TATA MEDICAL CENTER

ANNUAL
RESEARCH REPORT

RESEARCH SUPPORT DIRECTORATE
2019 - 2020

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Research Support Directorate

Tata Translational Cancer Research Centre

FROM THE DIRECTOR'S DESK

I have great pleasure in writing this foreword to the Annual Research Report 2021 which gives the reader a snapshot of the breadth of research that is being carried out at the Tata Medical Center. This year is special since we will complete ten years of institution building after being inaugurated on the 16th of May 2011.

TMC is now involved with many research projects both investigator initiated and pharma sponsored: the former receives funding from DBT, ICMR and also many international consortia. The pharma sponsored studies will allow TMC to be a part of many international Phase II studies allowing faculty to become conversant with new drugs and making these available to patients. The clinical units continue to conduct regular audits of outcomes and this is essential for comparison with international benchmarks.

Prof. Dr. Mammen Chandy
Director, Tata Medical Center

Most of the faculty and fellows are keen to be involved with research and attendance at GCP courses is high. The IRB continues to perform an important role in ensuring that all studies are scientifically and ethically sound.

TMC is working with INTAS to develop a CAR T Cell program and this has been funded by DBT-BIRAC. TTCRC continue to provide a major platform for research on childhood leukemia and is improving outcomes through the ICICLE collaboration In India.

Research is an attitude of mind where one is constantly asking questions, reviewing literature, formulating hypotheses and testing them with laboratory experiments and clinical trials: TMC must continue to foster this scientific approach..

DEPARTMENT OF ANESTHESIA, CRITICAL CARE & PAIN

Dr Jyotsna Goswami

MBBS, MD, Senior Consultant & HEAD ANESTHESIA, CRITICAL CARE & PAIN

Dr Rakhi Khemka Mittal

MBBS, MD, Senior Consultant, Anaesthesia

Dr Sonal Rastogi Das

MBBS, MD, PDCC in Neuro Anaesthesia, Senior Consultant, Anaesthesia

Dr Anshuman Sarkar

MBBS, MD, Senior Consultant, Anaesthesia

Dr Arunangshu Chakraborty

MBBS, MD, Associate Consultant, Anaesthesia

Dr Aditi Gupta

MBBS, FCARCSI, Consultant, Anaesthesia

Dr Viplab Patro

MBBS, DNB, Associate Consultant, Anaesthesia

Dr Neha Desai

MBBS, DA, DNB Anaesthesia, Junior consultant, Anaesthesia

Dr Angshuman R Pal

MBBS, MD, Junior consultant, Anaesthesia

Dr Suparna Mitra Barman

MBBS, MD, Junior consultant, Anaesthesia

Dr Sumantra Sarathi Banerjee

MBBS, MD, Junior consultant, Anaesthesia

Dr. Rudranail Nandi

MBBS, MD, DM (Onco-Anesthesia) (AIIMS) Junior Consultant, Anaesthesia & Pain

Dr Sudipta Mukherjee

MBBS, MD, Junior consultant, Critical Care

Dr Pralay Shankar Ghosh

MBBS, MD, Junior consultant, Critical Care

Dr Shantanu Bagchi

MBBS, MD-Anaesthesia, FNB (Critical Care Medicine), Junior consultant, Critical Care

RESEARCH PROJECTS

1. Anemia: Impact on Morbidity (AIM) (Investigator initiated, PI Dr Suparna Mitra Barman)
2. ERAS in colorectal surgeries. (Investigator initiated, PI Dr Angshuman Rudra Pal).
3. Restrospectivery analysis of compliance of Enhanced Recovery Protocol in major head and neck cancer surgery with Free Flap reconstruction. (Investigator initiated, PI Dr Sumantra Sarathi Banerjee).
4. Goal Directed Fluid Therapy in HIPEC surgeries. (Investigator initiated, PI Dr Viplab Patro).
5. Awareness with recall during Major abdominal surgery. (Investigator initiated, PI Dr Jyotsna Goswami).
6. Oxygen Insufflation Through Nasopharyngeal Airway V/S Nasal Cannula During Anesthesia in EBUS-TBNA Procedures (OXYNAS-EBUS). (Investigator initiated, PI Dr. Neha Desai).
7. Pre-procedural ultrasound for IJV access- a pilot study. (Investigator initiated, PI Dr. Sumantra Sarathi Banerjee).
8. Impact of Perioperative factors on Postoperative Mechanical Ventilation (POMV) of patients undergoing hyperthermic intraperitoneal chemotherapy (HIPEC): A retrospective analysis (Investigator initiated, PI Dr. Suparna Mitra Barman).
9. Ultrasound guided transverses abdominisplane (TAP) block for patients undergoing roboticgynecological oncosurgery: A Pilot study. (Investigator initiated, PI Dr. Sonal Das).
10. Post-operative delirium in cancer patients: incidence and risk factors-a prospective observational cohort study. (Investigator initiated, PI Dr. Sudipta Mukherjee; Co-Investigators: Dr. Sumantra Sarathi Banerjee, Dr. Jyotsna Goswami)
11. Intraoperative Fluid Practice and its effect on post-operative renal function and coagulation. (Investigator initiated, PI Dr. Angshuman Rudra Pal; Co-Investigators: Dr Monotosh Pramanik, Dr Anshuman sarkar, Dr Aditi Gupta, Dr Mayukh Chattopadhyay)
12. Restrictive or Individualized Goal-Directed Fluid Replacement Strategy in Ovarian Cancer Cytoreductive Surgery– A prospective randomized controlled trial (RIGoROCS). (Investigator initiated, PI Dr. Jyotsna Goswami; Co-Investigators: Dr. Asima Mukhopadhyay, Dr. Angshuman Rudra

Pal, Dr. Viplab Patro, Dr. Anshuman Sarkar, Dr. Suparna Mitra Barman)

13. Initiating Antimicrobial Stewardship activities in hospitals in India. (Investigator initiated, PI Dr. Sudipta Mukherjee)
14. Estimating Incremental Cost of treating Antimicrobial Resistant infections in India. (Investigator initiated, PI Dr. Sanjay Bhattacharya; Co-Investigator: Dr. Sudipta Mukherjee)
15. Expansion of antimicrobial stewardship (AMSP) and infection control program (ICP) of ICMR in secondary care hospitals. (Investigator initiated, PI Dr. Sanjay Bhattacharya; Co-Investigator: Dr. Sudipta Mukherjee)
16. Pre-operative respiratory care and outcomes for patients undergoing high risk abdominal surgery: A 2*2 factorial, international pragmatic randomized trial(PENGUIN)- (Investigator initiated, PI Dr. Viplab Patro)
17. Opioid sparing effect of low dose ketamine for peri-operative analgesia in free flap reconstruction of head and neck defects: A randomized control trial. (Investigator initiated, Dr. Rakhi Khemka Mittal).
18. Evaluation of informed consent for peripheral nerve block in a high volume tertiary care center: an observational study. (Investigator initiated, Dr. Rakhi Khemka Mittal).
19. Ultrasonic Measurement of Optic Nerve Sheath Diameter in prolonged abdominal surgery: A prospective observational study. (Investigator initiated, Dr. Arunangshu Chakraborty).
20. A case series of gnana LMA: our Experience at a tertiary care cancer centre. (Investigator initiated, Dr. Suparna Mitra Barman).

RESEARCH PUBLICATIONS

1. **Goswami J**. Insulinoma. *Anästh Intensivmed*. 2020;61: S349–S357. DOI: 10.19224/ai2020.S349
2. **Goswami J, Sarkar A, Mukherjee S.** Perioperative management of renal tumour surgeries/Nephrectomy. *Perioperative Critical Care*. June 2020.
3. **Mukherjee S, Ghosh PS, Goswami J.** Assessment of airway by ultrasonography. *ISCCM Manual of Critical Care Ultrasound*. April-2020.
4. Solanki SL, Thota RS, Garg R, Pingle AA, **Goswami J,** Ranganath N, Mukherjee S, Gupta S, Patkar S, Chikkalingegowda RH, Jindal T, Ray MD, Upadhye SM, Divatia JV**.** Society of Onco-Anesthesia and Perioperative Care (SOAPC) advisory regarding perioperative

management of onco-surgeries during COVID-19 pandemic. *Indian J Anaesth*. 2020;64: S97-102.
doi: 10.4103/ija.IJA_447_20

5. **Pal AR, Mitra S, Aich S, Goswami J**. Existing practice of perioperative management of colorectal surgeries in a regional cancer institute and compliance with ERAS guidelines. *Indian J Anaesth.* 2019; 63:26-30.
doi: 10.4103/ija.IJA_382_18
6. **Pramanik M, Sarkar A, Gupta A, Chattopadhyay M.** Postoperative Pulmonary Complications in robot assisted uro-oncological surgery: Our experience in a tertiary cancer care center. *Indian J Anaesth*. 2020; 64:238-41.
doi: 10.4103/ija.IJA_527_19
7. **Mandal S, Barman SM, Sarkar A, Goswami J**. Spontaneous Respiration using Intravenous Anesthesia and Hi-Flow nasal oxygen (STRIVE Hi) in tracheal stenting: Experience of ten cases in a regional cancer center. *Indian J Anaesth*.2019;63:941-944.
doi: 10.4103/ija.IJA_386_19
8. **Khemka R, Chakrborty A, Agrawal S, Ahmed R**. Is COMBIPECS the answer to Perioperative analgesia for breast surgery? A double blinded randomized controlled trial. *Indian J Anaesth*. 2019; 63: 530–536.
DOI: 10.4103/ija.IJA_222_19
9. **Khemka R, Chakrborty A**. Ultrasound guided modified serratus anterior plane block for perioperative analgesia in breast oncoplastic surgery: A case series. *Indian J Anaesth*. 2019; 63: 231–234.
doi: 10.4103/ija.IJA_752_18
10. **Khemka R, Rastogi S, Chakraborty A, Sinha S.** Ultra sonographic assessment of altered anatomical relationship between internal jugular vein and common carotid artery with supraglotic airway in children: LMA vs R i-gelTM. *Indian J Anaesth*. 2019; 63: 114–118.
doi: 10.4103/ija.IJA_747_18
11. **Solanki SL, Mukherjee S, Agarwal V, Thota RS, Balakrishnan K, Shah SB, Desai N, Garg R, Ambulkar RP, Bhorkar NM, Patro V, Sinukumar S, Venketeswaran MV, Joshi MP, Chikkalingegowda RH, Gottumukkala V, Owusu-Agyemang P, Saklani AP, Mehta SS, Seshadri RA, Bell JC, Bhatnagar S, Divatia JV.** Society of Onco-Anesthesia and Perioperative Care consensus guidelines for perioperative management of patients for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS+HIPEC). *Indian J Anaesth*. 2019; 63:972-87.
doi: 10.4103/ija.IJA_765_19

12. **Roy S, Das P, Das S, Roy S, Pal S, Joy VM, Mukherjee S, Bhattacharyya A, Goel G, Bhattacharya S, Mathur P, Walia K, Chandy M**. Detection of the emergence of mcr-1–mediated colistin-resistant Escherichia coli and Klebsiella pneumoniae through a hospital-based surveillance in an oncology center in eastern India. *Infect Control Hosp Epidemiol*. 2020 Mar;41(3):378-380. doi: 10.1017/ice.2019.363
13. **Das S, Roy S, Roy S, Goel G, Walia K, Mukherjee S, Bhattacharya S, Chandy M.** Rapid and economical detection of eight carbapenem-resistance genes in Enterobacteriaceae Pseudomonas spp, and Acinetobacter spp directly from positive blood cultures using an internally controlled multiplex-PCR assay. *Infection Control & Hospital Epidemiology*. 2019 Jun;40(6):737-739.
doi: 10.1017/ice.2019.79
14. Viswan A, **Ghosh P,** Gupta D, Azim A and Sinha N**.** Distinct Metabolic Endotype Mirroring Acute Respiratory Distress Syndrome (ARDS) Subphenotype and its Heterogeneous Biology. *Nature*. 2019 Feb 14;9(1):2108.
doi: 10.1038/s41598-019-39017-4
15. Ashokka B, **Chakraborty A,** Subramanian BJ, Karmakar MJ, Chan V. Reconfiguring the Scope and practice of regional anesthesia in a pandemic the Covid-19 perspective. *Reg Anesth Pain Med.* 2020 Jul;45(7):536-543.
doi: 10.1136/rapm-2020-101541.
16. **Nandi R,** Misra S, Garg R, Kumar V, Gupta N, Bharati SJ**.** Intavenous Lignocaine Fentanyl Versus Epidural Ropivacaine-Fentanyl for Postoperative Analgesia After Major Abdominal Oncosurgery: A Pilot Prospective Randomized Study. *Turkish Journal of Anaesthesiology and Reanimation*. 2020.
DOI:10.5152/TJAR.2020.23326.
17. **Nandi R,** Misra S, Biswas S, More S, Gupta R, Bharati SJ. Caring the Cancer Caregivers in the Era of COVID-19 Outbreak. *Asian Pacific Journal of Cancer Care*. 2020 Aug24,5(SI):203-8.
DOI: 10.31557/APJCC.2020.5. S1.203.
18. **Nandi R,** Das S, Nag A, Datta A. Jaundice after cytoreductive surgery along with hyperthermic intra-peritoneal chemotherapy in an ovarian cancer patient. *Indian J Anaesth*. 2020 Nov; 64(11): 997–999.
doi: 10.4103/ija.IJA_418_20

EXTERNAL ACADEMIC MEETINGS

1. CME+ Workshop Adult Difficult Airway Management (ADAM) February 2020

ORCID ACCOUNT

1. Dr. Jyotsna Goswami (0000-0003-0572-9821)
2. Dr. Arunangshu Chakraborty (0000-0002-0069-700X)
3. Dr. Angshuman Rudra Pal (0000-0002-1352-7632)
4. Dr. Rudranil Nandi (0000-0002-2698-2503)

DEPARTMENT OF SURGICAL ONCOLOGY (BREAST)

Dr Rosina Ahmed

MBBS, MD (Sheffield), FRCS (Eng), FRCS (Gen Surg), Senior Consultant

Dr Sanjit Agrawal,

MBBS, MS (Gen Surg), Fellowship in Surgical Oncology, Breast Surgery Qualification (European Board) Senior Consultant

Dr Abhishek Sharma

MBBS, MS (Gen. Surg.), MRCS), Associate Consultant.

RESEARCH PROJECTS

1. Additional Biomarker for TNBC (Prospective Observational- NIBMG). (PI, Dr Sanjit Agrawal).
2. Vascular remodelling in cancer patients: Role of BRAP gene in the vascular smooth muscle cells after chemotherapy-associated vascular dysfunction. (Prospective Cohort- ICMR). (PI, Dr Sanjit Agrawal)
3. A prospective single-arm study of lymphatic drainage patterns in patients undergoing SLNB with fluorescent dye using indocyanine green (ICG) in breast cancer patients. (Prospective Observational). (PI, Dr Abhishek Sharma)

RESEARCH PUBLICATIONS

1. **Bakkach J, Pellegrino B, Elghazawy H, Novosad O, Agrawal S, Bennani Mechita M**. Current overview and special considerations for second breast cancer in Hodgkin lymphoma survivors. Critical Reviews in Oncology/Hematology. 2021 Jan 1; 157:103175.
2. **Agrawal SK, Hashlamoun I, Karki B, Sharma A, Arun I, Ahmed R.** Diagnostic Performance of Indocyanine Green Plus Methylene Blue Versus Radioisotope Plus Methylene Blue Dye Method for Sentinel Lymph Node Biopsy in Node-Negative Early Breast Cancer. JCO Glob Oncol. 2020 Jul; 6:1225-1231. doi: 10.1200/GO.20.00165
3. **Agrawal SK, Shakya SR, Nigam S, Sharma A, Datta SS, Ahmed R.** Chest wall perforator flaps in partial breast reconstruction after breast

conservation surgery: an additional oncoplastic surgical option. Ecancermedicalscience. 2020; 14:1073. doi:10.3332/ecancer.2020.1073

4. **Ahmed R, Chatterjee S Et al**. Hypofractionated radiation therapy comparing a standard radiotherapy schedule (over 3 weeks) with a novel 1-week schedule in adjuvant breast cancer: an open-label randomized controlled study (HYPORT-Adjuvant)-study protocol for a multicentre, randomized phase III trial. Trials vol. 21,1 819. 30 Sep. 2020. doi:10.1186/s13063-020-04751-y
5. **Ahmed R, Tewary S, Arun I, Chatterjee S.** AutoIHC-Analyzer: computer-assisted microscopy for automated membrane extraction/scoring in HER2 molecular markers. Journal of Microscopy, 281: 87-96. https://doi.org/10.1111/jmi.12955

EXTERNAL ACADEMIC MEETINGS

1. CME Biostatistics and Clinical Research methodology September Virtual due to COVID pandemic

DEPARTMENT OF CENTRAL STERILE SUPPLY DEPARTMENT

Debabrata Basu,

Associate Scientific Officer M.Sc. (Environmental Science)

RESEARCH PUBLICATIONS

1. **Basu D, Das A, Rozario JD.** A brief discussion on environmental quality monitoring required in a central sterile supply department: Evidence from a cancer center in eastern India. *Infection Control & Hospital Epidemiology*. 2020. https://doi.org/10.1017/ice.2020.41
2. **Das TK, Laha SK, and Basu D**. Potential problems of inadequate air removal and presence of non-condensable gasses in a steam sterilization process: A brief discussion. *Infection Control & Hospital Epidemiology*. 2020. https://doi.org/10.1017/ice.2020.88
3. **Basu D, Dhara M, and Dutta SK**. Reprocessing of single-use medical devices and their associated problems: an experience from a cancer center in eastern India. *Infection Control & Hospital Epidemiology.* https://doi.org/10.1017/ice.2020.54

ORCID ACCOUNT

1. Debabrata Basu (0000-0002-1250-4973)

DEPARTMENT OF CYTOGENETICS

Dr Mayur Parihar
MBBS, MD, PDF, Senior Consultant

Dr Tanvi Gupta
MBBS, MD, DNB, Fellow

Dr Ashish Babu Gorantla
MBBS, MD, Fellow

Dr Barun Kumar Chakrabarty
MBBS, MD, DNB, Fellow

Arun S R
MSc Biotechnology, Associate Scientific Officer

Sumanta Kumar Patel
MSc Biotechnology, Scientific Officer

Sipra Rani Patel
MSc Biotechnology, Scientific Officer

Pranay Gurung
MSc Genetics, Scientific Officer

OVERVIEW OF RESEARCH

The year 2020 saw us completing our DBT project on Precursor B Cell ALL. The department is striving continuously to develop low cost, efficient sensitive and specific strategies for diagnosis and risk stratification of cancers.

Our strategy of using 3 FISH probes integrated with flow ploidy successfully risk stratifies BCP ALL patients. The same strategy was published in Paediatric Blood and Cancer Journal. We have further expanded this strategy to include more number of FISH probes and use a strategy based on flow cytometry to diagnosis recently described entities like ZNF384 and MEF2D rearranged leuakemias.

Our strategy to diagnosis hidden hypodiploidy using flow and targeted FISH has been published in Indian Journal of Haematology and Blood Transfusion.

The team is an integral part of the ALTITUDE project, the objective being risk stratification and Minimal Residual Disease Estimation (MRD) measurement in Acute Myeloid Leukaemias.

RESEARCH PROJECTS

1. Tumour genome profiling and minimal residual disease estimation in acute haematological malignancies using single-platform next generation sequencing strategies (PI, Dr Mayur Parihar)

RESEARCH PUBLICATIONS

1. **Gupta P, Saha K, Vinarkar S, Banerjee S, Choudhury SS, Parihar M, Midha D, Mukherjee G, Lingegowda D, Chatterjee S, ArunsinghS M, Shrimali R, Ganguly S, Dabkara D, Biswas B, Mishra DK, Arora N. Full text Gupta P, Saha K, Vinarkar S, Banerjee S, Choudhury SS, Parihar M, Midha D, Mukherjee G, Lingegowda D, Chatterjee S, ArunsinghS M, Shrimali R, Ganguly S, Dabkara D, Biswas B, Mishra DK, Arora N**. Next generation sequencing in lung cancer: An initial experience from India. *Curr Probl Cancer*. 2020 Jun;44(3):100562. doi: 10.1016/j.currproblcancer.2020.100562.
2. **Vipparthi K, Patel AK, Ghosh S, Das S, Das C, Das K, Sarkar A, Thatikonda V, Pal B, Remani ASKN, Arora N, Parihar M, Vijayakumar MV, Bhat MK, Boppana R, Bhattacharjee S, Biswas NK, Arun P, Sharan R, Singh S Full text Vipparthi K, Patel AK, Ghosh S, Das S, Das C, Das K, Sarkar A, Thatikonda V, Pal B, Remani ASKN, Arora N, Parihar M, Vijayakumar MV, Bhat MK, Boppana R, Bhattacharjee S, Biswas NK, Arun P, Sharan R, Singh S.** Two novel cell culture models of buccal mucosal oral cancer from patients with no risk-habits of tobacco smoking or chewing. *Oral Oncol*. 2020; 30; 113:105131. doi: 10.1016/j.oraloncology.2020.105131.
3. **Kapatia G, Sasikumar A, Nair R, Naseem S, Parihar M, Sreedharanunni S**. Myeloid Neoplasm with t (8; 22) (p11; q11): A Mimicker of Chronic Myeloid Leukaemia in Blast Crisis. *Indian Journal of Hematology and Blood Transfusion.* 2020.
4. **Saha K, Patel K, Banerjee S, Santra P, Bhave S, Radhakrishnan V, Nair R, Chandy M, Parihar M, Mishra D, Arora N.** Validation and Implementation of NGS-Based Combined DNA and RNA Sequencing in Myeloid Neoplasms. *Journal of Molecular Diagnostics*. 2020; S23-S23.
5. **Patel K, Arora N, Pall B, Gupta P, Thamtam VK, Dey D, Roy P, Parihar M, Mallath M, Chawla T, Roy M, Ganguly S, Mannan A, Mishra DK.** Two Cases of Germline EPCAM Mutation (s) as a Rare Cause of Hereditary Colorectal Adenocarcinoma (Lynch Syndrome). *Journal of Molecular Diagnostics*. S20-S20
6. **Radhakrishnan VS, Bhaduri A, Arora N, Nair R, Bhattacharya S, Sanyal S, Veldore V, Parihar M, Bhave SJ,**

Kumar J, Ramprasad VL, Mishra DK, Chandy M. Genomic profile at diagnosis by targeted high throughput sequencing, and real-world clinical outcomes in patients diagnosed with acute myeloid leukemia at a tertiary care. *Journal of Clinical Oncology*. e19515-e19515

7. **Patel K, Arora N, Pall B, Gupta P, Thamtam VK, Dey D, Roy P, Parihar M, Mallath M, Chawla T, Roy M, Ganguly S, Mannan A, Mishra DK.** Two Cases of Germline EPCAM Mutation (s) as a Rare Cause of Hereditary Colorectal Adenocarcinoma (Lynch Syndrome). *Journal of Molecular Diagnostics*. S20-S20
8. **Patel K, Saha K, Bhave S, Radhakrishnan VS, Nair R, Chandy M, Parihar M, Mishra D, Arora N**. AML-142: Implementation of Combined DNA and RNA Sequencing in Myeloid Neoplasms. *Clinical Lymphoma Myeloma and Leukemia*. S184-S185
9. **Bajaj R, Radhakrishnan VS, Bhave S, Kumar J, Arora N, Dey D, Parihar M, Mishra D, Chandy M, Nair R.** HL-150: Brentuximab Vedotin and Bendamustine Combination Therapy as Salvage for Relapsed-Refractory Hodgkin Lymphoma: A Real-World Single-Center Experience. Clinical Lymphoma Myeloma and Leukemia. S246-S247.

HONOURS & FELLOWSHIPS

1. Dr Ashish Gorantla International Summit for Human Genetics and Genomics at NIH United States of America
2. Dr Tanvi Gupta Young Investigator Program at Texas
3. Dr Tanvi Gupta Award for ASH Asia Pacific at Vietnam

ORCID ACCOUNT

1. Dr Mayur Parihar (https://orcid.org/0000-0002-8059-0914)

DEPARTMENT OF CLINICAL HAEMATOLOGY & BMT

Prof Dr Mammen Chandy
Director, Tata Medical Center
M.D., FRACP, FRCPA, FRCP, D.Sc.

Prof Dr Reena Nair
M.D. (Medicine), Senior Consultant

Dr Vivek S. Radhakrishnan
M.D., D.M., PDF (Clinical Hematology and BMT), Senior Consultant

Dr Saurabh Jayant Bhave
M.D., PDF (Hem, BMT), Senior Consultant

Dr Jeevan Kumar
M.D., DNB (Hem), PDF (Clinical Hem, BMT), Associate Consultant

Dr Rizwan Javed
MD(Path), PDF (Transfusion Med), MSc, Junior Consultant

RESEARCH PROJECTS

1. Acute Myeloid Leukemia: Exploring the feasibility of Multi-Modal-Omics based Genomic characterization, MRD evaluation and Computational drug modelling to inform Disease management. ALTITUDE Study. (PI Dr Vivek S. Radhakrishnan)
2. Effect of Pomalidomide- Bortezomib-Dexamethasone Induction on MRD status in patients with newly diagnosed Multiple Myeloma, PRIME Study. (PI Dr Vivek S. Radhakrishnan)
3. Cancer Immunotherapy and Precision Oncology (CRIMSON) Project. (PI Dr Vivek S. Radhakrishnan)

RESEARCH PUBLICATIONS

1. **Chandy M, Radhakrishnan VS, Sukumaran R (eds.)** Contemporary Bone Marrow Transplantation, Organ and Tissue Transplantation. *Springer Nature Switzerland AG*. 2020. https://doi.org/10.1007/978-3-319-64938-2
2. **Omidvar N, Tekin N, Conget P, Bruna F, Timar B, Gagyi E, Basak R, Auewarakul C, Sritana N, Julio J Cerci, Dimamay M P, Gyorke T, Redondo F,**

Nair R, Gorospe C, Paez D, Fanti S, Ozdag H, Padua R A, Carr R. Identification of a relapse cohort with PET-CT in low IPI-DLBCL using the two-gene scoring system of LMO2/TNFRSF9. *Acta Hematologica*. 2020.

3. **Devadas S, Jain H, Bagal B, Sengar M, Dangi U, Khatry N, Amre P, Patker N, Subramaian PG, Nair R, Menon H.** Sequential treatment of Arsenic trioxide followed by All tranretinoic acid with anthracyclines has excellent long-term cure in Acute promyelocytic leukemia. *Indian Journal of Hematology and Blood Transfusion*. 2020. http://doi.org/10.1007/s12288-020-01311-x
4. **Nayar N, Nair R, Mallath MK.** Truth telling and fully disclosing to cancer patients in India: A pragmatic approach. *The National Medical Journal of India*. 2020: 33.
5. **Bajpai J, Mailankody S, Nair R, T Surappa S, Gupta S, Prabhash K, Banavali SS, Malhotra H, Bhattacharyya GS, Bk Smruti, Babu G.** Gender climate in Indian oncology: national survey report. *ESMO Open*. 2020 Apr;5(2): e000671. doi: 10.1136/esmoopen-2020-000671.
6. **Radhakrishnan VS, Nair R, Goel G, Ramanan V, Chandy M, Nair R**. COVID-19 and haematology services in a cancer centre from a middle-income country: adapting service delivery, balancing the known and unknown during the pandemic. *Ecancer medical science*. 2020 Sep 24; 14:1110. doi: 10.3332/ecancer.2020.1110.
7. **Radhakrishnan VS, Agrawal N, Bagal B, Patel I.** Systematic Review of the Burden and Treatment Patterns of Adult and Adolescent Acute Lymphoblastic Leukemia in India: Comprehending the Challenges in an Emerging Economy. *Clin Lymphoma Myeloma Leuk*. 2020 Sep 18: S2152-2650(20)30513-9. doi: 10.1016/j.clml.2020.08.023.
8. **Modak K, Garg JK, Mishra DK, Radhakrishnan VS.** Blastic plasmacytoid dendritic cell neoplasm in a young female: Rare and challenging. *Indian J Med Paediatr Oncol*. 2020; 41:761-3
9. **Damodar S, Radhakrishnan VS, John MJ, Malhotra P, Jain R. Melinkeri S, Easow J, Malhotra P.** HSCT guidelines for transplant practices during covid-19 pandemic in India. *Blood cell therapy*. 2020; 4. DOI:10.31547/bct-2020-003
10. **Chaudhary A, Bag S, Arora N, Radhakrishnan VS, Mishra D and Mukherjee G**. Hypoxic Transformation of Immune Cell Metabolism Within the

Microenvironment of Oral Cancers. *Front. Oral. Health*. 2020; 1:585710. doi: 10.3389/froh.2020.585710

11. **Kathrotiya M, Radhakrishnan VS, Bhave SJ, Nair R et al.** Relapsed plasmablastic lymphoma in a HIV-negative patient: Pushing the envelope. *Clinical Case Reports*. 2020. DOI: 10.1002/ccr3.3673
12. **Grosicki S, Simonova M, Spicka I, Pour L, Kumar J, Jagannath S.** Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial. *Lancet*. 2020; 396: 1563–73.
13. **Nag A, Radhakrishnan VS, Kumar J, Bhave S, Mishra DK, 2, Nair R, Chandy M.** Thalidomide in Patients with Transfusion-Dependent E-Beta Thalassemia Refractory to Hydroxyurea: A Single-Center Experience. *Indian J Hematol Blood Transfus*. 2020; 36, 399–402. https://doi.org/10.1007/s12288-020-01263-2
14. **Javed R, Ahmadi F, Jawed A.** Precious platelets: The utility of cold-stored and cryopreserved platelets. *Glob J Transfus Med*. 2020; 5:17-21.
15. **Javed R, Radhakrishnan V, Basu S, Chandy M**. Challenges in transfusion and the role of Thalidomide in E-β-Thalassemia—A case report. *Clin Case Rep*. 2020; 00:1–3. https://doi. org/10.1002/ccr3.3141

CONFERENCE PRESENTATIONS

1.ASH 2020:

Reghu K Sukumaran Nair, Vivek S Radhakrishnan, Avijeet K Mishra, Vinay A Guntiboina, Saurabh J Bhave, Jeevan Kumar Garg, Indu Arun, Lateef Zameer, Debdeep Dey, Neeraj Arora, Deepak K Mishra, Arpita Bhattacharyya, Niharendu Ghara, Rimpa B Achari, Shekhar Krishnan, Mammen Chandy, Reena Nair; Adolescent and Young Adult Hodgkin Lymphoma: Is More Better? Blood 2020; 136 (Supplement 1): 26–27. doi: https://doi.org/10.1182/blood-2020-142276

2.SOHO 2020:

Poster: AML-142; Implementation of Combined DNA and RNA Sequencing in Myeloid Neoplasms; Kunjal Patel, Kallol Saha, Saurabh Bhave, et. al.

Poster HL- 150; Brentuximab Vedotin and Bendamustine Combination Therapy as Salvage for Relapsed-Refractory Hodgkin

Lymphoma: A Real-World Single-Center Experience; Rajat Bajaj, Vivek Radhakrishnan, Saurabh Bhave, et. al.

3.ASCO 2020:

Genomic profile at diagnosis by targeted high throughput sequencing, and real-world clinical outcomes in patients diagnosed with acute myeloid leukemia at a tertiary care cancer center; Vivek S Radhakrishnan, Arunima Bhaduri, Neeraj Arora, et.al.

4.APBMT 2020:

Relapsed Refractory Lymphoma and Transplantation Outcomes from A Tertiary Care Cancer Centre; Shailesh H Bamborde, Arijit Nag, Vivek S Radhakrishnan et. al.

5.Hematocon 2020:

- Buffy Coat Derived Granulocyte Transfusions During Intensive Chemotherapy of AML; Jay Y. Sheth, Arijit Nag, Suvro S. Dutta, Jeevan Kumar, Mayur Parihar, Vivek Radhakrishnan, Sabita Biswas, Deepak K. Mishra, Reena Nair, Mammen Chandy, Saurabh J. Bhave.
- Kumar J, Nair R. Image 001 Study Multicentric Study to Assess the Survival Statistics of Newly Diagnosed Multiple Myeloma Patients from Real World Settings. Indian J Hematol Blood Transfus https://doi.org/10.1007/s12288-020-01384-8]
- Targeted RNA Gene Fusion Variant Sequencing Metrics and Clinical Perspective in Myeloid Neoplasms at a Tertiary Care Centre; Kunjal Patel, Kallol Saha, Vamshi Thamtam, Saheli Banerjee, Vivek S Radhakrishnan, Saurabh Bhave, Jeevan Kumar, Reena Nair, Mammen Chandy, Neeraj Arora, Mayur Parihar, Deepak K Mishra.
- Immunophenotyping Directed Fish Strategy to Identify Znf384 Fusions; Arun SR Tanvi Gupta, Sipra P Patel, Subhajit Brahma, Niharendu Ghara, Reghu KS, Shekhar Krishnan, Arpita Bhattacharya, Vivek S. Radhakrishnan, Saurabh B. Jayant, Deepak K. Mishra, Mammen Chandy, Mayur Parihar.
- Blastic Plasmacytoid Dendritic Cell Neoplasm Presenting as Leukemia Without Skin Involvement: Role of Flow Cytometry in Diagnosis of a Rare Entity with Unusual Presentation; Rakesh B Demde, Deepak K Mishra, Mayur Parihar, Jeevan Kumar, Mammen Chandy, Vivek S Radhakrishnan, Saurabh Bhave, Neeraj Arora.

- Comprehensive Characterization of BCR-ABL1 Tkd Mutations: A Single Center Experience; Vamshi Krishna Thamtam, Poonam Santra, Biswajoy Pal, et. al.
- Outcome of SARS-COV2 Infection in Hematological Disorders: A Tertiary-Care Cancer Center Experience; Naveed Tamboli, Arijit Nag, Vivek Radhakrishnan, Jeevan Kumar, Saurabh Bhave, Rizwan Javed, Sanjay Bhattacharya, Gaurav Goel, Soumyadip Chatterji, Sudipta Mukherjee, Arna Das, MayurParihar, Deepak Mishra, Reena Nair, Mammen Chandy.
- Polatuzumab Vedotin in Relapsed/Refractory High-Grade B-Cell Non Hodgkin Lymphoma; Rajat Pincha, Vivek Radhakrishnan, Arijit Nag, Jeevan Kumar, Saurabh J. Bhave, Indu Arun, M A Lateef Zameer, Debdeep Dey, Mammen Chandy, Reena Nair.
- Multiparameter Flowcytometry; A Major Tool for Detection of Plasma Cell Neoplasm; Subhajit Brahma, Deepak Mishra, Sambhu N. Banerjee, Rakesh Demde, Raka Hota, Akshaya Mandloi, Saurabh Bhave, Vivek Radhakrishnan, Mammen Chandy, Reena Nair, Jeevan Kumar, Naveed Tamboli.
- Image 001 Study Multicentric Study to Assess the Survival Statistics of Newly Diagnosed Multiple Myeloma Patients from Real World Settings Jeevan Kumar, Dinesh Bhurani, Rayaz Ahmed, Saurabh J.Bhave, Reena Nair, et. al.
- Treatment Outcomes of Patients with Hodgkin Lymphoma: The Oncocollect Lymphoma Registry; Susmita Dasgupta et. al.
- Oncocollect Lymphoma Registry: Treatment Outcomes of Diffuse Large B-Cell Lymphoma; Pranita Mishra et. al.

6.Transmedcon

Javed R, Chowdhury MR, Radhakrishnan VS, Bhave SJ, Chandy M Et al. Older age does not influence the efficacy and safety of autologous peripheral blood stem cell collection

AWARDS & FELLOWSHIPS

1. Prof. Mammen Chandy, National Civilian Honour: Padma Shri, D. Sc: Jadavpur University, Kolkata.
2. Prof. Reena Nair, Invited - International Advisory Board Member of the Lancet Hematology 2020 to 2022.

3. Dr. Vivek Radhakrishnan, Invited – Expert on Cellular Therapy (CAR-T Cells), Dept. of Biotechnology and BIRAC, Govt. of India
4. Faculty – Australia and Asia-pacific Clinical Oncology Research Development (ACORD), Protocol development Workshops, Australia
5. Jt. Secretary: Immuno-Oncology Society of India
6. Dr. Jeevan Kumar, National Board of Examinations - Gold medal in DNB final examinations19th Convocation of National Board of Examinations.
7. Dr. Rizwan Javed, Awarded the Harold Gunson Fellowship by the International Society of Blood transfusion(ISBT) on 4th April 2019 at Basel, Switzerland.

ORCID ACCOUNT

1. Dr. Rizwan Javed (https://orcid.org/0000-0002-1961-3259)

DEPARTMENT OF DIGESTIVE DISEASES

Dr Mohandas K Mallath
MD, DNB, Senior Consultant

Dr Shiva Shankar Gangi Reddy
MD, DNB, Associate Consultant

OVERVIEW OF RESEARCH

Clinical research work continued in our department in 2020 with new roadblocks posed by the COVID-19 Pandemic and the Lockdown. Three ongoing research projects from the previous year were completed and support was given for a cancer vaccine trial in the clinical pharmacology department. The abstract of one completed project was accepted for poster presentation in the annual meeting of American Society for Hematology and the abstract was published in Blood. Several book chapters were published in 2020.

RESEARCH PROJECTS

1. An Open Label, Multicenter, Non-Comparative, Phase IV Study of Panitumumab to Characterize its Safety, Tolerability and Activity in Indian Subjects with Previously Treated Wild-Type RAS (KRAS and NRAS), Metastatic Colorectal Cancer. (PI, Dr. Mohandas K Mallath).
2. A prospective observational study to determine the impact of malnutrition on excess costs, financial burden and short-term clinical outcomes of lymphoma chemotherapy. (PI, Dr. Mohandas K Mallath).
3. A prospective observational study to determine the impact of malnutrition on excess costs, financial burden and short term clinical outcomes of GI cancer surgery. (PI, Dr. Mohandas K Mallath).

RESEARCH PUBLICATIONS

1. **Mallath MK, Chandy M et al. (eds.).** Nutritional Support and Issues Related to Hematopoietic Stem-Cell Transplantation. *Contemporary Bone Marrow Transplantation, Organ and Tissue Transplantation.* 2021. https://doi.org/10.1007/978-3-319-64938-2_9-1
2. **Mallath MK, Pitchumoni CS, Dharmarajan TS (eds.).** Gastric cancer. *Geriatric Gastroenterology*. https://doi.org/10.1007/978-3-319-90761-1_77-1

3. **Mallath MK.** Socioeconomic factors and cancer prevention in India Book Chapter Reviewer World Cancer Report. Edited by Wild CP, Weiderpass E, Stewart BW. International Agency on Research on Cancer, WHO. 2020.

EXTERNAL ACADEMIC MEETINGS

1. Master Class of Indian Society of Gastroenterology Gastrointestinal Lymphomas - October
2. National Board of Exam Lecture in Gastroenterology Gall bladder cancer- December

ORCID ACCOUNT

1. Mohandas K Mallath (https://orcid.org/0000-0001-5757-7220)

DEPARTMENT OF GASTRO INTESTINAL-HPB SURGERY

Dr Manas Roy

MS FRCS(Glas) FRCS(Edin) MCh(Cardiff), Senior Consultant

Dr Sudeep Banerjee

MS (PGI) DNB-(GI Surgery (CMC Vellore), Senior Consultant

Dr Robin Thambudorai

MS, Senior Consultant

Dr Bipradas Roy

MS, MRCS, Junior Consultant

Dr Amrit Pipara

MS, Junior Consultant

RESEARCH PROJECTS

1. **Biomarker discovery in gallbladder cancer.** (PI Prof Dr Vaskar Saha)
2. Studies undertaken as a part of an initiative of Global Surg and The NIHR Global Health Research unit on Global Surgery, Birmingham, United Kingdom:
    - CovidSurg Cancer Study: recruitment and data entry completed
    - CovidSurg Week Study: recruitment and data entry completed
    - CROCODILE: Aims to assess expenditure incurred during colorectal cancer treatment; recruitment started.
    - CRANE: Pilot study to assess nutritional status in cancer patients in low income countries; recruitment started.
    - CHEETAH: To assess the impact of changing of gloves and using new set of instruments prior to closure of laparotomy on the incidence of skin and soft tissue infection.

RESEARCH PUBLICATIONS

1. **Roy MK, Pipara A, Kumar A.** Surgical management of adenocarcinoma of the transverse colon: What should be the extent of resection? *Annals of Gastroenterological Surgery*. 2020;00: 1–8. https://doi.org/10.1002/ags3.12380

2. **Maru P, Roy, B, Sen S, Chatterjee A**. Lymph Node Mapping in Gastric Carcinoma. *Journal of Gastrointestinal and Abdominal Radiology.* DOI: 10.1055/s-0040-1722795
3. COVIDSurg Collaborative; GlobalSurg Collaborative. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. *Anaesthesia.* 2021 Mar 9. doi: 10.1111/anae.15458.

DEPARTMENT OF GYNAECOLOGICAL ONCOLOGY

Dr Jaydip Bhaumik

MS, DNB, FRCOG, MPH,

Senior Consultant and ***HOD***

Dr Anik Ghosh

MS, Fellowship- Gynae- Oncology

Associate Consultant

Dr Shweta Rai

MD, DNB (Obs& Gyn),

Mch Gynae-Oncology, Associate Consultant

Dr Arunava Roy

DGO, DNB, (Obs & Gyn)Fellowship in Gynae-Oncology, Associate Consultant

Dr Basumita Chakraborti

MD, DNB (Obs & Gyn),

Fellowship- Gynae-Oncology,

Associate Consultant

RESEARCH PROJECTS

1. Sentinel lymph node dissection in high risk endometrial cancer, prospective observational study. (PI, Dr Arunava Roy)

RESEARCH PUBLICATIONS

1. **Lucksom, P.G., Mathai, S., Bhaumik, J. et al**. Evaluation of CA-125 as an Indicator of Imaging During Follow-up of Carcinoma Ovary: Original Research. *J Obstet Gynecol India* 2020; 70, 289–294. https://doi.org/10.1007/s13224-020-01321-9
2. **Katwal P, Rai S, Mukherjee S, Ghosh P, Ghosh J, Bhaumik J.** Germ Cell Tumour of the Ovary Presenting with Chylothorax and Central Vein Thrombosis: A Case Report. *Indian Journal of Gynecologic Oncology*. 2020 18(1) DOI: 10.1007/s40944-020-0377-z
3. **Rout S, Rai S, Dabkara D, Ghosh J, Chakraborti B, Roy A, Ghosh A, Bhaumik J**. Managing brain lesions in gynaecological cancers: A case series. Indian Journal of Gynecologic Oncology. 2020; 18(3). DOI: 10.1007/s40944-020-00409-4

AWARDS & FELLOWSHIPS

1. Dr Basumita Chakraborti Certificate of completion of Fellowship in Gynaecological Oncology- Comprehensive Applied Science and Online Training, UKSH, Germany

DEPARTMENT OF HEAD & NECK SURGERY

Dr Pattatheyil Arun

MBBS, DLO, MS, MCh., Senior Consultant

Dr Kapila Manikantan

MBBS, MS, Senior Consultant

Dr Rajeev Sharan

MBBS, MS, MCh, Senior Consultant

Dr Prateek Jain

MBBS, MS, DNB, Senior Consultant

RESEARCH PROJECTS

1. Modified Radical Neck Dissection Vs Selective Neck Dissection in management of N+ neck in patient with oral SCC (SENPOS Study) (Investigator Initiated, PI, Dr. Pattatheyil Arun)
2. A study of Quality of Life in patients of Carcinoma Buccal mucosa who underwent Segmental mandibulectomy with and without Bony Reconstruction (SQOL Study) (Investigator Initiated, PI, Dr. Kapila Manikantan)
3. Preventing Alar Necrosis in Nasotracheal Intubation: A Prospective Observational Study (PANPOS STUDY)" (Investigator Initiated, PI, Dr. Rajeev Sharan)
4. Exploratory Phase Ib/IIa Study of Intratumourally Administered TigilanolTiglate to Assess Safety, Tolerability and Tumour Response in Patients with Head and Neck Squamous Cell Carcinoma (QBIOTIC) (QB 46C-H03) (PI, Dr. Pattatheyil Arun)
5. Outcomes research on oral squamous cell carcinoma: Multicentre Retrospective Study (HNRETRO) (Investigator Initiated, PI Dr. Pattatheyil Arun)
6. Surviving beyond treatment completion assessing reliability and validity of standardized dysphagia of communication questionnaires in head and neck cancer(READER) (Investigator Initiated, PI Dipanwita Roy; Dr. Pattatheyil Arun)
7. Delay in Presentation and Treatment of Head and Neck Cancer in India: A Multicenter Prospective Analysis of Factors and Impact on Survival (LATENT) (Investigator Initiated, PI Dr. Pattatheyil Arun)
8. Efficacy of Baseline Measures for Predicting Early Recovery of Swallowing after Surgery for Tongue Cancer: A Prospective Study(WATCA)

(Investigator Initiated, PI Dr. Pattatheyil Arun)

9. Free Thyroid Lobe Transfer for Prevention of Radiation Induced Hypothyroidism in patients of Oral carcinoma: A Phase I/II study (THRYFT Study) (Investigator Initiated, PI, Dr. Kapila Manikantan)
10. A Phase IIb/III study to determine efficacy of Curcumin and Metformin to reduce the incidence of second primary tumors of aero-digestive tract in patients with history of head and neck squamous cell carcinoma" (SPT Study) (Investigator Initiated, PI, Dr. Kapila Manikantan)
11. Determinants of speech outcome following closure in tongue carcinoma-A retrospective study (SPECTOR) (Investigator Initiated, PI Dr. Pattatheyil Arun)
12. Pre-operative speech score in Ca Tongue predicting post-operative speech outcome: A pr0spective Study (PRESPOT Study) (Investigator Initiated, PI Dr. Rajeev Sharan)
13. Determination of genomic signatures associated with treatment failure in oral squamous cell carcinoma of the gingivo-buccal region (OSCC-GB) (RECORD) (Investigator Initiated, PI Dr. Pattatheyil Arun)

RESEARCH PUBLICATIONS

1. **Ghosh RD, Arun P, Roychowdhury S.** Functional Landscape of Dysregulated MicroRNAs in Oral Squamous Cell Carcinoma: Clinical Implications. Front. Oncol. 10:619. doi: 10.3389/fonc.2020.00619.
2. **Jain PV, Sharan R, Manikantan K, Clark GM, Chatterjee S, Mallick I, Roy P, Arun P**. Redefining adequate margins in oral squamous cell carcinoma: outcomes from close and positive margins. *European Archives of Oto-Rhino-Laryngology*. 2020 Apr;277(4):1155-1165. doi: 10.1007/s00405-019-05779-w. https://doi.org/10.1007/s00405-019-05779-w
3. **Verma H, Arun P, Sharan R, Manikantan K, Jain P.** Risk of Hypocalcemia and the Need to Augment Calcium Supplementation After Total Thyroidectomy. *Indian Journal of Surgical Oncology*. 2020. DOI: 10.1007/s13193-020-01098-3 https://doi.org/10.1007/s13193-020-01098-3.
4. **Jain PV, Roy D, Manikantan K, Sharan R, Tshering P, Arun P.** Contribution of Weight and Volume of the Extirpated Thyroid Gland on Voice Alterations After Total Thyroidectomy in Patients

with Papillary Carcinoma of the Thyroid. *J Voice*. 2020 Mar 19; S0892-1997(20)30066-7. doi: 10.1016/j.jvoice.2020.02. 014. https://doi.org/10.1016/j.jvoice.2020.02.014.

5. **Arun I, Maity N, Hameed S, Jain PV, Manikantan K, Sharan R, Arun P**. Lymph node characteristics and their prognostic significance in oral squamous cell carcinoma. *Head & Neck*. 2020;1–14.
6. **Kewlani V, Jain P, Biswas G, Sharan R, Manikantan K, Panchal K, Arun P**. Impact of Covid-19 on Oral cancer stage at presentation in India: Experience from a tertiary cancer center. European Society of Surgical Oncology Conference (Virtual conference, 23-24th October 2020).

ORCID ACCOUNT

1. Dr. Pattatheyil Arun (0000-0002-7828-5777)
2. Dr Rajeev Sharan (0000-0002-3487-3884)
3. Dr Prateek Jain (0000-0002-9829-8583)
4. Dr Kapila Manikantan (0000-0001-6011-9175)

DEPARTMENT OF HISTOPATHOLOGY

Dr Geetashree Mukherjee

MBBS; MD (Pathology), Histopathology, Senior Consultant

Dr. Debdeep Dey

MBBS (Hons), FRCPath (UK), CCT(UK), Histopathology, Senior Consultant

Dr Indu Arun

MD, PDF (Oncopathology) Histopathology, Senior Consultant

Dr. Divya Midha

MBBS, MD (Path), PDF, Histopathology, Senior Consultant

Dr. Paromita Roy

MD Histopathology, Senior Consultant

Dr. M A Lateef Zameer

MD, PDF (Oncopathology), Histopathology, Associate Consultant

OVERVIEW OF RESEARCH

PROJECT ON ORAL CANCER - OVERVIEW

Dr. Geetashree Mukhejee

- The study investigates the relationship between genomic alterations and tumor immune microenvironment in oral squamous cell carcinoma – gingivo buccal (OSCC-GB) with the aim to identify prognostic and predictive biomarkers. The Primary Objective is to determine whether the burden of genomic/epigenomic alterations in the tumor correlates with immunological diversity in treatment naïve, OSCC-GB patients.
- Methodologies being used at Tata Medical Center (TMC) are a) Immunohistochemistry (IHC) and b) Flow Cytometry (FACS).
- Sequencing is being done at NIBMG, the results of which will be integrated.

RESEARCH PROJECTS

1. Excavating the relationship between genomic alterations and tumor immune microenvironment in oral squamous cell carcinoma – gingivo buccal (OSCC-GB) to inform future immunotherapy (PI Dr. Geetashree Mukherjee)

2. The predictive value of tumour pattern of invasion for intra-oral carcinoma. (PI Dr. Margaret Brandwein)
3. Microsatellite instability in Pediatric Glioblastoma (PI Dr Paromita Roy)
4. Clinicopathological characteristics of perineural invasion in oral squamous cell carcinoma (PI Dr.Indu Arun)
5. Radiomics features analysis of PET images for categorization of Hodgkin's Lymphomas and aggressive Non-hodgkin's Lymphomas (PI Dr Jayanta Das)

RESEARCH PUBLICATIONS

1. **Mukherjee G, Bag S, Chakraborty P, Dey D, Roy S, Jain P, Roy P, Soong R, Majumder PP, Dutt S.** Density of CD3+ and CD8+ cells in gingivo-buccal oral squamous cell carcinoma is associated with lymph node metastases and survival. *PLoS One.* 2020 Nov 19;15(11): e0242058. *doi: 10.1371/journal.pone.0242058* https://doi.org/10.1371/journal.pone.0242058
2. **Chaudhary A, Bag S, Arora N, Radhakrishnan VS, Mishra D, Mukherjee G**. Hypoxic Transformation of Immune Cell Metabolism within the Microenvironment of Oral Cancers. *Front. Oral. Health*. 2020 Dec 16; 1:585710. doi: 10.3389/froh.2020.585710 https://doi.org/10.3389/froh.2020.585710
3. **Biswas A, Mukherjee G, Kondaiah P, Desai VK.** Both EZH2 and JMJD6 regulate cell cyclegenes in breast cancer. *BMC Cancer*. 2020 Nov 27;20(1):1159. doi: 10.1186/s12885-020-07531-8 https://doi.org/10.1186/s12885-020-07531-8
4. **Roy P, Mallick I, Arun I, Zameer L, Dey D, Singh A, Chatterjee S, Jain P, Manikantan K, Sharan R, Pattatheyil A**. Nodal yield and topography of nodal metastases from oral cavity squamous cell carcinoma - An audit of 1004 cases undergoing primary surgical resection. *Oral Oncol*. 2020 Dec 16; 113:105115. doi: 10.1016/j.oraloncology.2020.105115.
5. **Parekh D, Kukreja P, Mallick I, Roy P**. Worst pattern of invasion - type 4 (WPOI-4) and Lymphocyte host response should be mandatory reporting criteria for oral cavity squamous cell carcinoma: A re-look at the American Joint Committee of Cancer (AJCC) minimum dataset. *Indian J Pathol Microbiol*. 2020 Oct-Dec;63(4):527-533.

doi: 10.4103/IJPM.IJPM_662_19.PMID: 33154300

6. **Bulten W, Balkenhol M, Belinga JA, Brilhante A, Çakır A, Egevad L, Eklund M, Farré X, Geronatsiou K, Molinié V, Pereira G, Roy P, Saile G, Salles P, Schaafsma E, Tschui J, Vos AM; ISUP Pathology Imagebase Expert Panel, van Boven H, Vink R, van der Laak J, Hulsbergen-van der Kaa C, Litjens G.** Artificial intelligence assistance significantly improves Gleason grading of prostate biopsies by pathologists. *Mod Pathol*. 2021 Mar;34(3):660-671. doi: 10.1038/s41379-020-0640-y.
7. **Saha G, Singh R, Mandal A, Das S, Chattopadhyay E, Panja P, Roy P, DeSarkar N, Gulati S, Ghatak S, Ghosh S, Banerjee S, Roy B, Ghosh S, Chaudhuri D, Arora N, Biswas NK, Sikdar N**. A novel hotspot and rare somatic mutation p. A138V, at TP53 is associated with poor survival of pancreatic ductal and periampullary adenocarcinoma patients. *Mol Med*. 2020 Jun 17;26(1):59. doi: 10.1186/s10020-020-00183-1.
8. **Singh A, Das A, Chatterjee A, Achari RB, S RK, Roy P**. A Nonchordomatous-looking Chordoma: When INI-1 and Radiology Came to the Rescue. *J Pediatr Hematol Oncol*. 2020 Apr;42(3):218-219. doi: 10.1097/MPH.0000000000001721.PMID: 32011562
9. **Kukreja P, Parekh D, Roy P**. Practical Challenges in Measurement of Depth of Invasion in Oral Squamous Cell Carcinoma: Pictographical Documentation to Improve Consistency of Reporting per the AJCC 8th Edition Recommendations. *Head Neck Pathol*. 2020 Jun;14(2):419-427. doi: 10.1007/s12105-019-01047-9.
10. **Arun I, Maity N, Hameed S, Jain PV, Manikantan K, Sharan R, Arun P.** Lymph node characteristics and their prognostic significance in oral squamous cell carcinoma. *Head Neck.* 2021 Feb;43(2):520-533. doi: 10.1002/hed.26499.
11. **Ghosh J, Ganguly S, Dabkara D, Biswas B, Chatterjee A, Mukhopadhyay S, Chandra A, Sen S, Dey D.** Case report & review of literature. Metachronous Muscle metastasis in a case of metastatic gall bladder cancer with TP53 gene mutation; a rare case report. *South Asian J Cancer.* 2019 Oct-Dec;8(4):240. doi: 10.4103/sajc.sajc_139_19.
12. **Jindal T, Dey D, Pawar P, Subedi N.** Ureteric sarcomatoid urothelial carcinoma with chondrosarcomatous differentiation: a rare entity. Case report & review of literature. *Indian*

Journal of Pathology and Microbiology. 2020; 10.4103/IJPM.IJPM_378_20.

13. **Singh A, Dey D.** An unusual case of a Solitary Fibrous Tumor showing dense collagenisation mimicking osteoid & aberrant SATB2 positivity: A diagnostic pitfall. Case report & review of literature. *Indian Journal of Pathology and Oncology*. 2021;8(1):170–172.
14. **Dey D, Mitra B, Sengupta S**. Wilms tumour- a rare case presentation Case report & review of literature *Indian Journal of Pathology and Oncology*. 2020;7(2):335-337.
15. **Chatterjee S, Chakraborty S, Dey D**. HYPOfractionated radiation therapy Comparing a Standard Radiotherapy schedule (over three weeks) with Novel one-week Schedule in Adjuvant Breast cancer: An Open-Label Randomised Controlled Study (HYPORT-Adjuvant): Study protocol for a Multicenter, Randomised Phase III Trial. HYPORT Adjuvant Author Group. *Trials*. 2020 Sep 30;21(1):819. doi: 10.1186/s13063-020-04751-y. https://doi.org/10.1186/s13063-020-04751-y
16. **Ambekar A, Rao V, Pai SA, Bindhu MR, Midha D, Kaushal S, Patil S, Jagdale R, Soni S, Kulkarni B, Sundaram S, Kumar RM, Desai S, Menon S**. Grossing and reporting of testicular tumor specimens: An evidence-based approach. *Indian J Cancer*. 2020 Jan-Mar;57(1):7-12. doi: 10.4103/ijc.IJC_1072_19. PMID: 32129294.
17. **Das J, Ray S, Tapadia R, Midha D, Mallick I**. Prostate-specific Membrane Antigen-expressing Hepatic Lesion: Metastatic or Hepatocellular Carcinoma. *Indian J Nucl Med*. 2020;35(1):58-60. doi: 10.4103/ijnm.IJNM_145_19.
18. **Ganguly S, Biswas B, Bhattacharjee S, Ghosh J, Mukhopadhyay S, Midha D, Dabkara D.** Clinicopathological characteristics and treatment outcome in small cell lung cancer: A single institutional experience from India. *Lung India*. 2020 Mar-Apr;37(2):134-139. doi: 10.4103/lungindia.lungindia_370_19.
19. **Gupta P, Saha K, Vinarkar S, Banerjee S, Choudhury SS, Parihar M, Midha D, Mukherjee G, Lingegowda D, Chatterjee S, ArunsinghS M, Shrimali R, Ganguly S, Dabkara D, Biswas B, Mishra DK, Arora N.** Next generation sequencing in lung cancer: An initial experience from India. *Curr Probl Cancer*. 2020 Jun;44(3):100562. doi: 10.1016/j.currproblcancer.2020.100562.

20. **Nakra T, Mehta A, Bal A, Nambirajan A, Mishra D, Midha D, Gupta N, Arora N, Gupta P, Gupta P, Singh V, Jain D.** Epidermal growth factor receptor mutation status in pulmonary adenocarcinoma: Multi-institutional data discussion at national conference of "Lung Cancer Management in Indian context". *Curr Probl Cancer*. 2020 Jun;44(3):100561. doi: 10.1016/j.currproblcancer.2020.100561.
21. **Dayanandal L, Gehani, A, Mukhopadhyay S, Divya M, Banerjee S, Bharat G.** Intraductal Papillary Neoplasm of the Bile Ducts: Case Reports with Review of the Literature. *World J Gastroenterol.* 2015 Nov 21; 21(43): 12498–12504. doi: 10.3748/wjg. v21.i43.12498.
22. **Jindal T, Dhanalakshmi M, Pawar P, Panda J, Midha D**. Inflammatory Pseudotumor of the Renal Pelvis. *Journal of Endourology Case Reports*. 6. 10.1089/cren.2020.0144.
23. **Ganguly S, Alphones S, Ghosh P, Midha D, Ghosh J, Biswas B.** Rectal cancer with breast metastasis: A case report with review of literature. *Cancer Research Statistics and Treatment*. 2020;3. 627-629.

EXTERNAL ACADEMIC MEETINGS

1. Virtual education to Pathology Fellows of medical colleges of Yenepoya University, Mangalore Topics on pathology of soft tissue, lung and Gynec cancers. (Once a month from June to September 2020)
2. Dermatopathology Conference CAPPCON 2020, Kolkata Approach to Cutaneous lymphoproliferative disorders. (March 2020)
3. Faculty speaker at IIT Kharagpur as part of microcredit course Workflow in Modern Histopathology lab and computational pathology. (January 2020)
4. Diagnostic challenges of High grade B cell NHL Eastern Haematology group. (Dec 2020)
5. Pathological aspects of aggressive T cell lymphomas that have a clinical impact (Panelists) Bombay Hematology group. (Dec 2020)
6. Pathological aspects of aggressive B cell lymphomas that have a clinical impact (Panellists) Bombay Hematology group. (Dec 2020)

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DEPARTMENT OF MEDICAL ONCOLOGY

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Dr. Sandip Ganguly

MBBS, MD (General Medicine), DM (Medical Oncology), Consultant

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Dr. Somnath Roy

MBBS MD (Radiotherapy), DM (Medical Oncology), DNB (Medical Oncology), Consultant

OVERVIEW OF RESEARCH

The department currently running a vibrant academic program with 1st batch of DNB super-specialty in Medical Oncology started from Sept'2019 and 2nd batch of students already joined the program in Dec'2020. In spite of COVID-19 pandemic, the departmental routine academic program, research & publication continued. We are currently running numerous clinical trials (mostly sponsored) involving various organ specific solid tumors. In few of the clinical studies, our department has the maximal national contribution in terms of recruitment. We have published and/or contributed to 36 publications during the last 1-years amidst the pandemic. We have participated in a few multicentric investigator initiated clinical studies and subsequent publications. Four consultants are in the Editorial Board of Indian Journal of Medical & Paediatric Oncology (official journal of Indian Society of Medical & Paediatric Oncology). Dr. Deepak Dabkara and Dr. Bivas Biswas have been assessor of DNB Medical Oncology Examination conducted by National Board of Examination. Two student dissertations are currently ongoing as part of DNB (ss) Medical Oncology Course.

RESEARCH PROJECTS

1. A phase III multicenter, randomized study of oral LDK378 versus standard chemotherapy in previously untreated adult patients with ALK rearranged (ALK-positive), stage IIIB or IV, non-squamous non-small cell lung cancer. (PI Dr. Deepak Dabkara).
2. A Multicenter Phase 4, Open-label, single-arm, Safety and Efficacy Study of Enzalutamide in Indian patients with Progressive Metastatic Castration-Resistant Prostate Cancer (PI Dr. Deepak Dabkara)
3. A phase III, multicenter, randomized, double blind, placebo controlled study evaluating the efficacy and safety of canakinumab versus placebo as adjuvant therapy in adult subjects with stages AJCC/UICC v. 8 II-IIIA and IIIB (T>5cm N2) completely resected (R0) non-small cell lung cancer (NSCLC) (PI Dr. Deepak Dabkara)
4. A prospective, multicenter, Phase-IV clinical trial to assess safety of TAGRISSO (Osimertinib) in Indian adult patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC) (PI Dr. Deepak Dabkara).
5. A Phase 3, Randomized Study of Amivantamab and Lazertinib Combination Therapy Versus Osimertinib Versus Lazertinib as First-Line Treatment in Patients with EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer (PI Dr. Deepak Dabkara)
6. A Randomized, Open-label Phase 3 Study of Combination Amivantamab and Carboplatin-Pemetrexed Therapy, compared with Carboplatin-Pemetrexed, in Patients with EGFR Exon 20ins Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer. (PI Dr. Deepak Dabkara)
7. An open lebel, Single arm, Multicenter, Safety study of Atezolizumab in Locally Advanced or Metastatic Urothelial or Non Urothelial Carcinoma of the Urinary Tract. (PI Dr. Bivas Biswas)
8. A Phase III, Double-blind, Placebo-controlled, Multi-center International Study of Neoadjuvant / Adjuvant Durvalumab for the Treatment of Patients with Resectable Stages II and III Non-Small Cell Lung Cancer (AEGEAN) (PI Dr. Bivas Biswas)
9. A Phase III, Randomized, Open Label,Controlled, Multi-Center,Global Study of First-Line Durvalumab in Combination with Standard of Care Chemotherapy and Durvalumab in Combination with Tremelimumab and Standard of Care Chemotherapy Versus Standard of Care

Chemotherapy Alone in Patients with Unresectable Locally Advanced or Metastatic Urothelial Cancer(NILE) (PI Dr. Bivas Biswas)

10. A Phase III, Randomized, Double-Blind, Placebo-Controlled, Multi-Centre, International Study of Durvalumab or Durvalumab and Tremelimumab as Consolidation Treatment for Patients with Limited Stage Small Cell-Lung Cancer Who Have Not Progressed Following Concurrent Chemoradiation Therapy (ADRIATIC) (PI Dr. Bivas Biswas)
11. A randomized, open label, multicenter phase II study evaluating the efficacy and safety of Capmatinib (INC280) plus Pembrolizumab versus Pembrolizumab alone as first line treatment for locally advanced or metastatic non-small cell lung cancer. (PI Dr. Bivas Biswas).
12. A Phase III, Randomised, Double-Blind, Placebo-Controlled, Multicentre Study Of Durvalumab As Consolidation Therapy In Patients With Locally Advanced, Unresectable, on -Small Cell Lung Cancer (Stage III) Who Have Not Progressed Following Definitive, Platinum- Based, Chemoradiation Therapy (Pacific 5). (PI Dr. Bivas Biswas).
13. A Phase II, Single Arm Study Assessing the Efficacy of Osimeritinib in Combination with Savolitinib in Patients with EGFRm+ and MET+, Locally Advanced or Metastatic Non-Small Cell Lung Cancer Who Have Progressed Following Treatment with Osimertinib (The Savannah Study). (PI Dr. Bivas Biswas).
14. An Observational, Multicentric, Prospective Study to Evaluate Concordance of Detecting EGFR Mutation by Circulating Tumor Free DNA Versus Tissues Biopsy in NSCLC(CONCORDANCE). (PI Dr. Bivas Biswas).
15. Pazopanib Real-World Assessment of Clinical Effectiveness and Safety in Patients Who Have Undergone Treatment in Different Settings in Advanced Renal Cell Carcinoma; A Prospective, Non-Interventional, Observational Study(PARACHUTE). (PI Dr. Bivas Biswas)
16. A Phase III, Open-label, Randomized Study of Osimertinib with or without Platinum Plus Pemetrexed Chemotherapy, as First-line Treatment in Patients with Epidermal Growth Factor Receptor (EGFR) Mutation-Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer (FLAURA2). (PI Dr. Bivas Biswas)
17. A Phase III, Randomized, Double Blind, Placebo-Controlled, Multicentre, International Study of Osimertinib as

Maintenance Therapy in Patients with Locally Advanced, Unresectable Egfrmutation-Positive Non-Small Cell Lung Cancer (Stage III) Whose Disease Has Not Progressed Following Definitive Platinum -Based Chemoradiation Therapy (LAURA). (PI Dr. Bivas Biswas).

18. Single Arm Study to Evaluate the Safety of Dacomitinib for The First Line Treatment of Participants in India with Metastatic Non-Small Cell Lung Cancer with Epidermal Growth Factor Receptor "(EGFR) Activating Mutations. (PI Dr. Bivas Biswas).
19. Single-Arm Study to Evaluate the Safety of Lorlatinib in Alk Inhibitor-Treated Unresectable Advanced and/or Recurrent Alk-Positive Non-Small Cell Lung Cancer Participants in India. (PI Dr. Bivas Biswas).
20. A Phase III Double-blind Randomized Study Assessing the Efficacy and Safety of Capivasertib + Paclitaxel Versus Placebo + Paclitaxel as First-line Treatment for Patients with Histologically Confirmed, Locally Advanced (Inoperable) or Metastatic Triple-Negative Breast Cancer(TNBC) (Capitello290). (PI Dr. Joydeep Ghosh).
21. A Prospective, Multicentre, Phase -IV Clinical Trial of Olaparib in the Indian Patients with Platinum Sensitive Relapsed Ovarian Cancer who are in Complete or Partial Response Following Platinum Based Chemotherapy and Metastatic Breast Cancer with Germline BRCA 1/2 Mutation (Soli Study). (PI Dr. Joydeep Ghosh).
22. A Phase III Randomized, Double-Blind, Placebo-Controlled, Multi-Regional, International Study of Durvalumab in Combination with Gemcitabine plus Cisplatin versus Placebo in Combination with Gemcitabine plus Cisplatin for Patients with First-Line Advanced Biliary Tract Cancers (TOPAZ-1). (PI Dr. Joydeep Ghosh).
23. A Single Arm, Multicentric, Open Label, Efficacy and Safety Study of Doceaqualip (Docetaxel Lipid Suspension for Injection of Intas Pharmaceuticals Limited, India) Based Regimens in Metastatic Gastric Adenocarcinoma Patients (PI Dr. Joydeep Ghosh).
24. A Multicenter, Double Blind, Randomized, Parallel-Group, Active-Controlled, Two Part, Phase III, Global Study to Evaluate the Pharmacokinetics, Efficacy and Safety of BP 02 (Trastuzumab) in comparison with Herceptin – EU in Patients with HER2 Positive Early Breast Cancer (EBC) and Metastatic Breast Cancer (MBC) (PI Dr. Joydeep Ghosh).

25. A Randomized, Double-Blind, Placebo-Controlled, Phase III Study Evaluating the Efficacy and Safety of Pembrolizumab Plus Platinum-Based Chemotherapy with or without Canakinumab as First Line Therapy for Locally Advanced or Metastatic Non-Squamous and Squamous Non-Small Cell Lung Cancer Subjects (CANOPY-1). (PI Dr. Sandip Ganguly).
26. A Phase III, Randomized, Double-Blind, Placebo-Controlled, Multi-center Study of Durvalumab Monotherapy or in Combination with Bevacizumab as Adjuvant Therapy in Patients with Hepatocellular Carcinoma Who Are at High Risk of Recurrence After Curative Hepatic Resection or Ablation (EMERALD-2). (PI Dr. Sandip Ganguly).
27. A Descriptive Study of PIK3CA Mutations in Patients with HR+/Her2- Advanced Breast Cancer. (PI Dr. Sandip Ganguly).

RESEARCH PUBLICATIONS

1. **Kumar S, Joga S, Biswas B, Dabkara D, Prasad KT, Singh N, Malik PS, Khurana S, Ganguly S, Muthu V, Batra U.** Immune checkpoint inhibitors in advanced non-small cell lung cancer: A metacentric experience from India. *Curr Probl Cancer*. 2020 Jun;44(3):100549. doi: 10.1016/j.currproblcancer.2020.100549.
2. **Prasad KT, Muthu V, Biswas B, Malik PS, Dabkara D, Ganguly S, Ghosh J, Kataria B, Khurana S, Verma S, Singh N.** Utility and safety of maintenance chemotherapy in advanced non-small cell lung cancer across various performance status categories: real-world experience. *Curr Probl Cancer*. 2020 Jun;44(3):100565. doi: 10.1016/j.currproblcancer.2020.100565.
3. **Patel A, Batra U, Prasad KT, Dabkara D, Ghosh J, Sharma M, Singh N, Suresh P, Jain P, Malik PS, Choudhary P, Ganguly S, Khurana.** Real world experience of treatment and outcome in ALK-rearranged metastatic non-small cell lung cancer: A multicenter study from India. *Curr Probl Cancer*. 2020 Jun;44(3):100571. doi: 10.1016/j.currproblcancer.2020.100571.
4. **Gupta P, Saha K, Vinarkar S, Banerjee S, Choudhury SS, Parihar M, Midha D, Mukherjee G, Lingegowda D, Chatterjee S, ArunsinghS M, Shrimali R, Ganguly S, Dabkara D, Biswas B,**

Mishra DK, Arora N. Next generation sequencing in lung cancer: An initial experience from India. *Curr Probl Cancer*. 2020 Jun;44(3):100562. doi: 10.1016/j.currproblcancer.2020.100562.

5. **Biswas B, Dabkara D, Sengupta M, Ganguly S, Ghosh J, Arunsingh S M, Sen S**. Multimodality treatment outcome in patients with primary malignant mediastinal germ cell tumor in adults. *Cancer Rep (Hoboken*). 2020 Oct 8: e1306. doi: 10.1002/cnr2.1306.
6. **Ghosh J, Ganguly S, Mondal D, Pandey P, Dabkara D, Biswas B.** Perspective of Oncology Patients During COVID-19 Pandemic: A Prospective Observational Study from India. *JCO Glob Oncol.* 2020 Jun; 6:844-851. doi: 10.1200/GO.20.00172.
7. **Ganguly S, Biswas B, Bhattacharjee S, Ghosh J, Mukhopadhyay S, Midha D, Dabkara D.** Clinicopathological characteristics and treatment outcome in small cell lung cancer: A single institutional experience from India. *Lung India*. 2020 Mar-Apr;37(2):134-139. doi: 10.4103/lungindia.lungindia_370_19.
8. **Pushpam D, Garg V, Ganguly S, Biswas B.** Management of Refractory Pediatric Sarcoma: Current Challenges and Future Prospects. *Onco Targets Ther*. 2020 Jun 8; 13:5093-5112. doi: 10.2147/OTT.S193363.
9. **Verma H, Sehgal K, Panchal KB, Chakraborty S, Biswas B, Mukherjee G, Midha D, Biswas G.** Presentation and Management of Dermatofibrosarcoma Protuberans: A Single Center Protocol. *Indian J Surg Oncol*. 2020 Mar;11(1):35-40. doi: 10.1007/s13193-019-01007-3.
10. **Patel A, Tannock IF, Srivastava P, Biswas B, Gupta VG, Batra A, Bhethanabhotla S, Pramanik R, Mahindru S, Tilak T, Das CK, Mehta P**. Low-Dose Abiraterone in Metastatic Prostate Cancer: Is It Practice Changing? Facts and Facets. *JCO Glob Oncol*. 2020 Mar; 6:382-386. doi: 10.1200/JGO.19.00341.
11. **Ganguly S, Alphones S, Ghosh P, Midha D, Ghosh J, Biswas B.** Rectal cancer with breast metastasis: A case report with review of literature. *Cancer Res Stat Treat*. 2020; 3:627-9.
12. **Basu A, Chatterjee M, Ghosh J, Ganguly S, Biswas B, Dabkara D.** Leptomeningeal metastasis in lung cancer: Not always a gloomy picture. *Cancer Res Stat Treat*. 2020 Sep; 3:619-21.
13. **Ghosh J, Das J, Ganguly S, Biswas B, Dabkara D.** Cardiac metastasis from

squamous cell carcinoma of the buccal mucosa: A case report and review of the literature. *Cancer Res Stat Treat.* 2020; 3:617-9.

14. **Ghosh S, Ganguly S, Ghosh J, Biswas B, Dabkara D.** A novel oxaliplatin desensitization protocol: Short, safe, and effective. *Indian J Med Paediatr Oncol*. 2020; 41:287-8
15. **Ganguly S, Ghosh J, Biswas B, Dabkara D**. Ado-trastuzumab emtansine – The monoclonal drug conjugate in human epidermal growth factor receptor 2-positive breast cancer. *Indian J Med Paediatr Oncol*. 2020; 41:218-20.
16. **Dabkara D, Ganguly S, Ghosh J, Patel A, Batra A, Das Ck, Tilak TVSVGK, Biswas B.** How We Treat Genitourinary Cancers During COVID-19 Pandemic? *Asian Pacific Journal of Cancer Care*. 2020; 5(Supplement 1):147-152. DOI: 10.31557/APJCC.2020.5. S1.147.
17. **Ghosh J, Ganguly S, Biswas B, Dabkara D, Srivastava P, Patel A, Batra A, Mehta P.** Systemic treatment of gastroesophageal cancer during SARS-CoV2. *Indian J Med Paediatr Oncol*. 2020; 41:141-3.
18. **Biswas B, Ganguly S, Dabkara D, Ghosh J, Srivastava P, Mehta P, Patel A, Bhethanabhotla S, Batra A, Pramanik R, Gupta VG, Das CK, Mahindru S.** How we treat lung cancer during SARS-Cov-2 (COVID-19) pandemic in India? *Indian Journal of Medical & Pediatric Oncology*. May 2020; DOI: 10.4103/ijmpo.ijmpo_122_20.
19. **Ghosh J, Ghosh A, Bhaumik J, Zameer L, Roy P, Chakraborty B, Roy A, Rai S, Mathai S, Ganguly S, Dabkara D, Ghosh P.** A rare case of hepatoid carcinoma of ovary with mini review of literature. *Indian Journal of Gynaecologic Oncology*. 2020;18,27(2020). DOI: 10.1007/s40944-020-0371-5.
20. **Kumar A, Biswas B, Chopra A, Kapil A, Vishnubhatla S, Bakhshi S.** Early Discontinuation versus Continuation of Antimicrobial Therapy in Low Risk Pediatric Cancer Patients with Febrile Neutropenia, Before Recovery of Counts: A Randomized Controlled Trial (DALFEN Study). *Indian J Pediatr*. 2021 Mar;88(3):240-245. doi: 10.1007/s12098-020-03377-x.
21. **Srivastava P, Tilak TVSVGK, Patel A, Das CK, Biswas B, Mahindru S, Pramanik R, Ghosh J, Mehta.** Advisory for cancer patients during the COVID pandemic. *Cancer Res Stat Treat*. 2020; 3:145-8.
22. **Batra A, Mehta P, Patel A, Bethanabhotla S, Biswas B, Pramanik R, Das CK.** Breast cancer treatment during the COVID-19 pandemic. *Indian*

Journal of Medical & Pediatric Oncology. May 2020.
DOI: 10.4103/ijmpo.ijmpo_111_20.

23. **Mahindru S, Das CK, Patel A, Mehta P, Biswas B, Batra A, Bandhopadhyay A.** Cancer surgery in challenging time of COVID-19 pandemic – A pragmatic approach. Indian Journal of Medical & Pediatric Oncology. May 2020.
DOI: 10.4103/ijmpo.ijmpo_121_20.
24. **Bethanabhotla S, Pramanik R, Srivastava P, Mehta P, Patel A, Biswas B, Batra A, Gupta VG, Das CK, Mahindru S**. Colorectal cancer chemotherapy during COVID-19 pandemic. *Indian Journal of Medical & Pediatric Oncology*. May 2020.
DOI: 10.4103/ijmpo.ijmpo_149_20.
25. **Das CK, Mahindru S, Patel A, Batra A, Biswas B, Mehta P, Pramanik R, Bethanabhotla S, Gupta VG.** How I treat epithelial ovarian cancer during COVID-19 pandemic. *Indian Journal of Medical & Pediatric Oncology*. May 2020.
DOI: 10.4103/ijmpo.ijmpo_112_20.
26. **Pramanik R, Srivastava P, Sharma A, Mehta P, Patel A, Bethanabhotla S, Biswas B, Batra A, Gupta VG, Das CK, Mahindru S**. Management of head-and-neck cancer during COVID-19 crisis: A medical oncology perspective. *Indian Journal of Medical & Pediatric Oncology*. May 2020.
DOI: 10.4103/ijmpo.ijmpo_134_20.
27. **Patel A, Batra A, Mehta P, Sharma A, Sirohi B, Biswas B, Gupta VG, Ganguly S.** Gallbladder cancer: Adjuvant and palliative treatment during Covid-19 pandemic in India. *Indian Journal of Medical & Pediatric Oncology*. May 2020.
DOI: 10.4103/ijmpo.ijmpo_110_20.
28. **Ghosh J, Ganguly S, Dabkara D, Biswas B, Chatterjee A, Mukhopadhyay S, Banerjee S, Sen S, Arun Case report Ghosh J, Ganguly S, Dabkara D, Biswas B, Chatterjee A, Mukhopadhyay S, Banerjee S, Sen S, Arun I.** Pancreatic adenocarcinoma with primary tumor calcification and calcified liver metastasis: Report of a rare case and review of literature. *Indian J Med Paediatr Oncol.* 2020; 41:738-740.
29. **Ghosh J, Batra A, Patel A, Mehta P.** Trastuzumab emtansine for residual invasive human epidermal growth receptor-2-positive breast cancer. *Indian J Med Paediatr Oncol*. 2020; 41:652-3.
30. **Rout S, Rai S, Dabkara D, Ghosh J.** Managing Brain Lesions in Gynecological Cancers: A Case Series. *Indian J Gynecol Oncolog*. 2020; 18, 83. https://doi.org/10.1007/s40944-020-00409-4
31. **Pandey A, Ghosh J.** Upfront maintenance poly (Adenosine

Diphosphate Ribose) polymerase inhibitors in ovarian cancer: A ray of hope or just a mirage! *Indian J Med Paediatr Oncol*. 2020; 41:173-81.

32. **Das J, Ray S, Ghosh J, Zameer L**. A Rare Case of Metastatic SuperScan from Signet Ring Cell Adenocarcinoma of Stomach. Int J Med Clin Imaging. 2020;5(1): 114-117.
33. **Chatterjee A, Biswas B, Gehani A, Das J, Sen S, Mukhopadhyay S, Chandra A, Ghosh P, Gupta B, Lingegowda D**. Oncoradiology preparedness in the COVID-19 pandemic: Perspective from a tertiary oncology referral center from Eastern India. *Indian J Med Paediatr Oncol*. 2020; 41(6). DOI: 10.4103/ijmpo.ijmpo_240_20.
34. **Basu A, Chatterjee M, Dabkara D, Biswas B, Ganguly S, Ghosh J, Ghosh P.** Adrenal metastasis in an older patient with seminoma. *Cancer Res Stat Treat*. 2020; 3:836-7.
35. **Ghosh J, Ganguly S**. Decline in the number of patients with cancer during the COVID-19 pandemic: A matter of concern or just a statistic? *Cancer Res Stat Treat*. 2020; 3:793-5.

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DEPARTMENT OF MICROBIOLOGY AND INFECTIOUS DISEASES

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MBBS, MD, DM, Consultant in Infectious Diseases

OVERVIEW OF RESEARCH – 2020

Diagnostic Microbiology in Medical Sciences hardly makes sense without an active and dynamic interface with Infectious Diseases, Clinical Medicine and the Surgical Sciences. In the current annual research report of the calendar year 2020 an attempt has been made to document the various activities of the Microbiology Department of Tata Medical Center, Kolkata. The research activities documented in this document is not necessarily the sole work of an individual or a small group of investigators. In many instances the data generated in clinical research is because of the work done and dedication shown by many staff at various levels of healthcare. We would like to thank students, laboratory technologists, scientific officers, scientists, medical colleagues within Microbiology or other departments, as well as colleagues of supporting departments such as Customer Care, Human Resources, Finance, Materials Management, Biomedical Engineering, Maintenance Engineering and Central Sterile Supply Department, Information Technology who have made the research works possible through their feedback guidance or support. Last but not least we would like to thank our Medical Administration and our Director Dr. Mammen Chandy for nurturing an ecosystem of research within the world of clinical care.

RESEARCH PROJECTS

1. ICMR Regional Center Project for Anti-Microbial Resistance Surveillance. (PI, Dr. Sanjay Bhattacharya) – Funded by Indian council of Medical Research
2. Capacity Building Project for Healthcare Associated Infection Surveillance in India. (PI, Dr. Sanjay Bhattacharya) - Funded by Centres for

Disease Control and prevention USA (through ICMR- AIIMS, New Delhi)

3. Estimating Incremental cost of treating antimicrobial Resistant infection in India. (PI, Dr. Sanjay Bhattacharya) - Funded by Indian council of Medical Research- NARI (National AIDS Research Institute, Pune)
4. Integrated Cervical cancer prevention and treatment stratification study: systems medicine cluster approach. (PI, Dr. Mammen Chandy) - Funded by Department of Biotechnology, Govt of India.
5. ALTITUDE study: Microbiome in patients with AML and BMT recipients. (PI, Dr. Vivek Radhakrishnan) - Funded by Tata Trust.
6. Antimicrobial Stewardship Program (AMSP). (PI, Dr. Sudipa Mukherjee) - Funded by Indian council of Medical Research.
7. Serology and Sociology of Individuals with SARS-Cov-2 Infection: A Study of Igg Serology in Patients, Staff and Blood Donors in an Oncology Center in Eastern India Along with an Assessment of KAP (Knowledge Attitude and Practice) In Blood Donors. (PI, Dr. Sanjay Bhattacharya) – Funded by Tata Medical Center (intra-mural)
8. ICMR National Clinical Registry for CoVID 19. (PI, Dr. Soumyadip Chatterji) - Funded by ICMR.

RESEARCH PUBLICATIONS

1. **Das P, Dadwal R, Radhakrishnan Vs, Parihar M, Bhattacharya S, Mishra DK, Chandy M**. Comparison of Four High Throughput Sequencing Platforms in A Medical Laboratory for Gut Microbiome Research. *Indian J. Anim. Hlth*. 2020; 59(2)89-99
   DOI: 10.36062/ijah.59.2SPL.2020.89-99
2. **Exner M, Bhattacharya S, Gebel J, Goroncy-Bermes P, Hartemann P, Heeg P, Ilschner C, Kramer A, Lin Ling M, Merkens W, Oltmanns P, Pitten F, Rotter M, Schmithausen RM, Sonntag HG, Steinhauer K, and Trautmann M.** Chemical disinfection in healthcare settings: critical aspects for the development of global strategies. *GMS Hyg Infect Control*. 2020;15: Doc36. doi:10.3205/dgkh000371
3. **Mukherjee S, Das S, Mukherjee S, Ghosh PS, Bhattacharya S**. Arterial blood gas as a prognostic indicator in patients with sepsis. *Indian J Med Microbiol*. 2020;38(3 & 4):457-460. doi: 10.4103/ijmm.IJMM_19_478.

4. **Bhattacharya S**. Positive aspects of the COVID-19 pandemic. *J Acad Clin Microbiol*. 2020; 22:2
DOI: 10.4103/jacm.jacm_9_20
5. **Bhattacharya S, Iyer R, Raja K, Joy VM, Bijulal SR, George K, Goel G, Santosh S, Madhavan A, Ardra M, Dash D, Oommen S, Joe G, Shetty AK, Gupta YK, Prabhakar M S, Vengilat DH, Philomina J B, Sujatha S R, Hotta S, Gandhi C, Sehgal R, Kirupa S, Sampath S, Mamtora DK, Kalyani M, Koppad M, Ashish J, Santhi M, Nair S, Sinha KK, Neetha T R.** A survey of practices to diagnose, manage, prevent and control COVID-19 from 28 centres. *J Acad Clin Microbiol*. 2020; 22:5-11.
DOI: 10.4103/jacm.jacm_21_20
6. **Bhattacharya S, Joy VM, Vivek P.** Personal-protective equipment priority list for developing countries in relation to the COVID-19 pandemic. *J Acad Clin Microbiol*. 2020; 22:56-8.
DOI: 10.4103/jacm.jacm_8_20
7. **Bhattacharya S, Vidyadharan A, Joy VM.** Inconclusive SARS-COV-2 reverse transcription-polymerase chain reaction test reports: Interpretation, clinical and infection control implications. *J Acad Clin Microbiol*. 2020; 22:59-61.
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8. **Mishra DK, Goel G, Arora N, Krishnan S, Bhattacharya S, Mathur P, Walia K, Chandy M.** The importance of intra- and inter-institutional networks for capacity building in severe acute respiratory syndrome coronavirus 2 reverse transcription polymerase chain reaction services: experience from an oncology centre in eastern India. *Indian J Med Microbiol*. 2020; 38:9-17.
DOI: 10.4103/ijmm.IJMM_20_255
9. **Vijayakumar S, Wattal C, Oberoi J K, Bhattacharya S, Vasudevan K, Anandan S, Walia K, Veraraghavan B.** Insights into the complete genomes of carbapenem-resistant Acinetobacter baumannii harbouring blaOXA-23, blaOXA-420 and blaNDM-1 genes using a hybrid-assembly approach. *AccessMicrobiol*.2020;2(8): acmi000140.
https://doi.org/10.1099/acmi.0.000140
10. **Bhattacharya S.** Improving Diagnostic and Laboratory Capacity Helps in Control of Infection: An Indian Perspective. Current Treatment Options in Infectious Diseases. 2020; 12,112–121
DOI https://doi.org/10.1007/s40506-020-00215-8
11. **Roy S, Das P, Das S, Roy S, Pal S, Joy VM, Mukherjee S, Bhattacharyya A, Goel G, Bhattacharya S, Mathur P, Walia K, Chandy M.** Detection of the

emergence of mcr-1-mediated colistin-resistant Escherichia coli and Klebsiella pneumoniae through a hospital-based surveillance in an oncology center in eastern India. *Infect Control Hosp Epidemiol*. 2020 Mar;41(3):378-380.
DOI: 10.1017/ice.2019.363

12. National Guidelines for Infection Prevention and Control in Healthcare Facilities. National Centre for Disease Control, Directorate General of Health Services. Ministry of Health and Family Welfare, Government of India. January 2020. Dr. Sanjay Bhattacharya of Tata Medical Center, Kolkata was one of the contributors and reviewers. http://www.mohfw.gov.in/National%20Guidelines%20for%20IPC%20in%20HCF%20-%20final%281%29.pdf
13. **Bhattacharya S, Das P, Goel G, Mukherjee, S, Ghosh PS, Singh R, Sinha S, Chandy M, Walia K, Chakrabarti A.** Candida auris Infection Among Patients with Cancer in an Oncology Center in Eastern India. *Infection Control & Hospital Epidemiology*. 2020; 41(S1), S146-S147. doi:10.1017/ice.2020.664
14. **Mathur P, Malpiedi P, Walia K, Malhotra R, Srikantiah P, Katoch O, Guleria R, et al.** Surveillance of Healthcare-Associated Bloodstream and Urinary Tract Infections in a National Level Network of Indian Hospitals. *Infection Control & Hospital Epidemiology*. 2020; 41(S1), S398-S399.
doi:10.1017/ice.2020.1043
15. **Bhattacharya S**. The Social Impact of the COVID Pandemic. ORF Issue Brief No. 406, October 2020, Observer Research Foundation.
16. **Datta SS, Mukherjee A, Ghose S, Bhattacharya S, Gyawali B.** Addressing the Mental Health Challenges of Cancer Care Workers in LMICs During the Time of the COVID-19 Pandemic. *JCO Glob Oncol*. 2020 Oct; 6:1490-1493.
doi: 10.1200/GO.20.00470.
17. **Gupta G, Chatterji S, Sinha S, Thukral H, Arumugaswami V, Guha SK, Basu A, Gupta S.** Possible Role of BCG-Induced Trained Immunity to Reduce the Prevalence and Severity of COVID-19 in High-Risk Population. *J Inf Dis Trav Med*. 2020; 4(S1): 000S1-005.
DOI: 10.23880/jidtm-16000S1-005
18. **Radhakrishnan VS, Nair R K S, Goel G., Ramanan V, Chandy M, Nair R.** COVID-19 and haematology services in a cancer centre from a middle-income country: adapting service delivery, balancing the known and unknown during the pandemic. *Ecancer.* 2020; 14:1110

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19. **Pal S, Bhattacharya S, Goel G, Chandy M.** Mycolicibacterium sp. (llatzerense) strain B3829 16S ribosomal RNA gene, partial sequence. *GenBank*. 2020. https://www.ncbi.nlm.nih.gov/nuccore/MT814053.1 https://www.ncbi.nlm.nih.gov/nuccore/MT814054.1
20. **Das P, Mandal S, Bhattacharya S, Goel G, Chandy M.** Saccharopolyspora tripterygii strain Blood Culture bottle 16S ribosomal RNA gene, partial sequence. GenBank. 2020; MT940447.1. https://www.ncbi.nlm.nih.gov/nuccore/MT940447.1
21. **Pal S, Das P, Mandal S, Bhattacharya S, Goel G, Chandy M.** Diutina catenulata isolate M5131 isolate 1 small subunit ribosomal RNA gene and internal transcribed spacer 1, partial sequence. GenBank Nucleotide sequence submission Pal S, Das P, Mandal S, Bhattacharya S, Goel G, Chandy M. GenBank: 2020. https://www.ncbi.nlm.nih.gov/nuccore/MW537818.1
22. **Bhattacharya S.** Dearth of Data. We don't know much about infections originating in hospitals. Dearth of Data. Down to Earth. Antibiotic Resistance. Pages 122-125. https://www.downtoearth.org.in/blog/health/dearth-of-data-we-don-t-know-much-about-infections-originating-in-hospitals-74265 (Nov 2020)
23. **Basu A, Das P**. Make life easy through telemedicine in COVID-19 crisis: An Indian perspective. International Journal of Community Medicine and Public Health
DOI:
http://dx.doi.org/10.18203/2394-6040.ijcmph20203957

EXTERNAL ACADEMIC MEETINGS

Resource Person - Dr Sanjay Bhattacharya

1. E-MICROCON - First Virtual Annual Congress of the Indian association of Medical Microbiologists an interview of Dr. Navin Dang- Clinical Microbiology Laboratory as an Entrepreneurship 11th December 2020.
2. Web based meeting organized by the Indian Council of Medical Research Target Product Profile of Sepsis and Neonatal Sepsis Diagnostics 24 November 2020.

Lecture - Dr Sanjay Bhattacharya

1. On-line Lecture organized by the Birla Industrial and Technological Museum, Kolkata Super Bugs and Global Problem of Antimicrobial Resistance (AMR) 01 Dec 2020.
2. On-line Lecture organized by the Mizoram College of Nursing Breaking the Pandemic Chain 19th November 2020.
3. On-line Lecture> Tata Clinical Research Methodology Course 2020 11th Sept 2020 Case Control Study and Cohort Study 11th Sept 2020.
4. On-Line lecture organized by Indian Institute of Technology, Kharagpur, India Biosafety in the COVID-19 era: what needs to be done in not just in the clinic but also in research laboratories 08-09 August 2020.
5. Meeting of INDIAN JOURNAL OF ANIMAL HEALTH, AMR- a global menace: one health approach Kolkata AMR in human health: An Indian perspective 07th March 2020.

Annual Conference 2020

6. Clinical Infectious Diseases Society of India Conference Nov 2020
7. Association of Physicians of India, West Bengal Chapter Nov 2020
8. Govt of West Bengal COVID update Weekly Webinar Sept 2020 Case discussion- Presenter and panellist

Lecture - Dr. Gaurav Goel

9. On-line Lecture> Tata Clinical Research Methodology Course 2020 5th Sept 2020 Diagnostic accuracy testing (Sensitivity, Specificity, predictive power, ROC curve) 5th Sept 2020

ORCID ACCOUNT

1. Dr. Sanjay Bhattacharya (https://orcid.org/0000-0003-4139-1039)
2. Dr. Gaurav Goel (https://orcid.org/0000-0002-5217-4083)
3. Dr. Soumyadip Chatterji (https://orcid.org/0000-0002-5291-1901)
4. Dr. Parijat Das (https://orcid.org/0000-0002-8916-1067)

DEPARTMENT OF NUCLEAR MEDICINE

Dr Soumendranath Ray

MBBS, DRM, DNB (NUCLEAR MEDICINE), Senior Consultant

Dr Jayanta Das

MBBS, MD (RADIODIAGNOSIS), Associate Consultant

RESEARCH PROJECTS

1. Intensifying radiation treatment in advanced/ poor prognosis laryngeal, hypopharyngeal (LH) and oropharyngeal cancers (OPC) using PET –CT based dose escalation strategies. (INTELHOPE)
2. Radiomics –Image analysis in Breast Cancer Texture analysis of PET-CT images of carcinoma breast and its relation with primary histopathological features(PE-CaB).
3. DBT Project: Phase II study to evaluate toxicity and clinical outcome of definitive helical tomotherapy for primarily unresected Cancer cervix using FDG PET based RT planning. (PI Dr Rimpa Achari).
4. DBTSyMec Project ---Cancer Cervix A multicenter multi parametric evaluation of locally advanced Ca Cervix.
5. HYPORT phase I/II study Hypofractionated Radiotherepy regimen in FDG PET based management of locally advanced breast cancer.
6. Comprehensive Digital Archive of Cancer Imaging (CHAVI RO). Department of Radiation Oncology. In collaboration with IIT, Kharagpur.

RESEARCH PUBLICATIONS

1. **Das J, Bhattacharyya T, Sayantani Sinha S, Ray S**. Aberrant origin of right vertebral artery from the arch of aorta. *Indian Journal of Thoracic and Cardiovascular Surgery*. 2021. https://doi.org/10.1007/s12055-020-01100-1
2. **Das J, Ray S, Ghosh J & Zameer L.** A Rare Case of Metastatic Super Scan from Signet Ring Cell Adenocarcinoma of Stomach. *Int J Med Clin Imaging*. 2020;5(1): 114-117.
3. **Das J, Ray S, Tapadia R, Midha D, Mallick I**. Prostate-specific membrane antigen-expressing hepatic lesion: Metastatic or hepatocellular carcinoma. *Indian J Nucl Med*. 2020; 35:58-60.

4. **Kathrotiya M, Radhakrishnan VS, Bhave S, et al**. Relapsed plasmablastic lymphoma in a HIV-negative patient: Pushing the envelope. Clinical Case Reports. 2021; 9:873–877. https://doi.org/10.1002/ccr3.3673
5. **Das J, Ghosh J, Zameer L, Ray S.** 18F Fluorodeoxyglucose positron emission tomography/computed tomography finding in a rare case of follicular carcinoma of thyroid with rhabdoid morphology. *Indian J Nucl Med*. 2021; 36:56-8.
6. **Mallick A, Das J, Shaw MK, Biswas B, Ray S**. Prognostic value of metabolic tumor parameters in pretreatment 18F fluorodeoxyglucose positron emission tomography–computed tomography scan in advanced non-small cell lung cancer. *Indian J Nucl Med*. 2020.

Review Article:

1. Nanoparticulate formulations of radiopharmaceuticals: Strategy to improve targeting and biodistribution properties. Datta P, Ray S. *J Label Compd Radiopharm*. 2020;1–23.

TEACHING & TRAINING

1. DNB Nuclear Medicine Assessment completed. Waiting for final approval from National Board.
2. MSc Nuclear Medicine Being conducted in collaboration with IIT, KGP since 2018. The students of second batch will join us in TMC for 4th semester training.

DEPARTMENT OF NURSING

Ms. Piyali Bose
Nursing superintendent

Ms. Chaitali Biswas
PG Co-ordinator

Ms. Chitra Sengupta
Deputy Nursing Superintendent

Ms. Sadhana Chattopadhyay
Nurse Educator

M.SC NURSING RESEARCH THESIS

1. A Study to Assess the Physical and Psychosocial Problems among Children with Leukemia Attending Out Patient Department in a Selected Hospital, Kolkata – Lalchhanmawii
2. A Study to Assess the Effect of Reiki Therapy on Pain and Fatigue among Hematological Cancer Patients in Selected Hospitals of Kolkata, West Bengal - Rinki Biswas
3. A Study to Assess the Effect of Using One Piece Versus Two Piece Ostomy Appliances on Self-Maintenance of Stoma Care Among Cancer Patients with Ostomy in Selected Hospital of Kolkata, West Bengal - Riba Haobam

JOURNAL PUBLICATIONS & PAPER PRESENTATION

INDIAN JOURNAL OF ONCOLOGY NURSING, VOLUME NO: 27
JANUARY – MARCH 2020

1. Effectiveness of Chlorhexidine Gluconate (CHG) based gel dressing in preventing CRBSI and local area skin changes on application among patients having Central Venous Access Device (CVAD): An Observational Report
   CRITICAL CARE NURSING TEAM, TMC
2. Clinical Audit on CLABSI prevention bundle
   Kumarika Maity, Ward In-charge, TMC
3. Clinical Audit on Prevention of SSI
   Shantilata Dalui, Ward In-charge, TMC
4. A Study to assess the effect of planned teaching programme on knowledge regarding prevention of colorectal

cancer among adults in selected urban areas of Manipur
Sijagurumayum Nirupama Devi, Staff Nurse, TMC

5. Audit checklist on ventilator associated pneumonia prevention and control bundle with intubated and tracheostomy patients
Arati Sahoo, Ward In-charge, TMC

INDIAN JOURNAL OF ONCOLOGY NURSING, VOLUME NO: 28
APRIL – JUNE 2020

6. Impact of COVID-19 on Hospital Administration
Sadhana Chattopadhyay, Nurse Educator, TMC
7. COVID-19 Crisis: Co-feelings about a front liner
Debjani Mukherjee, Nursing Supervisor, TMC
8. Comprehensive preparedness checklist for Corona Virus Disease 2019 (COVID-19) in Tata Medical Center (Nursing Perspective)
Sangita Choini, Nursing Supervisor, TMC
9. Health Thrives if WE live and it cries if WE leave – Measures aimed at preventing spread of COVID-19
Chitra Sengupta, Deputy Nursing Superintendent, TMC

PROMOTIONAL TEST - PROTOCOL PRESENTATION / DEMONSTRATION

1. MV Carboplatin protocol and any one drug from the protocol
Mousmi Saikia
2. AML- Induction protocol and one Chemo drug from the protocol
Pynshngain Habamut Tiewsoh
3. ABVD Protocol and any one drug fromthat protocol
Sijagurumayum Nirupama Devi
4. Drug Meropenem
Udita Chowdhury
5. Antimicrobial policy for VAP prevention and any one drug from the policy
Reetika Devi
6. VAD protocol for Multiple Myeloma and any one drug from VAD
Evelyn Darthanghnem
7. COPP protocol and any one drug from the protocol
Sanasam Luxmi Devi
8. Drug used in CPR and Noradrenaline
Taniya Atik

9. ICU insulin protocol and Drug study on Human Atrapid
   Baby Lalzokhumi
10. Drug Cordarone
    Roshni Chauhan
11. Commonly used Epidural anaesthetic drug and any one drug study
    Khundrakpam Roji Devi
12. Demonstration on Donning and Doffing of PPE for handling COVID-19 patient
    Anil Kumar N K
13. Project on- immediate nursing and collaborative measures/ action and it's outcome on immediate major post-operative patients during care in recovery unit
    Punyatoya Rout

NURSING IN-HOUSE WORKSHOP, SEMINAR

1. ICU WORKSHOP – "ACT ON THE SILENCE BEFORE STORM" 6th to 7th Feb'20 by Critical Care Team Nursing.
2. PICC LINE INSERTION TRAINING PROGRAMME conducted by PICC Nursing Team from 10th to 15th Feb'20.
3. Demonstration on Donning and Doffing of PPE for COVID-19 from March'2020 – July'2020.

TRAINING / PROGRAMME ATTENDED DETAILS 2020

1. Training - BLS' by Indian Academy of Pediatrics (IAP)

- Maitrayee Sarkar De
- Moumita Chakraborty
- Jaydipta Bera
- Payel Mazumder
- Pratap Mallick
- Keneisenuo Metha
- RC Laldihpui
- Balaram Rudra Paul
- Jithin Raj M
- Pritam Bhar
- Sangita Choini
- Mamumoni Kakati
- Ibahunlang Nongsiej
- Falguni Shil
- Namita Bindhani
- Khusbu Thapa
- Piyali Sahoo
- Soumya Swaroop Patra
- Rupali Debnath
- Upasana Das
- Punyatoya Rout
- Sriparna Giri
- Jenson Jose
- Chaitali Das
- Cordelica BD Rani
- Sangita Lama

- Suravi Debnath
- Ronali Purohit
- Tshering Ongmu Bhutia
- Sanasam Luxmi Devi
- Ramesh Nayak
- Rusia Ahmed
- Taniya Atik
- Pinku Halder
- Saswati Basak
- Pragyanmai Nayak

SPEAKERS

2. Cancer raising Awareness Programme & Sharing Information' - Cancer- know your risk and prevention
   Sriparna Giri
3. Cancer raising Awareness Programme & Sharing Information' - Palliative Care in Cancer Patients
   Sunipa Panja Gupta
4. Pre & Post op Stoma Counselling – Coloplast
   Sarmistha Roy
5. Organized by Assam Downtown University, Leadership Competencies for Health Care – 'I have to know What!'
   Piyali Bose
6. Society of Advanced Multidisciplinary Research & Practices in association with Astronomical Instruments Design Laboratory, IEE Dept-1st International Conference of Multidisciplinary Research 2020
   Piyali Bose
7. Breast Cancer & Cervical Cancer Awareness
   Moupiya Poriya
   Dimpi Hazarika
8. Annual Congress of the APBMT – Virtual Session- Basics of Transplant, Topic- HLA typing & its relevance in Transplant
   Mita Roy Chowdhury
9. Fluid Management'by Baxter
   Sucharita Maity
10. Development of EBP Guidelines for patient care: - Oral hygiene in cancer patient
    Chaitali Biswas
11. Opportunities and challenges of the exciting trends of virtual education
    Chitra Sengupta
12. 19th Annual International Conference (RG CON-2020)
    Mita Roy Chowdhury
13. Cancer Survivorship Programme
    Moupiya Poriya
14. Stoma Complications & Management'
    Dimpi Hazarika
    Sarmistha Roy
15. Guest Panelist - Cause-show on Cancer Care- “Love, Live, Conquer”. - Yeh mera India NGO
    Chitra Sengupta

16. 2nd National Congress -Immuno Oncology

- Piyali Bose
- Chitra Sengupta
- Sadhana Chattopadhyay
- Swapna Pal Sinha
- Kabita Mishra
- Joby Koshy
- Maitrayee Sarkar De
- Sangita Choini
- Monalisa Patra
- Angelina Lalhruaitluangi
- Prantika Deb
- Rojalini Kar

17. COVID Integrated Training – Faculty Development Program (FDP) session-2

Irengbam Nganthoibi Devi

DEPARTMENT OF PALLIATIVE CARE & PSYCHO-ONCOLOGY

Dr Soumitra Shankar Datta

MBBS DPM MD (Psychiatry) MNAMS, MRCPsych CCT in Child Psychiatry, Senior Consultant

Dr Shrikant Atreya

MBBS MD PDF, Fellowship in Palliative Medicine, PhD scholar, Associate Consultant

Dr Gaurav Kumar

MBBD MD PDF, Fellowship in Palliative Medicine, Junior Consultant

Dr Arnab Mukherjee

MBBS DPM MD, Junior Consultant

OVERVIEW OF RESEARCH

Research in psycho-oncology, psychiatry and mental health

- Communication in oncology specifically doctor-patient communications. Dr Datta was awarded the University College London Teaching Excellence Bursary and he further collaborated with researchers in UCL to develop a communication skills training programme for oncology clinicians in India. The work on role of families in cancer communications was published in international peer reviewed journals. Presently Dr Datta is leading another project on cancer communications in paediatric oncology.
- Decision making in oncology: The research on decision making in oncology has also been an area of investigation.
- Stigma in cancer and other diseases: One project focussed on stigma perceived in women with breast cancer and another project is currently quantifying stigma perceived by health care workers fighting the COVID-19 pandemic.
- Staff Mental Health has also been researched. A recent commentary from the clinicians of the department was published by the American Society of Clinical Oncology in the Journal of Clinical Oncology - Global Oncology.
- The department has taken the leadership in publishing two Cochrane reviews on child psychiatry. The review published in 2020 went on to become a featured review of the Cochrane Collaboration and the key message of the review has been translated to

French, Spanish, Malay, Chinese, Arabic, Portuguese and other languages.

- Another key strand of current research is in the area of patient and public involvement in clinical research and care in oncology.

Research in Palliative Care

- An exploratory study to understand the perception of Respiratory physicians for the need and integration of palliative care into respiratory medicine led by Dr Shrikant Atreya
- An observational study to understand the perception of Respiratory physicians for the need and integration of palliative care into respiratory medicine led by Dr Shrikant Atreya as part of his post-doctoral thesis
- A pragmatic clinical trial led by Dr Gaurav Kumar on Implementation of Home-based Palliative care in limited resource settings is a National Institutes of Health (NIH) USA funded R 21 Grant; an international collaborative research done by Tata Medical Center, Kolkata and Medical University of South Carolina, USA is a 2 years' project implementing WHO palliative care toolkit for enhancing community based palliative care

RESEARCH PROJECTS

1. Fear and Stigma of Healthcare workers in Oncology during COVID19 (FrStHealOnCO). (PI Dr Arnab Mukherjee).
2. Preference for Information Sharing and Participation in treatment decision Making of Children and Adolescents with Cancer and their Parents (PRISM-HEALTH study). (PI Dr Soumitra S Datta).
3. An exploratory study to understand the perception of Respiratory physicians for the need and integration of palliative care into respiratory medicine. (PI Dr Shrikant Y Atreya)
4. An exploratory study to understand the educational and training needs of general practitioners providing end of life care to adult patients in West Bengal. (PI Dr Shrikant Y Atreya).
5. Implementation of Home-based Palliative care in limited resource settings. (PI Dr Gaurav Kumar).

RESEARCH PUBLICATIONS

1. **Datta SS, Daruvala R, Kumar A**. Psychological interventions for psychosis in adolescents. 2020; Issue 7. Art. No.: CD009533. DOI: 10.1002/14651858.CD009533.pub2.
2. **Atreya S, Kumar G, Samal J, Bhattacharya M, Banerjee S, Mallick P, Chakraborty D, Gupta S, Sarkar S.** Patients'/Caregivers' perspectives on telemedicine service for advanced cancer patients during the COVID-19 pandemic: An exploratory survey. *Indian J Palliat Care*. 2020 Jun; 26(Suppl 1): S40–S44. doi: 10.4103/IJPC.IJPC_145_20.
3. **Datta S.S., Mukherjee A., Randall J**. Psychosocial Management of Patients Undergoing HSCT and Donors of Stem Cells. 2020. https://doi.org/10.1007/978-3-319-64938- 2_10-1
4. **Atreya S, Kumar R, Salins N**. Community-based palliative care during the COVID 19 pandemic. *J Family Med Prim Care*. 2020; 9:3169-75.
5. **Datta SS, Mukherjee A, Ghose S, Bhattacharya S, Gyawali B**. Addressing the Mental Health Challenges of Cancer Care Workers in LMICs During the Time of the COVID-19 Pandemic. *JCO Global Oncology.* 2020 :6, 1490-1493.
6. **Qanungo S, Alejandra CS, McGue S, Singh P, Roy R, Bhattacharjee G, Panda N, Kumar G, Chowdhury R, Cartmell KB**. Barriers, Facilitators and Recommended Strategies for Implementing a Home-Based Palliative Care Intervention in Kolkata, India. *Am J Hosp Palliat Care.* 2020 Nov 10;1049909120969127. https://doi.org/10.25384/SAGE.c.5203786.v1
7. **Agrawal SK, Shakya SK, Nigam S, Datta SS, Ahmed**. Chest wall perforator flaps in partial breast reconstruction after breast conservation surgery: an additional oncoplastic surgical option. *Ecancermedicalscience*. 2020; 14: 1073.
8. **Patil CR, Atreya S.** Unilateral hypoglossal nerve palsy with Malignancy of Unknown Origin: A case report. *Med J DY Patil Vidyapeeth*. 2020; 13:685-7.
9. **Daruvala R, Kumar A, Datta SS.** Do Psychological Interventions Work for Psychosis in Adolescents? *Schizophr Bull*. 2020 Sep 25; sbaa132. doi: 10.1093/schbul/sbaa132.

EXTERNAL ACADEMIC MEETINGS

1. Conference Evidence Based Management of Cancers in India - EBM 2020 February 2020 Faculty Invite- Dr Shrikant Atreya
2. Pre-conference workshop Concept Development Workshop for clinical and early career researchers in palliative care February 2020 Lead faculty- Dr Shrikant Atreya

ORCID ACCOUNT

1. Soumitra Shankar Datta (https://orcid.org/0000-0003-1674-5093)
2. Arnab Mukherjee (https://orcid.org/0000-0002-6325-7116)

DEPARTMENT OF PEDIATRIC HEMATOLOGY-ONCOLOGY

Prof Dr Vaskar Saha

MBBS, MD, FRCPath, FRCPCh, PhD, Senior Consultant

Dr Shekhar Krishnan

MBBS, MRCP, FRCPath, PhD, Senior Consultant

Dr Niharendu Ghara

MBBS, DCH, MD, FRCPath, MRCPCh, Senior Consultant

Dr Parthasarathy Bhattacharyya

MBBS, DCH, MRCP, Senior Consultant

Dr Arpita Bhattacharyya

MBBS, DCH, MRCP, Senior Consultant

Dr Reghu K.S.

MBBS, DCH, MD, DM, Senior Consultant

Dr Debjani Ghosh

MBBS, MD, PDF, Junior Consultant

RESEARCH PROJECTS

1. Prospective Study for Neuroblastoma Registry and Biology. (PI, Dr Arpita Bhattacharyya).
2. A prospective collaborative Study for newly diagnosed patients with Retinoblastoma in India. (PI, Dr Arpita Bhattacharyya).
3. Randomised open label phase IV study for patients with newly diagnosed Acute Lymphoblastic Leukaemia. (PI, Prof. Dr. Vaskar Saha, Dr. Shekhar Krishnan).
4. Clinical Course, Pathological Spectrum and Outcomes in Paediatric Rare Tumours in India: A Prospective Observational Study. (PI, Dr. Reghu K.S.)
5. A multicentre study to standardise the management of relapsed acute lymphoblastic leukaemia in children and young people. PI, Dr. Niharendu Ghara)
6. Cancer Immunotherapy and Precision Oncology Database. (Pi, Dr. Reghu KS)

RESEARCH PUBLICATIONS

1. **Singh A, Das A, Chatterjee A, Achari R B, Sukumaran R K, Roy P**. A Nonchordomatous-looking Chordoma: When INI-1 and Radiology Came to the Rescue!!! *Journal of pediatric hematology/oncology*. 2020 Apr;42(3):218-219. DOI: 10.1097/MPH.0000000000001721.

2. **Patil V, Sukumaran R K, Roychowdhury M, Chaudhuri S, Kumar J, Bhave S, Javed R, Ghara N, Nair R, Radhakrishnan V, Chandy M.** Reduced intensity conditioning followed by haploidentical hematopoietic cell transplantation (RIC-HAPLO HCT) and post-transplant cyclophosphamide as graft versus host disease prophylaxis, for hematological disorders: single centre experience. The 46th Annual Meeting of the European Society for Blood and Marrow Transplantation: Physicians Poster Session (P001-P706). *Bone Marrow Transplantation*. 2020 Dec;55(1):181–714.
3. **Shah SP, Radhakrishnan VS, Jaishetwar GS, Sukumaran R K, Kumar J, Bhave SJ, Roychowdhury M, Chaudhuri S, Mishra D K, Nair R, Krishnan S, Chandy M.** Myeloablative haploidentical t-cell replete hematopoietic cell transplantation with post-transplant cyclophosphamide in high-risk hematological malignancies: Bending the learning curve in a middle-income setting. *Advances in Cell and Gene Therapy*. 2020. https://doi.org/10.1002/acg2.106
4. **Sukumaran R K, Radhakrishnan VS, Mishra AK, Guntiboina VA, Bhave S, Kumar J, Arun I, Zameer L, Dey D, Arora N, Mishra D, Bhattacharyya A, Ghara N, Basu R, Krishnan S, Chandy M, Nair R.** Adolescent and Young Adult Hodgkin Lymphoma: Is More Better? *Blood*. 2020 Nov 5;136(Supplement 1):26–7. DOI: 10.1182/blood-2020-142276
5. **Radhakrishnan V S, Sukumaran Nair R K, Goel G, Ramanan V, Chandy M, Nair R**. COVID-19 and haematology services in a cancer centre from a middle-income country: adapting service delivery, balancing the known and unknown during the pandemic. *Ecancer*. https://doi.org/10.3332/ecancer.2020.1110
6. Sukumaran R K, Chandy M, Radhakrishnan VS. Long term Follow-up and Complications. Contemporary Bone Marrow Transplantation. Cham: Springer International Publishing. 2020; p. 1–25. (Organ and Tissue Transplantation). https://doi.org/10.1007/978-3-319-64938-2_13-1
7. **Bamborde S, Radhakrishnan V S, Kumar J, Bhave SJ, Nag A, Sukumaran Nair R K, Roychowdhury M, Javed R, Parihar M, Ghara N, Mishra D K, Nair R, Chandy M**. Relapsed Refractory Lymphoma and Transplantation Outcomes from a Tertiary Care Cancer Centre at APBMT Virtual conference.

https://doi.org/10.1007/s12288-020-01384-8

8. **Bhattacharyya P.** Multisystem Inflammatory Syndrome of Children Related to SARS-CoV-2: A Novel Experience in Children with a Novel Virus. *Indian J Crit Care Med*. 2020;24(11): 1010–1011. **doi: 10.5005/jp-journals-10071-23652**
9. **Zugbi S, Ganiewich D, Bhattacharyya A, Aschero R, Ottaviani D, Sampor C, Cafferata E G, Mena M, Sgroi M, Winter U, Lamas G, Suñol M, Daroqui M, Baialardo E, Salas B, Das A, Fandiño A, Francis J H, Lubieniecki F, Lavarino C, Garippa R, Podhajcer OL, Abramson D H, Radvanyi F, Chantada G, Llera A S, Schaiquevich P**. Clinical, Genomic, and Pharmacological Study of MYCN-Amplified RB1 Wild-Type Metastatic Retinoblastoma. *Cancers (Basel).* 2020 Sep 22;12(9). DOI: 10.3390/cancers12092714
10. **Mishra A, Krishnan S, Ghara N, Bhattacharyya A, Das P, Modi S, Das A, Sukumaran R, Tuladhar S.** A Single center experience of treating children with AML with majority receiving mitoxantrone based induction. *Pediatric Hematology Oncology Journal*. 4. S34-S35. DOI: 10.1016/j.phoj.2019.08.097.
11. **Gupta T, Arun SR, Babu GA, Chakrabarty B K, Bhave S J, Kumar J, Radhakrishnan V, Krishnan S, Ghara N, Arora N, Mishra D K, Parihar M**. A Systematic Cytogenetic strategy to identify Masked Hypodiploidy in Precursor B Acute Lymphoblastic Leukemia in Low Resource Settings. *Indian Journal of Hematology and Blood Transfusion*. 2021. DOI: 10.1007/s12288-021-01409-w.

EXTERNAL ACADEMIC MEETINGS

Dr Partha Sarathi Bhattacharya

1. Global Critical Care Monthly Meeting-Talk on COVID, September 2020
2. Global ID network Case Kiosk Case Presentation -MDR TB in a Child with Osteosarcoma, September 2020.
3. Global Critical Care Monthly Meeting Palliative Care and Shared Decision-Making at the time of Pandemic. Case Presentation: November 2020.
4. St. Jude Global Alliance Virtual Convening. December 10 & 11 Featured in St. Jude Global Alliance video named “Inspiring Hope”. December 2020

5. Faculty, 22nd National Conference of IAP Pediatric Intensive Care Chapter (PediCritiCon 2020). Pediatric Intensive Care: Infodynamics in Pandemic 2020". December 4-7. (E-Conference).
6. Judge/Expert: P2P Febinar (Peer to Peer Webinar for the Fellows) by IAP-PICC Chapter. 9 Dec, 2020. " Case based discussion - Acute CNS Manifestations of Tropical Infections " Case based discussion - Acute CNS Manifestations of Tropical Infections" December 2020
7. Head Examiner, Indian Diploma in Pediatric Critical Care Medicine (IDPCCM) and Indian Fellowship in Pediatric Critical Care Medicine (IFPCCM). St. John's Medical College and Hospital, Bengaluru. IAP Critical Care Chapter. Fellowship exit exam 9-10 January 2021

Dr Arpita Bhattacharya

8. Joint presentation with St. Jude Children's Research Hospital, Memphis Tuberculosis in the Immunocompromised Host, March 2020
9. IAP-PHO Lecture Series Malignant Bone Tumours, August 2020
10. Recorded on 11th for dIAP Online Teaching Platform Digital IAP Lecture Series Acute Leukaemia, August 2020
11. Rotary International online meeting on 24th Life Beyond Cancer, September 2020
12. Infection prevention and control: the key to better outcomes in cancer care-Talk for St. Jude Cancer Care India staff, October 2020

Dr Reghu KS

13. Panelist at IAP PHO Teaching Series Malignant Bone tumors, August 2020
14. Speaker, Management of GvHD in 2020 BMT update, Virtual Conference, June 2020
15. Panelist, West Bengal IAP conference HURDLES IN HEMATOLOGY OFFICE PRACTICE, August 2020
16. Panelist, BeshCon 2020 Challenges of blood transfusion in clinical practice, Feb 2020
17. Speaker and Moderator, IAP Cochin, Paediatric Potpourri Series Long term follow up in Paedaitric ALL-Paediatric ALL virtual symposium, July 2020

AWARDS & FELLOWSHIPS

Dr Partha Sarathi Bhattacharya

1. Awarded a scholarship by St. Jude Global Academy in Pediatric Onco-Critical Care (GA-POCC) to attend the Symposium (Virtual Symposium)., March 2020
2. Pediatric Oncology Critical Care Symposium (POCCS 2020), St. Jude April 2-3, 2020. Awarded a scholarship by St. Jude Global Academy in Pediatric Onco-Critical Care (GA-POCC) to attend the Symposium (Virtual Symposium).
3. Awarded a scholarship by St. Jude Global Academy in Pediatric Onco-Critical Care (GA-POCC) to attend the Congress and the Workshops on Ultrasound (USG) and CRRT at 10th World Congress of the World Federation of Pediatric Intensive & Critical Care Societies (WFPICCS 2020). 14-17 June. Mexico City. Virtual Congress.

ORCID ACCOUNT

1. Prof. Dr Vaskar Saha (0000-0002-2916-9649)
2. Dr Shekhar Krishnan (0000-0002-6769-3847)

DEPARTMENT OF PLASTIC AND RECONSTRUCTIVE MICROSURGERY

Dr Gautam Biswas

MBBS, MS, MCh, Dip NB, Head of Department & Senior Consultant

Dr Karnav Panchal

MBBS, MS, DNB, Junior Consultant

RESEARCH PROJECTS

1. Speech outcomes in tongue reconstruction by free flaps. (PI, Dr Rajeev Sharan).
2. Free Thyroid Lobe Transfer for prevention of Radiation Induced Hypothyroidism in patients of Oral Carcinoma: A phase I/II). (PI, Dr Kapila Manikantan).
3. Opioid Sparing Effect of Low Dose Ketamine for Peri Operative Analgesia in Free Flap Reconstruction of Head and Neck Defects: A Randomised Control Trial. (PI, Dr. Rakhi Mittal).

RESEARCH PUBLICATIONS

1. **Biswas G**. Mid Face Reconstruction: Planning and Outcome. *Indian J PlastSurg*. 2020; 53(03): 324-334
2. **Biswas G, Panchal KB, Jain PV, Manikantan K, Sharan R, Arun P.**Fabricating Flap is Forearm prior to Tracheal Reconstruction. *Indian J PlastSurg*; November 2020.
3. **Ganguly S,Biswas B,Biswas G.**Early experience with dabrafenib-trametinib combination in patients with BRAF mutated malignant melanoma- a single centre experience. 2020.

EXTERNAL ACADEMIC MEETINGS

1. Intra and perioperative decision making in DIEP flap salvage
2. Breast Reconstruction and aesthetic Surgery Conference –BRASCON VADADORA – January, 2020
3. Reconstruction in complicated post irradiated cases
4. Tongue reconstruction –changing concepts.
5. Planning of double paddle Fibular Free flap.
6. Perforator based free flaps in Head and Neck reconstruction- Onco recon 2020 1-2 Feb Jaipur

Invited WEBINARS-due to COVID PANDAMIC

Dr. Gautam Biswas

1. APLAST WEBINAR Facial Palsy Reconstruction May 2020 Organised by Amrita Institute of MedicalSciences
2. Indian Society for Reconstructive Microsurgery Principals of Mid Face Reconstruction, July 2020.
3. Indian Society for Reconstructive Microsurgery My approach to acute Foot Trauma, Sep 2020. Indian Society for Reconstructive Microsurgery Nuances in Penile Reconstruction, August 2020
4. Indian Society for Reconstructive Microsurgery Facial Resurfacing, Nov2020

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DEPARTMENT OF RADIATION ONCOLOGY

Dr Sanjoy Chatterjee

MRCP (Lond), FRCP (Edin), FRCR (UK), PGCE (Dundee), CCT (Clin Onc), Senior Consultant

Dr Rimpa Basu Achari

MD, DNB, Senior Consultant

Dr Indranil Mallick

MD, DNB, Senior Consultant

Dr Santam Chakraborty

M.D., Senior Consultant

Dr Tapesh Bhattacharyya

M.D., DNB, Junior Consultant

Dr Moses Arunsingh S

MD, FRCR (UK), PGCE (Dundee), Junior Consultant

RESEARCH PROJECTS

1. Intensifying Radiation Treatment in Advanced/ Poor Prognosis Laryngeal, Hypopharyngeal and Oropharyngeal Cancers Using Pet –CT Based Dose Escalation Strategies. Phase III Randomised Trial. (PI, Dr. Sanjoy Chatterjee).
2. Comprehensive Digital Archive of Cancer Imaging - Radiation Oncology. (Dr. Jayanta Mukhopadhyay; Dr. Sanjoy Chatterjee; Dr. Indranil Mallick; Dr. Rimpa Achari; Dr. Santam Chakraboty). Image Bank Development.
3. Hypofractionated Radiation Therapy Comparing a Standard Radiotherapy Schedule (Over Three Weeks) With A Novel One Week Schedule in Adjuvant Breast Cancer: An Open-Label Randomised Controlled Study. Phase III Randomised Trial. (PI, Dr. Sanjoy Chatterjee).
4. Hypo-fractionated Radiotherapy Schedule of 26 Gy in 5 Fractions with Simultaneous Integrated Boost (6 Gy) In Advanced Incurable Breast Cancer: A Prospective Phase I/Ii Study. (PI, Dr. Sanjoy Chatterjee).
5. Prospective Evaluation of the Involved Side Versus Involved Node Target Volume Parameters for Deep Inspiration Breath Hold Mediastinal Radiation Therapy for Hodgkin's Lymphoma. Non-Drug Trial. (PI, Dr. Rimpa Achari).
6. A Phase III, Double-Blind, Placebo-controlled, Randomized Trial Assessing the Effects of Aspirin On Disease Recurrence and Survival After Primary Therapy in Common Non-Metastatic

Solid Tumours. Phase III Randomised Trial. (PI, Dr. Indranil Mallick).

7. A Phase III, Open-label, Multicenter, Randomized Study to Investigate the Efficacy and Safety of Atezolizumab Compared with Chemotherapy in Patients with Treatment-naïve Advanced or Recurrent (Stage Iiib Not Amenable for Multimodality Treatment) Or Metastatic (Stage Iv) Non-small Cell Lung Cancer Who Are Deemed Unsuitable for Platinum-containing Therapy. Phase III Randomised Trial. (PI, Dr. Moses Arunsingh).
8. A Phase III, Multicenter, Randomised, Double-blind, Placebo-controlled Study of Atezolizumab (Anti–PD-L1 Antibody) In Combination with Paclitaxel Compared with Placebo with Paclitaxel for Patients with Previously Untreated Inoperable Locally Advanced or Metastatic Triple-Negative Breast Cancer. Phase III Randomised Trial. (PI, Dr. Sanjoy Chaterjee).
9. An Open-label, Multicenter, Phase IIIb Study to Assess the Safety and Efficacy of Ribociclib (Lee011) In Combination with Letrozole for The Treatment of Men and Pre/Postmenopausal Women with Hormone Receptor-positive (Hr+) Her2-negative (Her2-) Advanced Breast Cancer (Abc) With No Prior Hormonal Therapy for Advanced Disease". Phase III Randomised Trial. (PI, Dr. Sanjoy Chatterjee).
10. Predicting Treatment Response of Lung Cancers Following Curative Chemo-radiation Using Serial Image Analysis. Radiomics Study. (Dr. Moses Arunsingh; Dr. Santam Chakraborty; Dr. Soumendranath Ray).
11. A Phase II, Multicenter, Open-label, Two-cohort, Non-comparative Study to Assess the Efficacy and Safety of Alpelisib Plus Fulvestrant or Letrozole in Patients with Pik3ca Mutant, Hormone Receptor (Hr) Positive, Her2 – Negative Advanced Breast Cancer (Abc), Who Have Progressed On or After Cdk 4/6 Inhibitor Treatment. Phase II Non Randomised Drug Trial. (PI, Dr. Sanjoy Chatterjee).
12. Ablative Therapy for Oligometastatic Cancers (Target) - A Prospective Data Registry. Prospective Observational Registry study. (PI, Dr. Moses Arunsingh S).
13. Phase II Study to Evaluate Toxicity and Clinical Outcomes of Definitive Helical Tomotherapy for Primarily Unresected Carcinoma Cervix Using Fluoro-deoxy Glucose Positron Emission Tomography Based Radiotherapy Planning. Phase II Department of Biotechnology (DBT) PET Study. (PI, Dr. Rimpa Achari).

14. A Phase III Randomised, Double-blind, Parallel Group, Multicentre Study to Compare the Efficacy, Safety, Pharmacokinetics and Immunogenicity Between SB3 (Proposed Trastuzumab Biosimilar) And Herceptin® In Women with Newly Diagnosed Her2 Positive Early or Locally Advanced Breast Cancer in Neoadjuvant Setting. Phase III Randomised Trial Drug Trial. (PI, Dr. Sanjoy Chatterjee).
15. Randomised Controlled Trial of Prostate Radiotherapy in High Risk and Node-Positive Disease Comparing Moderate and Extreme Hypofractionation. Phase III Randomised Radiotherapy Trial. (PI, Dr. Indranil Mallick).
16. Predictive Dashboards for Treatment Plan Evaluation and Prediction in Radiation Oncology. Technology Development. (PI, Dr. Indranil Mallick).
17. Parotid Sparing Adaptive Radiotherapy in Head and Neck Cancer Patients –A Study Evaluating the Resource Intensiveness and Impact On Quality of Life Dr. Phase II single-arm Interventional study. (PI, Moses Arunsingh S).
18. Radiomics as a tool for predicting outcomes in high-grade gliomas. Radiomics study. (PI, Dr. Rimpa Achari).
19. Conversational User Interface for Patient Communication in Oncology. Technology Development. (PI, Dr. Indranil Mallick).
20. A Long-term Follow-up Study for Cardiac Safety in the Patients with HER2 Positive Early or Locally Advanced Breast Cancer Who Have Completed the SB3-G31-BC. Observational Study. (PI, Dr. Sanjoy Chatterjee).
21. A prospective, multicenter, randomized, double-blind, parallel-group study to compare the efficacy and safety of biosimilar cetuximab versus innovator cetuximab in combination with platinum-based chemotherapy in patients with recurrent locoregional or metastatic squamous cell carcinoma of the head and neck (SCCHN) Phase III Randomised Trial Drug Trial. (PI, Dr. Sanjoy Chatterjee).
22. A Phase III, Double-Blind, Placebo-Controlled, Randomized study of Ipatasertib in combination with Atezolizumab and Paclitaxel as a treatment for patients with Locally Advanced Unresectable or Metastatic Triple-Negative Breast Cancer. Phase III Randomised Trial Drug Trial. (PI, Dr. Sanjoy Chatterjee).
23. A prospective, multicenter, randomized, double-blind, Phase III

study to compare the efficacy and safety of Biosimilar ENZ137 of Enzene Biosciences Ltd. versus Innovator Bevacizumab both in Combination with CAPEOX in Patients with Metastatic Colorectal Cancer. Phase III Randomised Trial Drug Trial. (PI, Dr. Moses Arunsingh S).

24. Identifying and potentially mitigating biologic and treatment-related disparities in head and neck squamous cell carcinoma (HNSCC) in India (with the University of Pittsburgh, for an NIH Supplementary Grant award). (PI, Dr. Indranil Mallick).

RESEARCH PUBLICATIONS

1. **Mallick I, Chakraborty S, Baral S, Saha S, Lal VH, Sasidharan R, Santosham RJM, Chhatbar S, Bhusal S, Goyal L, Maulik S, Phesao V, Arora S, Bhattacharyya T, Mahata A, Prasath S, Balakrishnan A, Mandal S, Arunsingh MA, Achari R, Chatterjee S**. Prioritizing Delivery of Cancer Treatment During a COVID-19 Lockdown: The Experience of a Clinical Oncology Service in India. JCO Glob Oncol. 2021 Jan; 7:99-107. doi: 10.1200/GO.20.00433. PMID: 33449800.
2. **Chatterjee S, Mallick I, Chakraborty S, Prasath S, Arunsingh M, Achari RB, et al.** Helical Radiotherapy in Early Laryngeal Cancers Could Lead to Excess Local Recurrence: Lessons from a Phase II Prospective Study. Clin Oncol. 2019 Nov 5;32(2): e67–75.
3. **Kundu S, Chakraborty S, Chatterjee S, Das S, Achari RB, Mukhopadhyay J, et al**. De-Identification of Radiomics Data Retaining Longitudinal Temporal Information. J Med Syst. 2020 Apr 2;44(5):99.
4. **Chatterjee S, Backianathan S, Lal P, Gupta S, Chakraborty S.** Can the FAST-Forward Trial Results be Generalised Across all Breast Cancer Patients? Clin Oncol. 2020 Sep 29. http://dx.doi.org/10.1016/j.clon.2020.09.006
5. **Chatterjee S, Chakraborty S.** Trials. Hypofractionated radiation therapy comparing a standard radiotherapy schedule (over 3 weeks) with a novel 1-week schedule in adjuvant breast cancer: an open-label randomized controlled study (HYPORT-Adjuvant)—study protocol for a multicentre, randomized phase III trial. 2020 Sep 30;21(1):819.
6. **Ghosh S, Maulik S, Chatterjee S, Mallick I, Chakravorty N, Mukherjee J**. Prediction of survival outcome based on clinical features and pre-treatment 18FDG-PET/CT for HNSCC patients.

Comput Methods Programs Biomed. 2020 Oct; 195:105669.

7. **Tewary S, Arun I, Ahmed R, Chatterjee S, Mukhopadhyay S.** AutoIHC-Analyzer: computer-assisted microscopy for automated membrane extraction/scoring in HER2 molecular markers. J Microsc. 2020 Aug 17. http://dx.doi.org/10.1111/jmi.12955
8. **Saha M, Arun I, Ahmed R, Chatterjee S, Chakraborty C**. HscoreNet: A Deep network for estrogen and progesterone scoring using breast IHC images *Pattern Recognit*. 2020 Jun 1; 102:107200.
9. **Coles CE, Aristei C, Bliss J, Boersma L, Brunt AM, Chatterjee S, et al.** International Guidelines on Radiation Therapy for Breast Cancer During the COVID-19 Pandemic. *Clin Oncol*. 2020 May;32(5):279–81.
10. **Jain PV, Sharan R, Manikantan K, Clark GM, Chatterjee S, Mallick I, et al.** Redefining adequate margins in oral squamous cell carcinoma: outcomes from close and positive margins. *Eur Arch Otorhinolaryngol*. 2020 Apr;277(4):1155–65.
11. **Mallick I, Arunsingh M, Chakraborty S, Arun B, Prasath S, Roy P, et al.** A Phase I/II Study of Stereotactic Hypofractionated Once-weekly Radiation Therapy (SHORT) for Prostate Cancer. *Clin Oncol.* 2020 Feb;32(2): e39–45.
12. **Das A, Arunsingh M, Bhattacharyya T, Prasath SS, Balakrishnan A, Mallick I.** Intensity modulated radiotherapy in anal canal squamous cell carcinoma: Implementation and outcomes. 2020. https://www.cancerjournal.net/preprintarticle.asp?id=298862
13. **Iyizoba-Ebozue Z, Murray LJ, Arunsingh M, Vaidyanathan S, Scarsbrook AF, Prestwich RJD**. Incidence and patterns of retropharyngeal lymph node involvement in oropharyngeal carcinoma. Radiother Oncol. 2020 Jan; 142:92–9.
14. **Prestwich RJD, Arunsingh M, Zhong J, Dyker KE, Vaidyanathan S, Scarsbrook AF.** Second-look PET-CT following an initial incomplete PET-CT response to (chemo)radiotherapy for head and neck squamous cell carcinoma. Eur Radiol. 2020 Feb;30(2):1212–20.
15. **Parekh D, Kukreja P, Mallick I, Roy P**. Worst pattern of invasion – type 4 (WPOI-4) and Lymphocyte host response should be mandatory reporting criteria for oral cavity squamous cell carcinoma: A re-look at the American Joint Committee of Cancer (AJCC) minimum dataset. *Indian J Pathol Microbiol*. 2020 Oct;63(4):527–33.

16. **Murthy V, Mallick I, Gavarraju A, Sinha S, Krishnatry R, Telkhade T, et al**. Study protocol of a randomised controlled trial of prostate radiotherapy in high-risk and node-positive disease comparing moderate and extreme hypofractionation (PRIME TRIAL). *BMJ Open*. 2020 Feb 28;10(2): e034623.
17. **Das J, Ray S, Tapadia R, Midha D, Mallick I.** Prostate-specific Membrane Antigen-expressing Hepatic Lesion: Metastatic or Hepatocellular Carcinoma. *Indian J Nucl Med*. 2020 Jan;35(1):58–60.
18. *Hagiwara Y, Yamada S, Isozaki Y, Takiyama H, Shinoto M, Kawashiro S, et al*. Efficacy and feasibility of re-irradiation using carbon ions for pancreatic cancer that recurs after carbon-ion radiotherapy. *Clinical and Translational Radiation Oncology*. 2021 Jan 1; 26:24–9.
19. **Hagiwara Y, Bhattacharyya T, Matsufuji N, Isozaki Y, Takiyama H, Nemoto K, et al**. Influence of dose-averaged linear energy transfer on tumour control after carbon-ion radiation therapy for pancreatic cancer. *Clin Transl Radiat Oncol*. 2020 Mar; 21:19–24.
20. **Bhattacharyya T, Koto M, Ikawa H, Hayashi K, Hagiwara Y, Tsuji H.** Assessment of risk factors associated with development of oronasal fistula as a late complication after carbon-ion radiotherapy for head and neck cancer. *Radiother Oncol*. 2020 Mar; 144:53–8.
21. **Isozaki Y, Takiyama H, Bhattacharyya T, Ebner D, Kasuya G, Makishima H, et al**. Heavy charged particles for gastrointestinal cancers*. J Gastrointest Oncol*. 2020 Feb;11(1):203–11.
22. **Hagiwara Y, Koto M, Bhattacharyya T, Hayashi K, Ikawa H, Nemoto K, et al**. Long-term outcomes and toxicities of carbon-ion radiotherapy in malignant tumors of the sphenoid sinus. *Head Neck*. 2020 Jan;42(1):50–8.
23. **Mallick I, Achari RB, Chakarborty S, Bhattacharyya T, Sundersingh Rajapand MA, Chatterjee S.** Design and Prospective Assessment of a Free Online Course on Radiological Anatomy for Target Volume Delineation. *Int J Radiat Oncol Biol Phys*. 2020 Nov 1;108(3): S124.
24. **De Laurentiis M, Borstnar S, Campone M, Warner E, Salvador Bofill J, Jacot W, et al.** Updated results from the phase IIIb complement-1 study of ribociclib (RIB) plus letrozole (LET) in the treatment of HR+, HER2-advanced breast cancer (ABC). *J Clin Orthod.* 2020 May 20;38(15_suppl):1055–1055.

25. **Mallick I, Paul S, Chakraborty S**. Stress and Burnout among Radiation Oncologists in India. *Int J Radiat Oncol Biol Phys*. 2020 Nov 1;108(3): e412.
26. **Sinha S, Laskar SG, Agarwal JP, Juvekar S, Murthy V**. Impact of pre-treatment imaging on outcomes of organ conservation in laryngopharyngeal cancers. 2020 Sep 17. https://www.researchgate.net/publication/344287407_Impact_of_pre-treatment_imaging_on_outcomes_of_organ_conservation_in_laryngopharyngeal_cancers
27. **Chakraborty S, Mallick I, Bhattacharyya T, Moses A, Basu Achari R, Chatterjee S**. Development and user experience testing of an electronic system for routine collection and use of electronic patientreported outcome measures. *International Society for Quality of Life Research*. 2020; p. S111–2.
28. **Sanosham R, Chatterjee S, Chakraborty S, Mahata A, Mandal S, Das A, Kumari A, Ray S, Ahmed R.** Hypofractionted radiotherapy with SIB in advanced incurable breast cancer - HYPORT B Study. Published Abstract.
29. **Maulik S, Arunsingh M, Prasath S, Arun B, Achari R, Chakraborty S, Chatterjee S, Mallick I**. Long term outcomes and predictors of relapse and toxicities after moderately hypofractionated radiotherapy for high-risk localized prostate cancer. Published Abstract.
30. **Mallick I, Saha S, Arunsingh M, Sarkar A, Guha D, Achari R.** Predicting Doses to organs at risk in prostate cancer intensity-modulated radiotherapy Published Abstract.
31. **Mallick I, Arunsingh M, Lal VH, Bhattacharya T, Chatterjee S, Chakraborty S, Achari R.** Predicting response to neoadjuvant chemoradiation in esophageal cancer using CT radiomic features. Published Abstract.
32. **Bhusal S, Chatterjee S, Chakraborty S, Kumari A, Bachianathtan S, Mahata A, Lal P, Gupta S, Solomon P, Das K.J Maria, Mandal S.** Dosimetric analysis of simultaneous integrated boost in the HYPORT Adjuvant Trial. Published Abstract.
33. **S. Chatterjee, M. Md Yusuf, T. Dejthevaporn, W-P. Chung, C.G. Galvez, P. Sunpaweravong6, A. Cheng, Abesamis-Tiambeng, S.O.Y. Michelle, L. Menon-Singh, J. Wu, K. Zhou, H. Azim.** Ribociclib (RIB) + letrozole (LET) in Asian patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor-2enegative (HER2L) advanced breast cancer (ABC):

Subgroup analysis of the phase IIIb CompLEEment-1 trial. *Annals of Oncology*. 2020; 31 (suppl_6): S1257-S1269. 10.1016/annonc/annonc353

34. **Mallick I, Achari RB, Arunsingh M.** The Bethesda Handbook of Clinical Oncology, South Asia Edition Contributions. *The Bethesda Handbook of Clinical Oncology*. South Asia Edition, Wolters Kluwer India Pvt. Ltd., 2020.
35. **Chakraborty S, Wadasadawala T, Ahmed R, Coles C, Chatterjee S.** Breast Cancer Demographics, Types and Management Pathways: Can Western Algorithms Be Optimally used in Eastern Countries? *Clin Oncol*. 2019 Aug;31(8):502-509. doi: 10.1016/j.clon.2019.05.024

ACADEMIC MEETINGS

1. FRCR Clinical Oncology Part 1 Course. (January 2020)
2. 11th Varian Advanced Imaging school (February 2020)
3. 12th Varian Advanced Imaging school (October 2020)
4. 13th Varian Advanced Imaging school (December 2020)
5. FRCR Clinical Oncology Part 2A Course (December 2020)
6. AVARO - Applied Virtual Anatomy for Radiation Oncology (Ongoing course - Started in 2018)
7. IGRT Online (Ongoing Course - Started in 2014)
8. Acute Oncology e-learning module for the Royal College of Radiology (Ongoing Course - Started in 2019)

AWARDS & FELLOWSHIPS

1. Dr Indranil Mallick - Grant received for project - Identifying and potentially mitigating biologic and treatment-related disparities in head and neck squamous cell carcinoma (HNSCC) in India (with the University of Pittsburgh, for an NIH Supplementary Grant award)
2. Dr Subecha Bhusal - Selected for the post of Clinical Fellow Oncology at Royal Marsden Hospital, London, United Kingdom
3. Dr Moses Arunsingh - Awarded “Best Use of Data/Evidence” and “The Sharpest Tongue” awards in the debate competition on EGFR mutated lung cancers at the Excellence in

Healthcare Communications (ECHO), 2020 conference organised by Pfizer

4. Dr Sanjoy Chatterjee - Competitive Research Grant for HYPORT Adjuvant study, Body: Women's Cancer Initiative and NAG foundation

ORCID ACCOUNT

1. Sanjoy Chatterjee (https://orcid.org/0000-0001-7402-8645)
2. Rimpa Basu Achari (https://orcid.org/0000-0002-1709-255X)
3. Indranil Mallick (https://orcid.org/0000-0002-5567-9204)
4. Santam Chakraborty (https://orcid.org/0000-0003-3580-5979)
5. Tapesh Bhattacharyya (https://orcid.org/0000-0002-3714-1195)
6. Moses Arunsingh S (https://orcid.org/0000-0002-4003-3259)
7. Sriram Prasath (https://orcid.org/0000-0001-5367-1543)
8. B Arun (https://orcid.org/0000-0002-1464-4507)
9. Anurupa Mahata (https://orcid.org/0000-0003-1127-312X)

DEPARTMENT OF RADIOLOGY AND IMAGING

Dr Saugata Sen
MD, Senior Consultant

Dr. Argha Chatterjee
MD, PDCC, Junior Consultant

Dr. Aditi Chandra
MD, Senior Consultant

Dr. Priya Ghosh
MD, FRCR, Junior Consultant

Dr. Sumit Mukhopadhyay
MD, Senior Consultant

Dr. Bharat Gupta
MD, DNB, Junior Consultant

Dr. Dayananda Lingegowda
DNB, PDCC, Senior Consultant

Dr Anisha Gehani
MD, Junior Consultant

RESEARCH PROJECTS

1. SODIUM Study. (PI, Dr. Dr. Dayananda Lingegowda)
2. Integrated Cervical Cancer Prevention & Treatment Stratification Study: Systems Medicine Cluster Approach. (PI, Dr. Dr. Mammen Chandy)

RESEARCH PUBLICATIONS

1. **Chatterjee A, Biswas B, Gehani A, Sen S**. Pembrolizumab-induced large duct cholangiopathy: Diagnosis and follow up imaging. *J Postgrad Med*. 2021; 67(1):43-45.
2. **Chatterjee A, Dutt TS, Ghosh P, Mukhopadhyay S, Chandra A, Sen S.** Inflammatory lesions mimicking chest malignancy: CT, bronchoscopy, EBUS, and PET evaluation from an oncology referral centre. *Curr Probl Diagn Radiol*. 2021; S0363-0188 (21) 00024-4.
3. **Khoda J, Sen S, Chatterjee A**. Incidental detection of Zinner syndrome in a patient with nonseminomatous germ cell tumor of testis. *Urol Annal*. 2020; 12(4):394.
4. **Chatterjee A, Ramanan RV, Mukhopadhyay S**. Imaging Postoperative Abdominal Hernias: A Review with a Clinical Perspective. *JGAR*. 2020; 3(S 01): S35-S48

5. **Dey M, Das S, Chatterjee A, Dutta A, Ghosh R, Dasgupta J**. Yield and Safety of Transjugular Versus Percutaneous Liver Biopsies in Suspected Cases of Diffuse Liver Disease and Correlation of Yield of Transjugular Liver Biopsy with Hepatic Venous Pressure Gradient. *JGAR*. 2020.
DOI: 10.1055/s-0040-1716605
6. **Chatterjee A, Biswas B, Gehani A, Das J, Sen S, Mukhopadhyay S, Chandra A, Ghosh P, Gupta Bharat, Lingegowda D.** Oncoradiology preparedness in the COVID-19 pandemic: Perspective from a tertiary oncology referral center from Eastern India. *IJMPO*. 2020; 20(6).
DOI: 10.4103/ijmpo.ijmpo_240_20
7. **Venkataramanan RV, Chatterjee A**. Medical Journalism at the Time of the COVID-19 Pandemic*. JGAR*. 2020; 3(2):115.
8. **Dayananda L, Gehani A, Mukhopadhyay S, Midha D, Banerjee S, Bharat Gupta.** Intraductal Papillary Neoplasm of the Bile Ducts: Case Reports with Review of the Literature**.** *JGAR*. 2020.
DOI: 10.1055/s-0040-1715777
9. **Srinivasan S, Chatterjee A**. Recent Advances in Pancreatic MR Imaging: A Guide on How, When, and Why to Perform. *JGAR*. 2020 3(1):2-13.
10. **Maru P, Roy B, Sen S, Chatterjee A**. Lymph Node Mapping in Gastric Carcinoma. *JGAR*. 2021.
11. **Prasad N, Sen S.** Gall bladder carcinoma: the facts and the mimics**.** *Egyptian Journal of Radiology and Nuclear Medicine*. 2021. 52 (1), 1-9.
12. **Biswas B, Dabkara D, Sengupta M, Ganguly S, Ghosh J, Moses Arunsingh S, Sen S**. Multimodality treatment outcome in patients with primary malignant mediastinal germ cell tumor in adults. *Cancer Reports*. 2021;4: e1306
13. **Ghosh J, Ganguly S, Dabkara D, Biswas B, Chatterjee A, Mukhopadhyay S, Banerjee S, Sen S, Arun I.** Pancreatic adenocarcinoma with primary tumor calcification and calcified liver metastasis: Report of a rare case and review of literature. *IJMPO*. 2020; 41(5):738.
14. **Lingegowda D, Gehani A, Sen S, Mukhopadhyay S, Ghosh P.** Centrally inserted tunnelled peripherally inserted central catheter: Off-label use for venous access in oncology patients. *J Vasc Acc*. 2020;21(5):773-777
15. **Arya S, Sen S, Engineer R, Saklani A, Pandey T**. Imaging and Management of Rectal Cancer. *Semin Ultrasound CT MR*. 2020; 41(2): 183-206
16. **Chatterjee S, Mallick I, Chakraborty S, Prasath S, Arunsingh M, Achari RB,**

Arun B, Nallathambi C, Pattatheyil A, Sen S. Helical Radiotherapy in Early Laryngeal Cancers Could Lead to Excess Local Recurrence: Lessons from a Phase II Prospective Study. *Clin Oncol*. 2020; 32(2): e67-e75.

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18. **Basu A, Chatterjee M, Dabkara D, Biswas B, Ganguly S, Ghosh J, Ghosh P**. Adrenal metastasis in an older patient with seminoma. *Canc Res Ther Treat*. 2020; 3(4): 836-837.
19. **Ganguly S, Alphones S, Ghosh P, Midha D, Ghosh J, Biswas B**. Rectal cancer with breast metastasis: A case report with review of literature. *Canc Res Ther Treat*. 2020; 3(3): 627-629.
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21. **Colak E et al**. The RSNA Pulmonary Embolism CT (RSPECT) Dataset. *Radiology: Artificial Intelligence.* 2021. https://doi.org/10.1148/ryai.2021200254

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4. Dr. Argha Chatterjee (0000-0001-5570-2737)
5. Dr. Anisha Gehani (0000-0002-7395-0766)

DEPARTMENT OF TRANSFUSION MEDICINE

Dr Sabita Biswas

MBBS.MD (Pathology), Senior Consultant

Dr Suvro Sankha Datta

MBBS.MD (Immunohematology & Blood Transfusion), Junior Consultant

OVERVIEW OF RESEARCH

The main focus of research in 2020 was to establish a platelet serology laboratory at Tata Medical Center, Kolkata for those patients who have refractoriness to platelet transfusion. The laboratory started functioning in April 2020, and underwent validation at multiple steps during the next three months. Platelet antibody screening and platelet cross-matching by SPRCA technique have been started since August'2020. Over the next 3 months, a novel diagnostic algorithm was developed for HSCT patients prior to initiation of the transplant. Platelet antibody screening followed by cross-matching is done in multi-transfused patients with anticipated platelet refractoriness. This helps to identify, potential plateletpheresis donors who would be cross match compatible with the patient. All future apheresis platelet transfusions are then from cross match compatible donors.

At present we are in the process of validating platelet cross-matching for across the ABO group platelets.

RESEARCH PROJECTS

1. Importance of type and screen policy in blood bank- an Indian Perspective. (Investigator initiated, PI, Dr. Suvro Sankha Datta)
2. Serology and sociology of individuals with SARS-CoV-2 infection: a study of IgG serology in patients, staff and blood donors in an oncology center in eastern India along with an assessment of KAP (Knowledge Attitude and Practice) in blood donors and staff (Investigator initiated, Co-PI: Dr. Sabita Biswas CI: Dr. Suvro Sankha Datta)

RESEARCH PUBLICATIONS

1. **Dogra K, Kaur G, Basu S, Chawla D.** Fresh Frozen Plasma and Platelet Transfusion Practices in Neonatal Intensive Care Unit of a Tertiary Care Hospital. *Indian J Hematology and Bl Transf*. 2020; 36:141-148
2. **Javed R, Radhakrishnan V, Basu S, Chandy M.** Challenges in transfusion

and the role of Thalidomide in E-β-Thalassemia—A case report. *Clin Case Rep*. 2020; 00:1–3. https://doi. Org/10.1002/ccr3.3141

3. **S.S. Datta, S. Basu, M. Reddy, K. Gupta, and S. Sinha.** Comparative evaluation of the conventional tube test and column agglutination technology for ABO antibody titration in healthy individuals: a report from India. *IMMUNOHEMATOLOGY*. Volume 37, Number 1, 2021
4. **Datta SS, Basu, Ghara N, Kole P, Khemka P**. Utility of platelet cross-matching in a case of neonatal alloimmune thrombocytopenia associated with a de novo MECOM variant. Blood Research 2021; 56(1): 1-3
5. **Datta SS, Basu S.** Randomization amid a pandemic - a critical appraisal regarding convalescent plasma therapy clinical trials for COVID-19 patients. Letter to Editor. *ISBT Science Series*. 2020; 15: 417-18. doi: 10.1111/VOXS.12564
6. **Datta SS, Basu S, Reddy M, Gupta K, Sinha S.** Comparative evaluation of the conventional tube technique and column agglutination technique for ABO antibody titration in healthy individuals - a report from India. 2020.
7. **Datta SS, Basu S, Ghara N, Kole P, Khemka P**. Utility of platelet cross-matching in a case of neonatal alloimmune thrombocytopenia associated with a de novo MECOM variant. Letter to Editor In-Press. 2020.
8. **Dogra K, Kaur G, Basu S, Chawla D**. Fresh Frozen Plasma and Platelet Transfusion Practices in Neonatal Intensive Care Unit of a Tertiary Care Hospital. *Indian J Hematology and Bl Transf*. 2020; 36:141-148
9. **Javed R, Radhakrishnan V, Basu S, Chandy M**. Challenges in transfusion and the role of Thalidomide in E-β-Thalassemia—A case report. *Clin Case Rep*. 2020; 00:1–3. https://doi. Org/10.1002/ccr3.3141
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11. **Datta SS, Basu S, Ghara N, Kole P, Khemka P**. Utility of platelet cross-matching in a case of neonatal alloimmune thrombocytopenia associated with a de novo MECOM variant. *Blood Research.* 2021; 56(1): 1-3.

BOOK CHAPTERS

Dr. Sabita Biswas

1. Basu S., Basu D., Ghara N. (2020) Blood Product Support in HSCT. In: Chandy M., Radhakrishnan V., Sukumaran R. (eds) Contemporary Bone Marrow Transplantation. Organ and Tissue Transplantation. Springer, Cham

   Publisher Name Springer, Cham
   Online ISBN 978-3-319-64938-2
   eBook Packages Medicine Reference Module Medicine
   DOI https://doi.org/10.1007/978-3-319-64938-2_8-1

EXTERNAL ACADEMIC MEETINGS

1. Haematocon'2020 Evaluating Three Methods for Enumeration of Residual WBCs in Single Donor Apheresis Platelets: A Pilot Study from Eastern India as a Part of Blood Components Quality Monitoring Process. Nasir N. Naikoo, Deepak K. Mishra, Sabita Basu, Suvro S. Datta. Indian J Hematol Blood Transfus (Nov 2020) 36(Suppl 1): S228. November'2020 E-Poster
2. Haematocon'2020 Buffy Coat Derived Granulocyte Transfusions during Intensive Chemotherapy of AML. Jay Y. Sheth, Arijit Nag, Suvro S. Datta, Jeevan Kumar, Mayur Parihar, Vivek Radhakrishnan, Sabita Basu, Deepak K. Mishra, Reena Nair, Saurabh J. Bhave, Mammen Chandy. Indian J Hematol Blood Transfus (Nov 2020) 36(Suppl 1): S25. November'2020 E-Poster
3. Appointed by DG ICMR, Member of Scientific Advisory Committee to review progress of the Project on National Rare Donor Registry.
4. Panelist for webinar on: Use of Convalescent Plasma in COVID-19 treatment - Overview & Way forward. Held on Tuesday, June 23, 2020, 5:10 pm. Organised by Dr. Cheirmaraj, National Manager, Ortho Clinical Diagnostics. Recording available at: https://orthoclinicaldx.webex.com/orthoclinicaldx/ldr.php?RCID=8ec794ff3984390155273574a8282b72
5. Faculty for National Workshop on recent advances on Blood Transfusion Services with special emphasis on GSR 166(E), held on 6th March 2021, The Astor, Kolkata

AWARDS & FELLOWSHIPS

1. Dr. Suvro Sankha Datta selected as a reviewer of following journals:

- Transfusion and Apheresis Science
- Journal of Translational Medicine

- Global Journal of Transfusion Medicine
- Journal of Blood Medicine
- Therapeutic Apheresis and Dialysis
- Future Rare diseases

2. Dr. Suvro Sankha Datta Selected as a member of special interest group of Immunohematology under Indian Society of Transfusion Medicine (SIG-ISTM).

3. Dr. Sabita Biswas, Reviewer for the following Journals –

- Indian Journal of Medical Research
- Global Journal of Transfusion Medicine
- Asian Journal of Transfusion Science

1. Dr. Sabita, Biswas Member National Advisory Board - Asian Journal of Transfusion Science

ORCID ACCOUNT

1. Dr. Suvro Sankha Datta (0000-0003-2094-6429)

DEPARTMENT OF URO-ONCOLOGY

Dr Sujoy Gupta

MBBS, MS (General Surgery), FRCS(England), FRCS(Edinburgh), FRCS(Urology), Senior Consultant

Dr Gaurav Aggarwal

MBBS, MS (General Surgery), FAGE, FELLOWSHIP (Surgical Oncology), DNB(Urology), Associate Consultant

Satyadip Mukherjee

MBBS, MS, MCh (Urology), Consultant

Dr Tarun Jindal

MBBS, MSS, MCh, Associate Consultant

RESEARCH PUBLICATIONS

1. **Aggarwal G, Gupta S**- as a part of the COVID Surg Collaborative. Elective Cancer Surgery in COVID-19–Free Surgical Pathways During the SARS-CoV-2 Pandemic: An International, Multicenter, Comparative Cohort Study. *Journal of Clinical Oncol*. 2020. https://doi.org/10.1200/JCO.20.01933 1
2. **Raleng M, Aggarwal G, Gupta S**. Lymphoepithelioma like Carcinoma of the Bladder – "A Case" Revisited. *Int J Immunother Cancer Res*. 2020; 6(1): 019-021.
   DOI: https://dx.doi.org/10.17352/2455-8591.000025
3. **Das S, Aggarwal G, Gupta S**. Para-stomal variceal bleed, 9 years' post-radical cystectomy: An Unusual emergency at a usually missed location. *Arch Urol Res*. 2020; 4(1): 090-092.
   DOI: https://dx.doi.org/10.17352/aur.000027
4. **Das S, Aggarwal G, Gupta S, Midha D**. Primary Renal Ewing's Sarcoma in an Adult: An Enigma. *Innovative Surgical Sciences*. 2020.
5. **Aggarwal G, Gupta S.** Cancer treatment vis-à-vis COVID-19: The ledge of a precipice!! *Arch Urol Res*. 2020; 4(1): 047-048.
   DOI: https://dx.doi.org/10.17352/aur.000018
6. **Jindal T, Meena M**. Laparosocpic and robotic Video-endoscopic inguinal lymphadenectomy by the lateral approach. *Asian J Endosc Surg*. 2020 Nov 16.
   doi: 10.1111/ases.12898.

7. **Solanki SL, Thota RS, Garg R, Pingle AA, Goswami J, Ranganath N, Mukherjee S, Gupta S, Patkar S, Chikkalingegowda RH, Jindal T, Ray MD, Upadhye SM, Divatia JV.** Society of Onco-Anesthesia and Perioperative Care (SOAPC) advisory regarding perioperative management of onco-surgeries during COVID-19 pandemic. *Indian J Anaesth*. 2020;64, S2:97-102.
8. **Jindal T, Dhanalakshmi M, Pawar P.** Pulmonary lymphangitis carcinomatosa in a patient with carcinoma of urinary bladder. *Indian J Urol*. 2020;36:216-8.
9. **Jindal T, Pawar P, Subedi N**. Unusual presentation of castrate resistant prostate cancer with urethral and inguinal nodal metastasis**.** *Indian J Urol*. 2021;37:95-6.
10. **Jindal T, Dhanalakshmi M, Pawar P, Panda J, Midha D**. Inflammatory pseudotumour of the renal pelvis*. Journal of Endourology Case Reports*. 2020;405-408. http://doi.org/10.1089/cren.2020.0144

EXTERNAL ACADEMIC MEETINGS

Dr Sujoy Gupta - Invited Lecture

1. Manipur Oncology Society Management of Muscle Invasive Bladder cancer, February 2020

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3. Gaurav Aggarwal (0000-0002-6524-700X)
4. Tarun Jindal (0000-0002-8723-7486)

Tata Translational Cancer Research Centre

Research Support Directorate

Annual Research Report - 2020

The Vision

The Research Support Directorate (RSD) was conceptualized in 2018 by Dr Chandy and Prof Saha for facilitating and supporting the wide range of research activities at the Tata Medical Center. Research Support Directorate (RSD) is set up with the broad aim of facilitating and supporting the wide range of research activities at the Tata Medical Center. This includes addressing the logistic requirements for the conduct of research, developing policies for research operations, facilitating development of collaborative research proposals especially in response to external grant calls, providing training and advice support especially for young investigators, conducting courses on various aspects of research (methodology, grant application etc.) for young researchers and communicating and summarising research activities carried out in the institution.

Our mission is to develop Tata Medical Center as one of the leading research institutions in the world and to provide a holistic environment for the training of the next generation of cancer researchers.

While the IRB (Institutional Review Board) seeks to evaluate the scientific or ethical questions raised by the research project proposal, key functions of the RSD are:

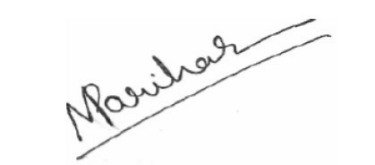
Key Functions

Address the logistic requirements for the conduct of research (Seek to ensure hospital is able to meet additional resource requirement, if any).
Develop policies for research operations.
Facilitate development of collaborative research proposals especially in response to external grant calls.
Provide training and advice support especially for young investigators.
Conduct courses on various aspects of research (methodology, grant application etc.) for young researchers.
Summarize and communicate research activities carried out in TMC.

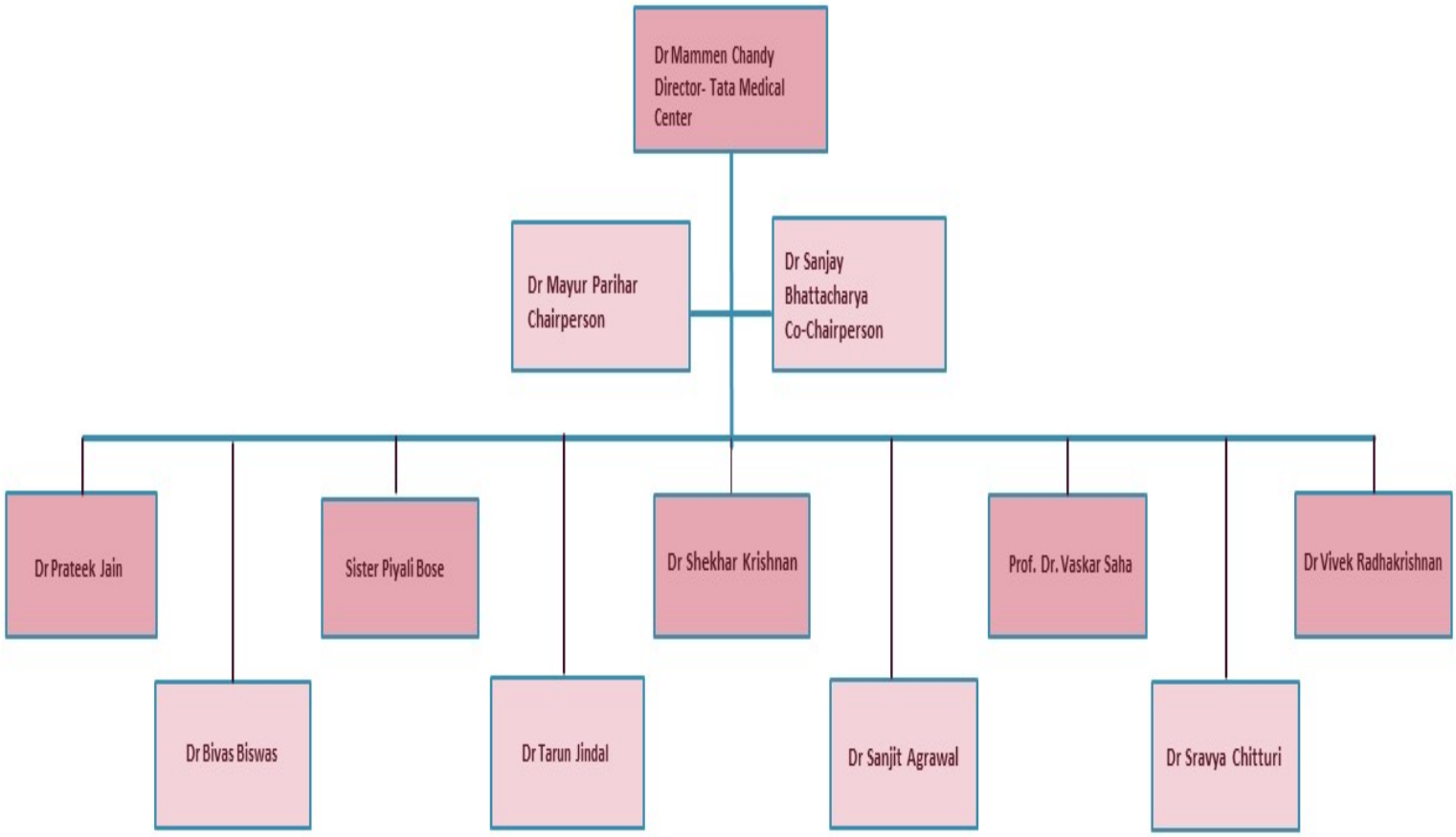
CHAIRPERSON'S FOREWORD

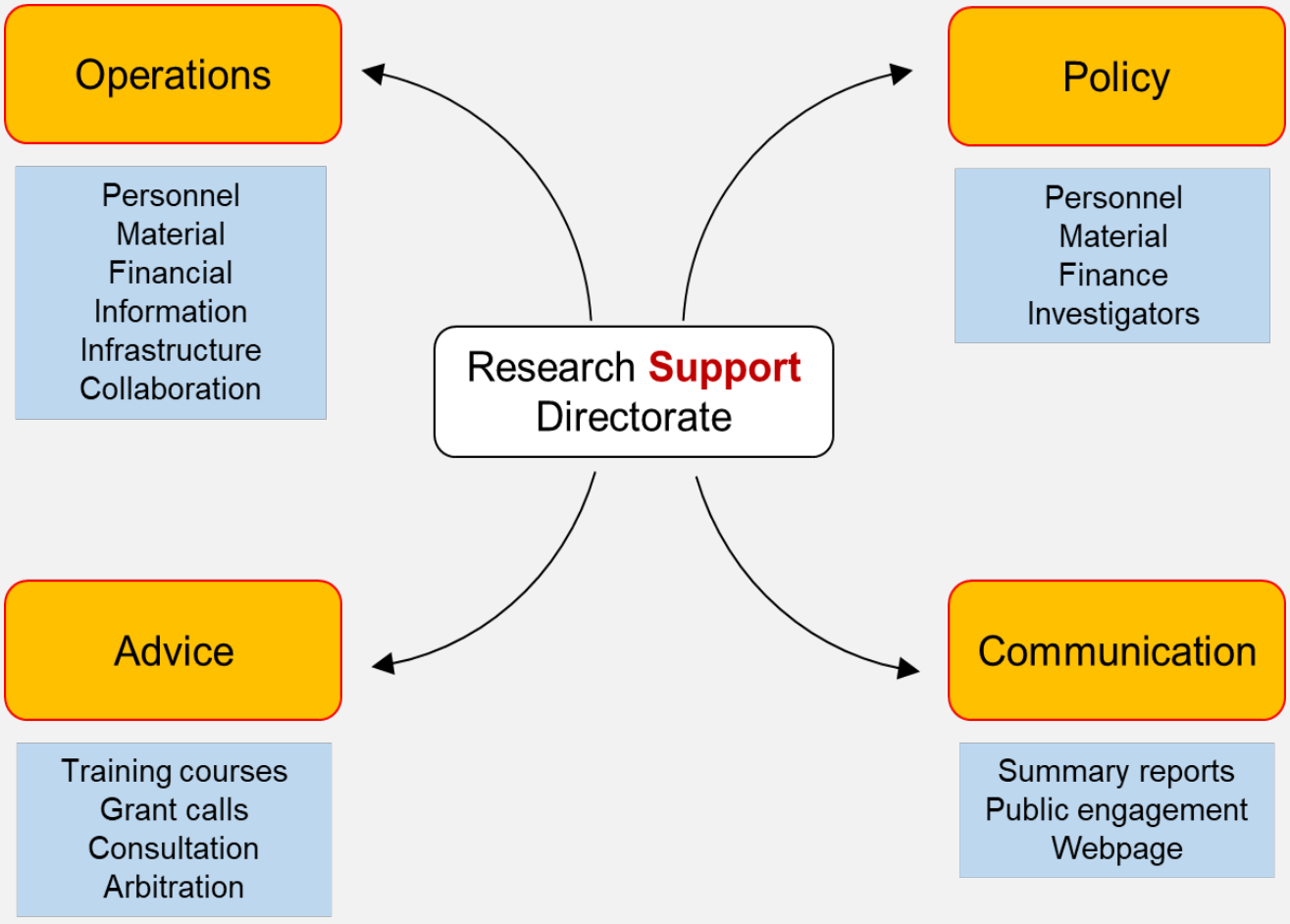
I am pleased to present the Annual report of the Research Support Directorate (RSD) for the year 2020. The report is a snapshot of the preamble, process and activities of the RSD in the last year. As the RSD completes its second year of existence we are delighted that the process of reviewing research proposals now is streamlined, consolidated and integrated with the IRB. In the coming year we strive to support research at TMC/TTCRC in a more pro-active way, focussing on research training especially for young researchers, NBE students and fellows. The RSD hopes to create a common platform where young researchers can share their research ideas, hypothesis and improvise their proposals. We plan to conduct workshops on manuscript writing, grant writing, and clinical trial management in the coming year, directing our efforts to provide a fertile environment that will encourage interdisciplinary research and provide stimulus to young researchers.

In the last year many new young members form different specialities have joined the RSD team, bringing with them a fresh wave of ideas and enthusiasm. I take this opportunity to thank all the members of the RSD team who are passionately driven to support and develop research at our institute.



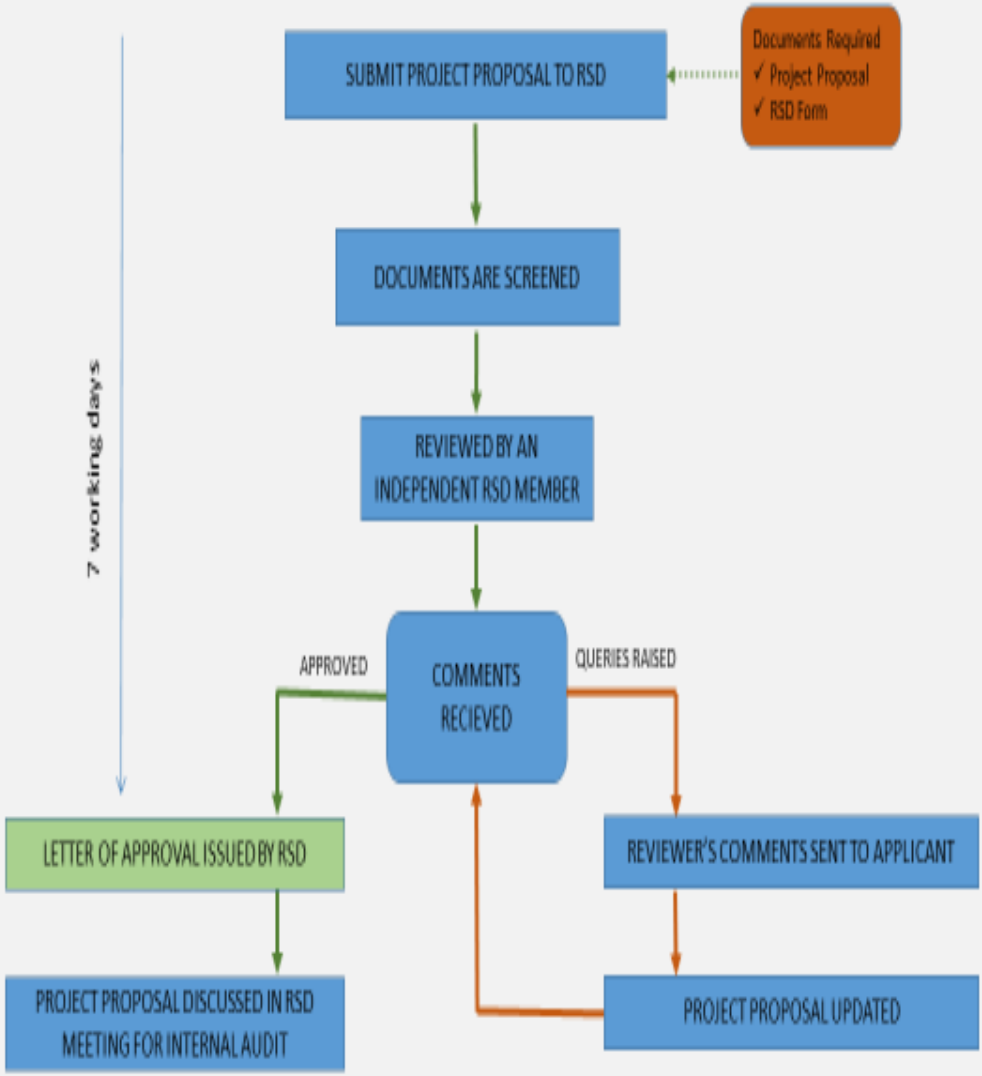
Dr Mayur Parihar


Research Support Directorate - Organizational Structure
Dr Mammen Chandy
Director- Tata Medical Center
Dr Mayur Parihar
Chairperson
Dr Sanjay Bhattacharya
Co-Chairperson
Dr Prateek Jain
Dr Bivas Biswas
Sister Piyali Bose
Dr Tarun Jindal
Dr Shekhar Krishnan
Dr Sanjit Agrawal
Prof. Dr. Vaskar Saha
Dr Sravya Chitturi
Dr Vivek Radhakrishnan



Inclusive, multidepartment representation, especially younger investigators

RSD SUBMISSION-REVIEW-APPROVAL PROCESS



PROJECT PROPOSAL SUBMISSIONS (2019-2020)

REFERENCE NUMBER	PROJECT TITLE	PI & DEPARTMENT	DATE SUBMITTED TO RSD	DATE APPROVED BY RSD
RSD/01/2019	Acute Myeloid Leukemia: Exploring the feasibility of Multimodal-omics based genomic characterization, MRD evaluation and computational drug modelling to inform disease management	Dr Vivek S Radhakrishnan - Clinical Haematology/Laboratory Haematology	01/04/2019	
RSD/02/2019	EFFECT OF POMALIDOMIDE-BORTEZOMIB-DEXAMETHASONE INDUCTION ON MRD STATUS IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA Acronym: PRIME	Dr Vivek S Radhakrishnan - Clinical Haematology Laboratory Haematology and Molecular Genetics-Cytogenetics, Biochemistry, Radiation oncology, Radio-diagnosis and Interventional Radiology	July, 2019	
RSD/03/2019	Establishing Academic Clinical Trails Units in India to transform the design and delivery of Clinical Trials (ACT Ind)	Dr Shekhar Krishnan - Tata Translationa;l Cancer Research Centre	01/06/2019	

RSD/04/2020	Intelligent Clinical Decision Support System for the Maintenance Phase of the Peadiatric Acute Lymphoblastic Leukemia (ALL)	Dr Shekhar Krishnan - Tata Translationa;l Cancer Research Centre	01/06/2019	
RSD/04/2019	Dissecting the Interactions of NFkB & TP53 in the Genesis of Gall Bladder Cancer in India	Prof Vaskar Saha -GI-HPB Surgery, Pathology & Radiology	01/05/2019	
RSD/05/2020	A prospective validation study for non-invasive diagnostic kit for breast, lung and oral cancers	Dr Jain Prateek Vijay - Head & Neck Surgery, Breast Surgery, Radiation Oncology	01/07/2020	
RSD/06/2019	Integrated strategies to address minimal residual disease in acute lymphoblastic leukaemia	Dr Jasmeet Sidhu - Paediatric oncology	01/09/2019	

RSD/07/2020	Identifying and potentially mitigating biologic and treatment-related disparities in head and neck squamous cell carcinoma (HNSCC) in India (with University of Pittsburgh, for an NIH Supplementary Grant award)	Dr Indranil Mallick - Department of Radiation Oncology Department of Laboratory Medicine/Molecular Biology Department of Histopathology	01/08/2020	06/08/2020
RSD/08/2020	Serology And Sociology Of Individuals With SARS-Cov-2 Infection: A Study Of Igg Serology In Patients, Staff And Blood Donors In An Oncology Center In Eastern India Along With An Assessment Of KAP (Knowledge Attitude And Practice) In Blood Donors	Dr. Sanjay Bhattacharya - Microbiology	09/09/2020	16/09/2020
RSD/09/2020	Identification Of Genomic Correlates Of Disease Severity In Covid-19	Dr. Sanjay Bhattacharya - Microbiology	08/09/2020	15/09/2020

RSD/10/2020	Evaluation Of The Commercial Sona Aspergillus Galactomannan Lateral Flow Assay And Novel-Aspergillus Lateral Flow Device For Diagnosis Of Invasive Aspergillosis	Dr. Sanjay Bhattacharya - Microbiology	09/09/2020	18/09/2020
RSD/11/2020	A Randomized, Double-Blind, Placebo-Controlled Phase Ill Multi-Center Study Of Azacitidine With Or Without MBG453 For The Treatment Of Patients With Intermediate, High Or Very High Risk Myelodysplastic Syndrome (MOS} As Per IPSS-R, Or Chronic Myelomonocytic Leukemia-2 (CMML-2) .	Dr. Vivek S. Radhakrishnan - Clinical Hematology and BMT	10/09/2020	16/09/2020
RSD/12/2020	Inpog – RB – 19 – 01	Dr Arpita Bhattacharya - Paediatric Haematology & Oncology	25/09/2020	01/10/2020
RSD/13/2020	Inpog Neuroblastoma Biology And Registration Study	Dr. Arpita Bhattacharyya - Paediatric Haematology & Oncology	25/09/2020	01/10/2020

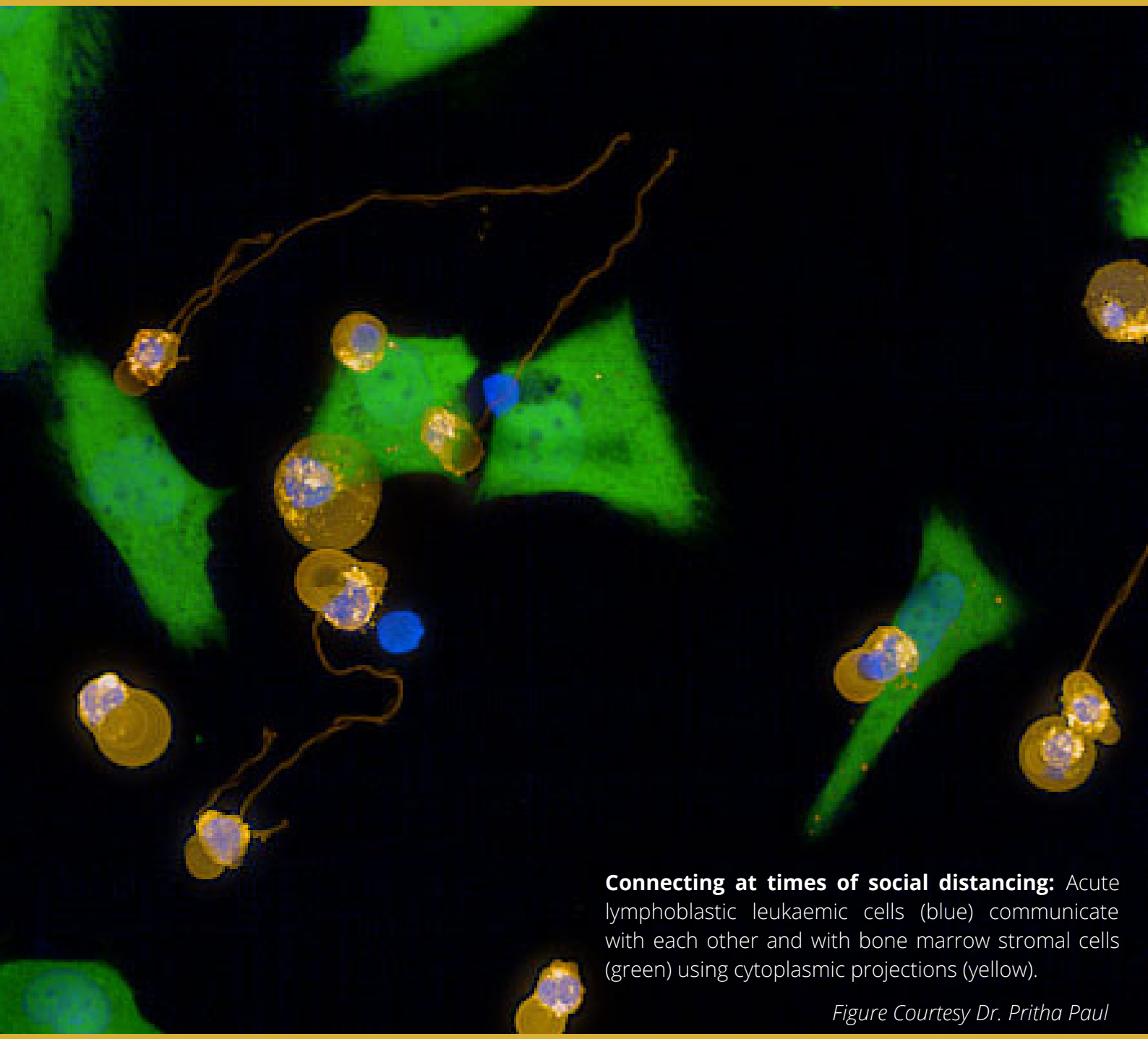
RSD/14/2020	A Pilot Study To Evaluate The Extent Of Analgesia After Sacral-Erector Spinae Peripheral Block (ASES)	Dr. Arunangshu Chakraborty - Anaesthesia	19/10/2020	29/10/2020
RSD/15/2020	73841937nsc3003 (Mariposa)	Dr. Deepak Dabkara - Medical Oncology	19/10/2020	29/10/2020
RSD/16/2020	61186372nsc3001(Papillon)	Dr. Deepak Dabkara - Medical Oncology	19/10/2020	29/10/2020
RSD/17/2020	CBYL719C2401	Dr. Sandip Ganguly - Medical Oncology	29/10/2020	03/11/2020
RSD/18/2020	Cbyl719h12301	Dr. Sandip Ganguly	29/10/2020	03/11/2020
RSD/19/2020	D361BC00001 (Capitello-281)	Dr. Deepak Dabkara - Medical Oncology	04/11/2020	06/11/2020
RSD/20/2020	D910dc00001 (AstraZeneca)	Dr. Sandip Ganguly - Medical Oncology	09/11/2020	13/11/2020
RSD/21/2020	A Real-World Utilization And Outcomes With Dacomitinib First-Line Treatment For EGFR Mutation-Positive Advanced Non-Small Cell Lung Cancer Among Asian Patients – A Multi-Center Chart Review.	Dr. Bivas Biswas - Medical Oncology	13/11/2020	25/11/2020
RSD/22/2020	EMERALD-D933gc00001	Dr. Sandip Ganguly - Medical Oncology	29/12/2020	07/01/2021

RSD/23/2021	DESTINY-D967vc00001	Dr. Bivas Biswas - Medical Oncology	13/01/2021	22/01/2021
RSD/24/2021	MERMAID-D910lc00001	Dr. Bivas Biswas - Medical Oncology	13/01/2021	18/01/2021
RSD/25/2021	D516AC00001	Dr. Bivas Biswas - Medical Oncology	12/02/2021	16/02/2021
RSD/26/2021	[CBYL719K12301] A Phase III, multi-center, randomized (1:1), openlabel, active-controlled study to assess the efficacy and safety of alpelisib (BYL719) in combination with olaparib as compared to single agent cytotoxic chemotherapy, in participants with no germline BRCA mutation detected, platinum-resistant or refractory, high-grade serous ovarian cancer	Dr Joydeep Ghosh - Medical Oncology	15/02/2021	22/02/2021
RSD/27/2021	A5481145	Dr Sandip Ganguly - Medical Oncology	03/03/2021	06/03/2021
RSD/28/2021	SERENA-4	Dr Joydeep Ghosh - Medical Oncology	05/03/2021	06/03/2021

- Quarterly Research Bulletin 2021 – Q1 (Published)

2020

ANNUAL SCIENTIFIC REPORT



Connecting at times of social distancing: Acute lymphoblastic leukaemic cells (blue) communicate with each other and with bone marrow stromal cells (green) using cytoplasmic projections (yellow).

Figure Courtesy Dr. Pritha Paul

TATA TRANSLATIONAL CANCER RESEARCH CENTRE

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From the Directors Desk

Vaskar Saha

Head - Paediatric Hematology
Director -TTCRC

What a year this has been! In early January, when we heard about the virus outbreak in Wuhan, we treated it as normal news, as we had done with SARS and MERS. We then went deep into the unknown as a global pandemic ensued. Over time, clarity emerged as to what the virus did, how it spread and more importantly how to treat those affected. Vaccines came rolling in – a triumph of medical science and technology. Mixed with a bit of hyperbole. As with all scientific knowledge, the more we learn, the more there is left to know. Above all that has come human resilience and the ability to work together to face the odds. We are not out of the woods yet, but a path has appeared.

Along with everyone else, TMC learnt to sift the good facts from the bad, set up the SARS2-COVID screening, arrange for PPE and develop protocols to keep patients and staff safe. Patient load dropped for a while, mostly due to the enforced lockdown. We are operational again running at almost full capacity – a testimony to the fortitude, courage, and ingenuity of all those involved. Despite that, all of us have been directly or indirectly affected by illness and death.

In March, just prior to the lockdown, TTCRC moved to shut operations. First to reduce the risk to staff and second to decrease the chance of bringing the infection into the hospital. For a couple of weeks, Shekhar was the last man standing, supporting both the clinical team as well as babysitting TTCRC. Pritha, on secondment to Manchester, managed to get the on the last inbound flight back to Kolkata. Skype gave away to zoom and we began working out how to work from home. As things settled down, staff found ways to get back to coming into work. Some, and here given what little we knew back then, had the courage and fortitude to help with the virus testing program. Others came in regularly to maintain equipment and essential activities. Even

Barun, my driver, stepped into ferry people who had no means of transport. By May, we had gradually begun work again, though biobank remained shut. The bank premise was the only site suitable to set up a secure area for the Covid PCR test and sample collection was deemed to be too risky. By August, the biobank team has set up a temporary facility within TTCRC and the labs were up and running. More staff began to come into work, some now travelling together, overcoming the sum of all their fears.

In late February, I had gone on what was to be a short visit to Germany and UK. I was only able to return on the second flight allowed from London to India in September. The fact that TTCRC was fully active by then speaks volumes of Shekhar's calm influence, the commitment of the senior TTCRC staff and the willingness of everyone to get back to work. For this I am humbled and truly grateful. We have had some scares, but then this is the new normal.

As you will see from the annual report, lockdown may have stymied, but it has not stopped the groups from making progress. CRU continues to recruit patients to the frontline trial and has expanded into exploring designs for early phase trials. Biobank is regrouped and reorganised, waiting to move back to its own area. The genomics lab has completed the analyses of High Hyperdiploid ALL and the MRD lab is moving to a NGS platform. Leukaemia Biology has developed new tools and techniques for analyses, generating new hypotheses on the way. Drug Discovery has come of age allowing us to identify alternative therapies for patients with a suboptimal response to frontline therapies. The organoid team has setup a multidisciplinary team to elucidate the pathogenesis of gallbladder cancer and successfully established a organoid laboratory. The mass spec has finally begun to sing. Ankita (Organoid Laboratory) became our first doctoral student, joint with IIT-Kharagpur. Jaydeep, who worked with biomaterials in the Organoid Laboratory, has joined for a PhD program working on biomaterials in CAR-T (IIT-Bombay with Monash University). Meanwhile Tushar and Kankana were awarded well deserved PhD's.

Bindhu, Chumki, Dipshikha, Shivani, Jaydeep, Ruma, Akash, Madhuparna, Parna, Piyali, Sayan, Soumita, and Susri left for fresh opportunities. I wish them every success. Abhirupa, Amrita, Ananya, Anushka, Aparajita, Arnav, Asama, Bishwaranjan, Dwijit, Manimaran, Pravin,

Saheli, Samik, Sayantani, Shreyasree, Shinjini, Srijita, and Subhoshree have joined.

We have a busy year ahead. All the best everyone, work hard and work together. Stay safe, keep others safe – we are not quite out of the woods yet.

I leave you with a quote from a lady who is an inspiration to all of us in the field of cancer "Nothing in life is to be feared. It is only to be understood. Now is the time to understand more, so we may remain fearless." What Marie Curie said a 100 years ago, resonates today.

Clinical Research Unit

Background

The Clinical Research Unit (CRU) at TTCRC leads and participates in the design, development, management, analysis and reporting of investigator-initiated and investigator-led clinical studies in cancer. These studies provide the platform for the translational research programme at TTCRC.

Research programmes

The CRU is involved in the following research programmes

A. Acute lymphoblastic leukaemia
B. Gallbladder cancer

Studies

A. Acute lymphoblastic leukaemia (ALL)

1. The Indian Paediatric Oncology Group's Indian Collaborative Childhood Leukaemia ALL-14 multicentre randomised clinical trial in children and young people with newly-diagnosed ALL (InPOG-ALL-15-01-ICiCLe-ALL-14; CTRI/2015/12/006434)
   a. Pre-trial phase: from March 2013
   b. Trial: opened in late October 2016, continuing enrolment

c. Investigators: Shekhar Krishnan (principal); Vaskar Saha (chief)
d. Funding: National Cancer Grid and Indian Council of Medical Research

2. The Indian Paediatric Oncology Group collaborative multicentre treatment protocol for children and adolescents with relapsed acute lymphoblastic leukaemia (InPOG-ALL-19-02-TMC-ALL-R1; CTRI/2019/10/021758)
   a. Pilot: from August 2016
   b. Study: opened in June 2019, continuing enrolment
   c. Investigators: Niharendu Ghara (principal); Vaskar Saha (chief)
3. Summary of activities in 2020
   a. Enrolment in the ICiCLe-ALL-14 clinical trial slowed substantially or was paused for 4-6 months between March and August 2020 on account of the SARS-CoV-2 pandemic, affecting the projected timeline for completion of target enrolment. A submission was made to the National Cancer Grid (March 2020) for extended funding for a fourth year. Trial observations demonstrate improvements in risk stratification diagnostics, a sustained lower rate of treatment-related mortality compared with the pre-trial phase and the pronounced adverse effect of anthracycline treatment in younger patients (<10 years).
   b. Analysis of outcomes of patients (N=~2500) treated in the pre-trial phase is underway. Preliminary observations confirm improvements in survival with risk stratified therapy but the outcomes do not match those reported in the west. The findings suggest opportunities to refine risk stratification diagnostics, investigate distinct biologic determinants of poor treatment response, improve the quality of generic cytotoxic drugs (specifically the biopharmaceutical L-asparaginase) and strengthen the outpatient supervision of the 96-week maintenance treatment phase.
   c. The remote data capture system for the ALL-R1 study is complete and awaits incorporation of a few corrections before going live. At least nine centres have indicated interest in participating in the study. The study protocol was reviewed at the NCG's CReDO 2020 workshop (Dr Ghara). Study enrolment is underway at the Tata Medical Center and increasingly, families opt for intensive

treatments aimed at cure or good quality remission.

d. An ICiCLe-ALL study website was designed and developed in early 2020 (ND, SP) and is accessed through the TTCRC homepage (https://icicle.ttcrc.org/)

4. Key proposed activities in 2021
   a. Interim analysis of the ICiCLe-ALL-14 trial is scheduled in mid-2021, four years from start of enrolment. Findings from the analysis will inform decisions on trial randomisations and enrolment.
   b. Rollout of ALL-R1 to participating centres is expected to begin in the second half of 2021.

B. Gallbladder Cancer Research Programme

Investigators: Dr Manas Roy; Dr Anindita Dutta

Collaborations: Medical Oncology; Digestive diseases; Diagnostic imaging; Histopathology

Gallbladder cancer is a malignancy of high endemicity and poor outcomes. The multidisciplinary translational research programme in gallbladder cancer aims to investigate the pathogenesis of this disease and discover new therapies, using suitable pre-clinical disease models. The role of the CRU in this programme is evolving. In 2020, the focus was on strengthening the tissue collection pathways required for development of the pre-clinical models. In 2021, the focus of the CRU would be on extending nascent efforts to create a clinical registry and consolidate the same with tissue banking and research laboratory records to develop an integrated study database.

Sub-studies / Projects

These projects and sub-studies are spin-offs of the CRU's clinical research programmes. The CRU is involved in two principal projects:

A. L-Asparaginase in ALL
B. Maintenance therapy in ALL

A. L-asparaginase in ALL

Investigators: Jasmeet Sidhu (principal); Shekhar Krishnan

CRU: MG; SS; ND

Laboratory: Arko Bhowal (from Nov 2019); Priyanka Bose (Jan 2018 – Sep 2019); Pritha Paul

Tissue banking: Ritam Siddhanta

Study 1: Investigating *E. coli* asparaginase (EcASNase) biogenerics in India

Study 2: Optimising dose and scheduling of an EcASNase biogeneric

Study 3: Clinical monitoring of PEG-EcASNase biogenerics (PEG, polyethylene glycol)

Study 4: Clinical trial to determine safety and efficacy of recombinant EcASNases

Study 1 highlighted the unsatisfactory quality and therapeutic activity of EcASNase biogenerics available in India (**Figure 1**). A draft manuscript has been prepared for submission.

Study 2 was halted on account of the SARS-CoV-2 pandemic (March 2020) but the observations confirm that switch to an alternate-day schedule of Leucoginase EcASNase (VHB Life Sciences; 10,000 IU/m^2/dose every 48 hours) provides adequate asparaginase activity in a majority of patients, importantly during the critical induction phase of ALL treatment. Analysis is ongoing and the findings will be communicated as part of the report on outcomes in the ICiCLe-ALL-14 pre-trial phase, as exemplar of strategies to optimise use of generic cytotoxic agents. Study 2 is supported by a grant from VHB Pharma.

Study 3 has been initiated and will be implemented in 2021. This will involve administration of PEG-conjugated EcASNase biogenerics marketed in India as part of a monitored study to determine drug activity, optimum dose, dosing schedule, toxicity and immunogenicity.

Study 4 is part of a collaboration with Gennova Biopharma Limited (Gennova) to develop affordable high-quality asparaginases. With part-funding from DBT's Biotechnology Industry Research Assistance Council, Gennova has developed recombinant EcASNase products (unconjugated and lyophilised PEG-conjugated formulations) that are likely to be approved soon for clinical testing. The proposed clinical study (target, second half of 2021) will investigate the safety and therapeutic activity of the recombinant products and determine the dose and schedule suitable for clinical use. This study will require additional personnel (coordination, lab studies), substantial preparatory work (protocol preparation, ethics approvals, data plans, laboratory studies) and dedicated funding.

B. Maintenance therapy in ALL

CRU: TM; MG; SP

Collaborations: Prof Sangeeta Das (IIT Kharagpur); Prof Kiranmoy Das (ISI Kolkata)

The CRU supports the clinical monitoring of the maintenance treatment phase in first-presentation and relapsed ALL. In parallel, research studies carried out by Tushar Mungle as part of his doctoral thesis highlighted the problem of suboptimal antimetabolite drug dosing in the majority of patients and identified potential strategies to address this

shortcoming. Three strategies have been proposed:

(a) Incorporation of visualisation tools (i) to monitor blood count trends and drug dose decisions in real-time and, (ii) to review weighted mean leucocyte counts against antimetabolite dose intensities at the completion of each maintenance cycle (12 weeks) as measures of optimal dosing practice (**Figure 2**)
(b) Development, testing and validation of an automated dose decision advice system based on protocol-based dose rules for initiation, continuation, interruption and escalation of antimetabolite drug doses based on longitudinal information from blood counts, dose tolerance and time elapsed from last dose changes
(c) Exploring computational modelling approaches to predict antimetabolite drug doses, based on traditional statistical modelling or through development of intelligent systems.

The SARS-CoV-2 pandemic has provided impetus for this work. As a result of pandemic-related travel restrictions, the proportion of ALL patients requiring remote supervision during the maintenance phase has increased sharply. An estimated two-thirds of patients now have their maintenance treatment supervised largely remotely, up from 25% last year. This transition has required development of data systems and strategies to record information longitudinally during the maintenance phase and reorganisation within the CRU to support remote dose advice clinics ('e-mail clinics'). The focus in 2021 will be to establish these data systems to support remote management of ALL maintenance, evaluate the use of visualisation and automated dose advice tools in maintenance management and publish the findings from TM's doctoral work. Findings from Prof Kiranmoy Das' joint modelling analyses highlighting the adverse impact of suboptimal 6-mercaptopurine dosing on the risk of ALL treatment failure will be communicated as part of the proposed publication on outcomes in the pre-trial phase, serving as exemplar of potential strategies to optimise treatment practice to improve ALL outcomes in India.

Other sub-studies undertaken in 2020 include

(a) Evaluation of impact of risk stratified therapy on direct treatment costs in patients with ALL treated at the Tata Medical Center: This work is complete and a draft manuscript is being prepared (ND; TM; SP)

(b) Evaluation of treatment toxicity in ALL in patients treated at the Tata Medical Center, including evaluating the frequency, nature and severity of infection and non-infection treatment toxicities and the influence of patient, disease and treatment variables on toxicity characteristics (ND; PD). Data collection is underway, analysis will begin in the second half of 2021, and a draft manuscript is targeted in early 2022.

(c) Observational study of the value of therapeutic drug monitoring with high-dose methotrexate schedules in first-presentation ALL (investigator, Dr S Chitturi, Fellow, Paediatric Haematology-Oncology). Contrary to other reports, findings from this work (76 patients, 290 infusions) emphasise the necessity of monitoring blood methotrexate levels in patients, especially in patients with T-ALL administered higher doses of intravenous methotrexate. Drug monitoring enabled timely intervention with augmented alkaline hyperhydration in nearly a quarter of infusions and extended leucovorin rescue in a further ~10% patients. Levels of serum creatinine were useful chiefly as negative predictors of supratherapeutic blood methotrexate levels. A draft manuscript is proposed (from CRU: ND, SC)

Sub-studies proposed in 2021 include the following

(a) Evaluation of the safety and efficacy of newer agents and therapies in ALL (SS, PD, ND)

The availability of generic targeted agents (dasatinib, venetoclax) and antibody therapies (blinatumomab, accessed as part of a donation programme in partnership with St Jude Global) and experience with newer agents (e.g. bortezomib in relapsed ALL) expands the therapeutic options for patients at high-risk of treatment failure including patients with high risk genetic subtypes and/or poor treatment response. These interventions will be introduced to deepen disease remission prior to allogeneic haematopoietic stem cell transplantation or where transplant treatment is not feasible, evaluated as potential strategies to extend disease-free remission. The use of these agents also provides an opportunity to prospectively evaluate their cost-effectiveness.

Others

1. The ICiCLe-ALL-14 (non-randomised) treatment protocol for risk-stratified management of children and young people with newly-diagnosed ALL at the NRS Medical College Hospital (Department of Haematology; Dr Rajib De, investigator)

   The CRU works with NRSMCH to support with coordination and funding of laboratory studies outsourced to the Tata Medical Center and advise on data management and analysis. CanKids India has committed to extend funding support for laboratory studies at TMC.
2. The CRU works closely with the tissue banking and laboratory groups to support laboratory-based research at TTCRC.

Figure Legends

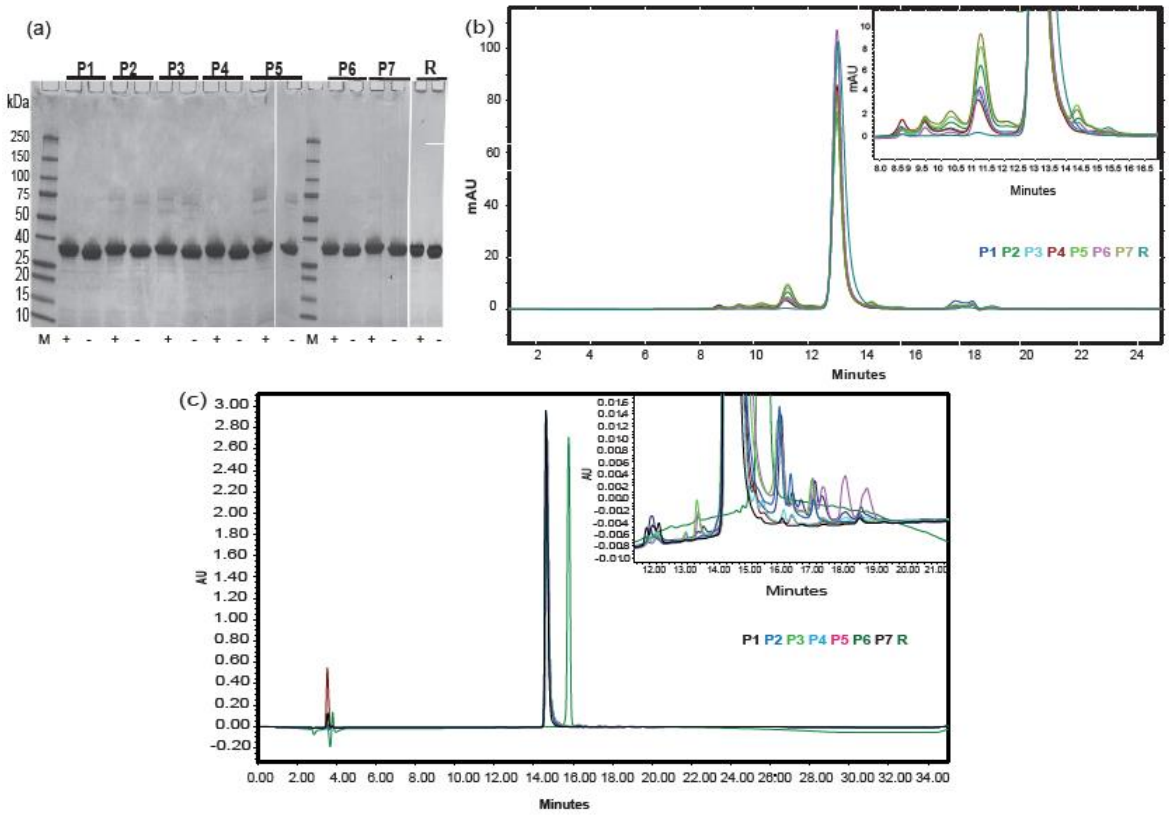


Figure 1: Analysis of EcASNase biogenerics P1-P7 and the reference EcASNAse (R) indicates impurities in the biogeneric products. (a) Coomassie-stained image of SDS-PAGE analysis of EcASNase products examined in reducing ('+') and non-reducing ('-') conditions confirms presence of the ~36kDa EcASNase subunit in all products, and shows additional higher molecular weight bands in the biogenerics suggesting presence of protein impurities (M, molecular weight marker); (b) SEC analyses of EcASNase products indicates that in addition to the primary peak of EcASNase, biogeneric products are characterised by additional smaller peaks with shorter retention times (inset, magnified view), suggesting the presence of higher molecular weight impurities, likely multimer aggregates of EcASNase (mAU, milli-absorbance unit); (c) RP-HPLC analyses of EcASNase products indicates difference in retention times (~1 minute) between EcASNase biogenerics and the reference product,

likely related to differences in hydropathicity owing to amino acid sequence variations in the biogeneric EcASNases. Additional smaller peaks with varying retention times are also observed in the biogeneric products, suggesting impurities (inset, magnified view). (AU, absorbance unit)

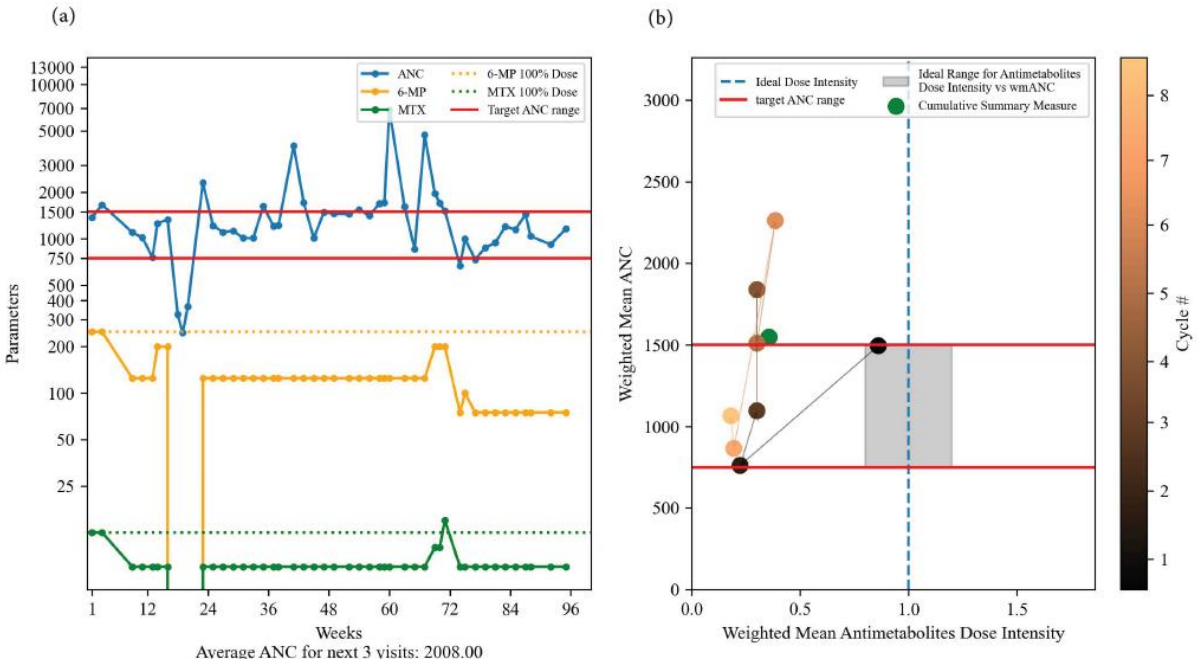


Figure 2: (a) Line graph showing longitudinal information of maintenance therapy over 96 weeks; (b) summary measure graph showing weighted means absolute neutrophil counts and antimetabolite dose intensity over 8 cycles

Biobank

Abhirupa Kar

Biobank Manager

Ritam Siddhanta

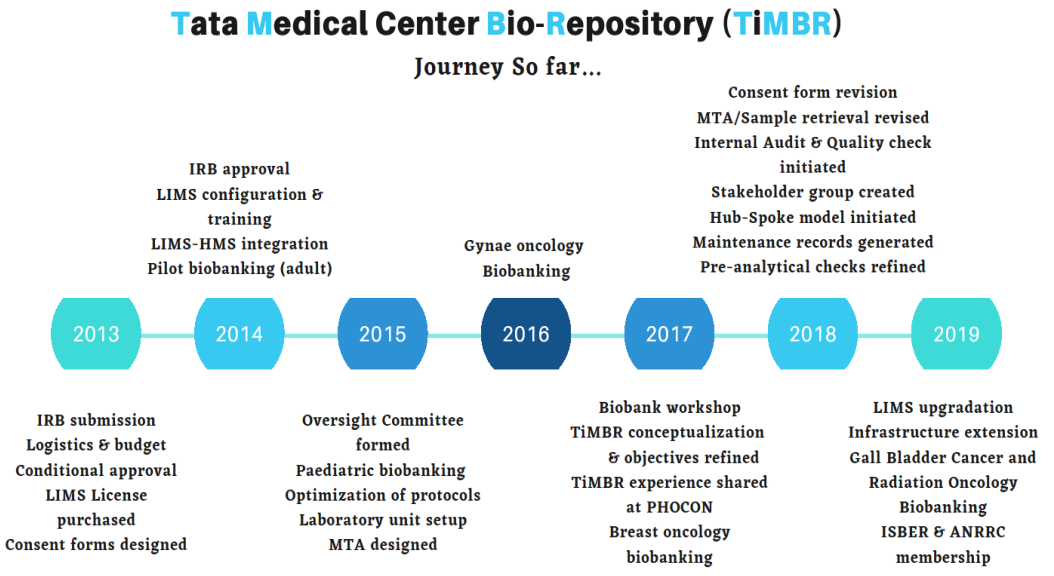
Biobank Technologist

Kankana Das

Research Assistant

Cancer Research Centre. TiMBR aims to facilitate access to high quality bio-specimens for translational cancer research leading to precision oncology, following international, national and institutional regulations involving operational, legal and ethical aspects of a biorepository.

TiMBR has come a long way since its inception. Being a single, organized, common resource, TiMBR provides samples to various research domains namely Genomics, Proteomics and Cell Biology for downstream experimental



TiMBR – Tata Medical Center Biorepository is a research infrastructure providing critical fuel to research activities performed at Tata Translational

procedures.

The year 2020-21 was full of ups and downs for TiMBR. The core team got reshuffled with new members joining force. The biobank oversight committee

was dissolved paving the path for introspection on the governance and operations of TiMBR. The current team is comprised of members from diverse backgrounds with expertise that not only makes our journey dynamic but also opens up avenues for branching out and evolve from routine biobanking processes. Mr. Ritam Siddhanta has joined TiMBR in 2018 and has been responsible for optimisation of biobanking protocols pertaining to paediatric leukaemia. He is overseeing the activities related to the quality of biospecimens. Dr. Kankana Das got introduced to TiMBR in 2019 starting off with paediatric leukaemia biobanking and later got involved in Gallbladder cancer biobanking as well as downstream research activities. Recently, Kankana received her doctoral degree from University of Calcutta. She is now responsible for quality assessment of extracted RNA and managing retrieval process of cryo preserved cells. For further validating the quality of the cryopreserved cells Dr. Kankana has undertaken post retrieval cell viability assays. Ms. Abhirupa Kar has recently joined TiMBR in August 2020 and is in-charge of managing the operational and structural aspects of the biobank.

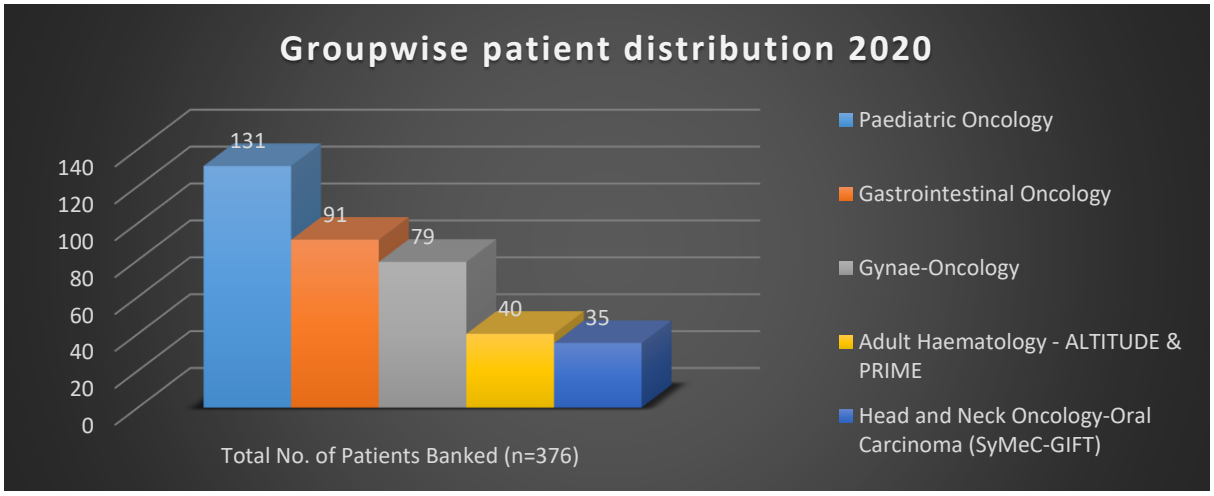
With the COVID-19 outbreak forcing the world to come to a halt, TiMBR extended its support to the institutional COVID-19 response strategy. As a unique facility built following international standards, TiMBR could be repurposed to meet regulatory guidelines to become a COVID-19 testing facility. In April 2020, TiMBR's processing facility was opened up for SARS CoV 2 RNA extraction and continues to do so. TiMBR resumed its activity after a month's gap with paediatric leukaemia group reinitiating banking in May 2020. With COVID-19 response taking centre-stage, biobanking was relocated to various TTCRC specialised laboratory units and to the diagnostic facility of TMC hospital unit. Despite the pandemic, TiMBR continues its banking services overcoming obstacles at multiple levels, from facility to personnel.

This report comprises of the following:

- Summary of the projects banking with TiMBR
- Information on samples collected and released
- Governance and audits
- Event and news (upcoming plans)

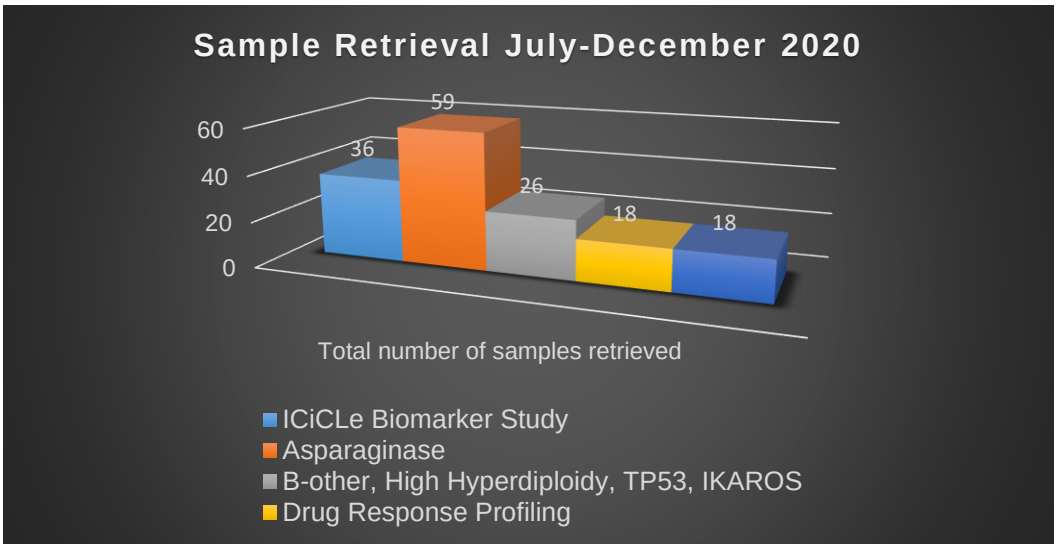
In 2020, TiMBR has actively banked for five departments at Tata Medical Center providing samples to 12 projects groups (details given below).

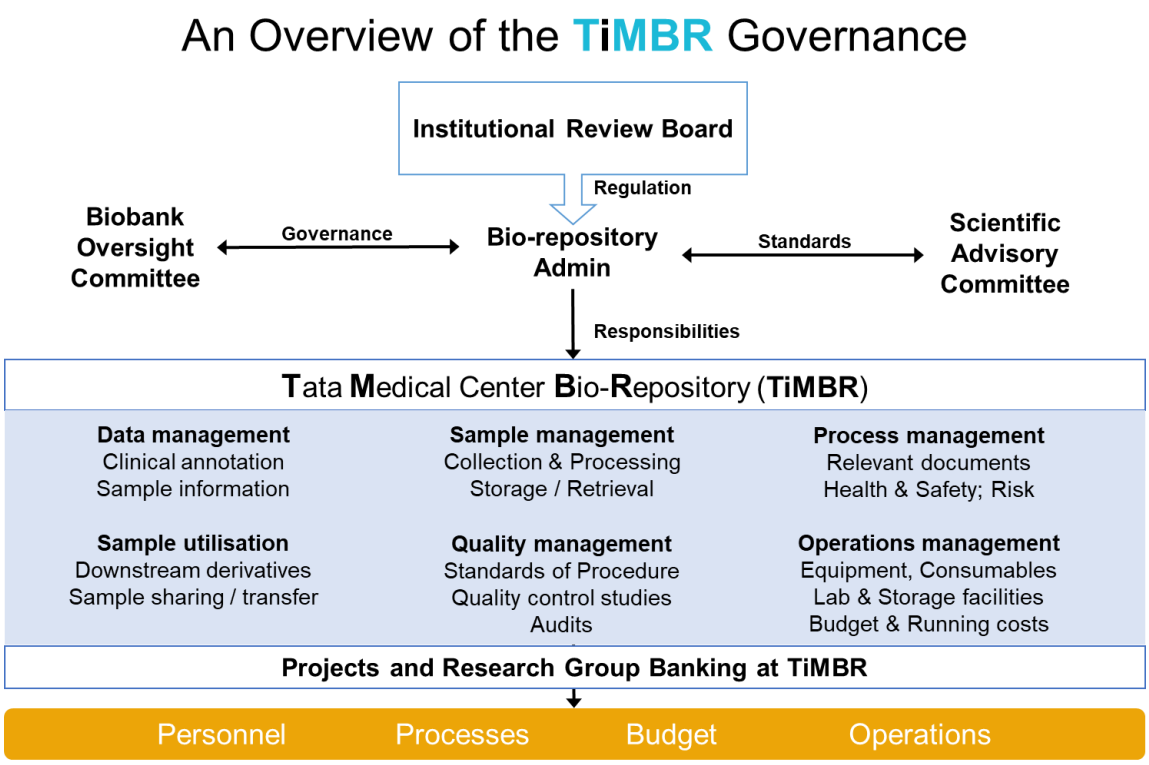
S. No.	Groups Banking with TiMBR	Project	Types of samples banked	Status
1.	Paediatric Oncology	ICiCLe Biomarker Study, Asparaginase	Bone marrow aspirate, Peripheral Blood, Cerebrospinal Fluid, Tissue	Active
		B-other, High Hyperdiploidy		Active
		Drug Response Profiling		Active
		TP53		Active
		IKAROS		Active
2.	Gastrointestinal Oncology	Gallbladder Carcinoma Biomarker Study	Tissue, Peripheral Blood, Hair, Nail, Gall Bladder stone, Bile	Active
3.	Gynae-Oncology	Cervix (SyMeC)	Cervical Scrape, Tissue, Peripheral Blood	Active
		Ovary (PROVAT)	-	Tenure complete
4.	Adult Haematology	ALTITUDE	Bone marrow aspirate, Peripheral Blood	Active
		PRIME		Active
5.	Head and Neck Oncology	Oral Carcinoma (SyMeC-GIFT)	Tissue, Peripheral Blood	Active
		miRNA Study	-	Tenure complete
6.	Breast Oncology	BREXO	-	Inactive
7.	Radiation Oncology	INTELHOPE HYPORT	-	Inactive



Along with sample storage, TiMBR has also witnessed high amount of retrieval in the last half of the year. In case of Gall Bladder cancer group, samples collected through TiMBR are directly used up for downstream processing and only excess samples are stored for retrospective analysis.

S. No.	Project	Type of derivative retrieved	Purpose of Retrieval
1.	ICiCLe Biomarker Study	DNA	Minimal residual disease tracking
2.	Asparaginase	Plasma	Therapeutic drug monitoring
3.	B-Other, High Hyperdiploidy, *TP53*, *IKAROS*	Cryo preserved mono nuclear cells (MNCs), DNA & RNA	RNA sequencing, SWATH-MS, SNP Array, TES
4.	Drug Response Profiling	Cryo preserved MNCs	Drug Response Profiling
5.	Oral Carcinoma (SyMeC-GIFT)	Tissue, Peripheral Blood	Transfer to NIBMG





At TiMBR, audits are undertaken internally every year by each project groups as well as by TiMBR admin. Last year, in order to overcome infrastructural shortcomings triggered due to the pandemic, quality check is adopted as a routine activity by the TiMBR core team. All retrieval carried out for in-house downstream research undergo quality checks. Two types of checkpoints have been set up for maintaining value of bio specimens.

- Direct quality assessment through estimation of DNA yield from mononuclear cells, RNA yield from cells in TRIzol, cell viability checks by flow cytometry.
- User group feedback on cryo-retrieved cells.

Events and news in TiMBR:

On 3rd December 2020, a hands-on-training of LabVantage was organised for user groups of Tata Medical Center. Professor Usha Menon graced the occasion as the keynote speaker followed by a technical session by Mr. Mayookh Sengupta from LabVantage.

TiMBR participated in a virtual symposium organised by International Society for Biological and Environmental Repositories (ISBER) in collaboration with UHN Biospecimen Services on 22nd -23rd October 2020.

Upcoming activities:

Operational:

1. Optimisation of bone marrow stromal cell culture as a research activity complimenting Paediatric Leukaemia group.
2. Exploring the possibility of organoid biobanking in collaboration with Gallbladder Cancer group.

Structural:

1. Refurbishment of the sample processing facility.
2. Activation of TiMBR oversight committee and scientific advisory or user committee.
3. Introduction of e-forms for efficient project management.

Flow Cytometry Facility

Arunima Maiti
Proteomics Technologist

The flow cytometry facility provides investigators with technological resources and assistance for high quality, multi-parametric flow cytometry acquisiton and analysis. The facility is equipped with a benchtop cell analyser, BD Accuri C6 Plus and a cell sorter, *BD FACSAria*. BD Accuri C6 Plus can simultaneously measure and analyse multiple physical characteristics, like, relative size, internal complexity, and fluorescence intensity. *BD FACSAria* is capable of cell sorting ensuring sterility, from heterogenous cell population based on their relative size, granularity and antigen expression using upto eighteen fluorochromes, sorting upto four separate populations simultaneously.

We support investigators in creating efficient and cost-effective experimental designs, through optimizing cytometry-specific reagent and fluorochrome selection, and provide assistance in operating both instruments, as well as in data analysis.

In 2020, we optimised standard operating procedures (SOPs) for some of the common flow cytometry experiments, for ready reference of users. We created equipment booking forms along with instrument setup guidelines for smooth running of the facility. Between the period of Jun 2020 - Dec 2020, BD Acurri C6 Plus was used to perform about 74 experiments assessing cell cycle, apoptosis, mitochondrial health, immunophenotyping of primary cancer cells. BD Aria Fusion was used for 35 experiments. Upto 7 parameters (2 scatter + 5 colours) immunophenotyping was performed in BD Aria Fusion. Drug resistant viable ALL cells were bulk sorted, while GFP+ cells were single sorted for clonal expansion. Data generated from both Accuri C6Plus and Aria Fusion were analysed using FCS Express 6.

Some of the data generated in-house are shown below:

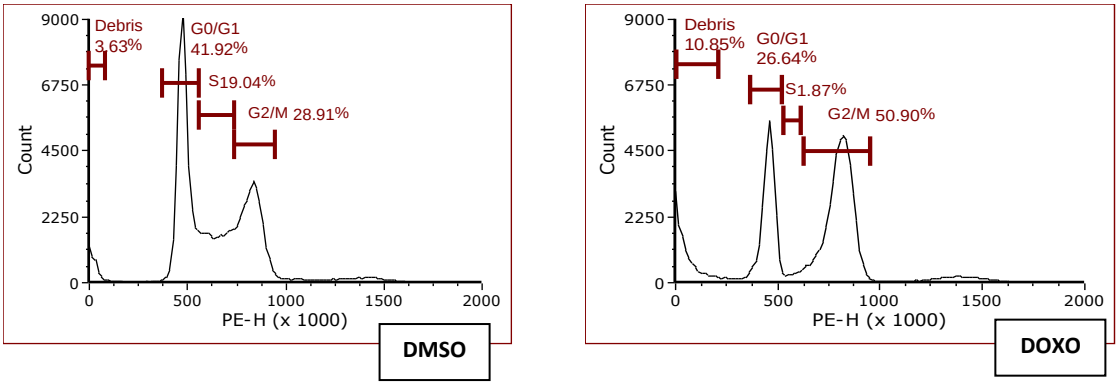


Figure 1: Cell cycle profiling of leukaemia cell line NALM-6 showing G2 arrest upon treatment with 100nM Doxorubicin (DOXO).

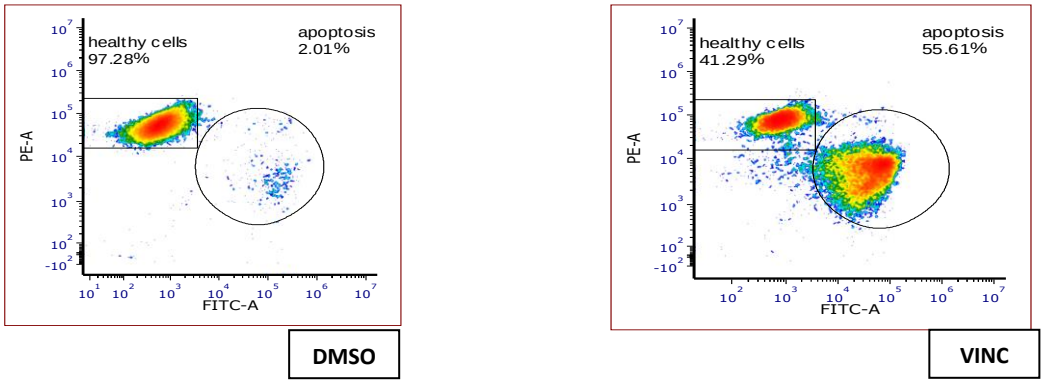


Figure 2: Mitotracker assay showing 97.28% cells containing healthy mitochondria in control REH cells. Upon treatment with 1µM Vincristine (VINC) for 48 hrs, proportion of healthy cells decreased to 41% with increment in cell apoptosis to 55.6%.

Proteomics biomarker discovery laboratory

Arunabha Chakraborty
IA Early Career Fellow

Arnav Bhattacharya
Research Assistant

Sangramjit Basu
Bioinformatics technologist

Development of high-throughput Mass Spectrometry for Discovery of Cancer Biomarkers

Aims and objectives:

- ✓ To develop high-throughput proteomics technologies for rapid identification of biomarkers in cancer.
- ✓ Detection of specific biomarker(s) in Biological samples for patient monitoring and development of targeted therapy.
- ✓ To complement genomic data for better functional implication of genetic abnormalities in cancer patients.
- ✓ Proteomics and metabolomics profiling of specific subtypes of cancer for therapeutic intervention.
- ✓ Qualitative and quantitative analyses of biological samples (both targeted and discovery) for small- and macromolecular expression in a specific time point or condition.
- ✓ **Types of samples:** Examples of types of samples which will be used for study using our mass spectrometer are provided below.

Types of samples	Examples
Cell	Cell lysates from: 1. Cell lines 2. Primary cells
Tissue	Solid tissue lysates from different cancer types e.g. Gall bladder cancer
Organoids	Gallbladder organoids from patients
Body fluids	Blood, CSF, Plasma

We started to develop our proteomics pipelines with analysis of cell lysates prepared from cell lines. Initial experiments were performed with leukaemia cell line NALM-6. Spectral library was generated using NALM-6 wild type cell line. We have created NALM-6 cell lines with different gene knock-outs (e.g. *IKZF1* and *P53* genes) as part of different projects. These knock-out cell lines were used to study differential proteomic expression compared to the wild type cell line. These initial data acquisition (both data dependent acquisition and data independent acquisition) are being used to develop data analysis pipelines to generate differential proteome data. Once streamlined, this pipeline can be used further to analyse DDA and SWATH data generated from different source of samples for both identification and quantitation purpose.

Experimental approaches:

Two types of experimental approaches we are currently following for both identification and quantification of proteins present in a particular sample- Data Dependent Acquisition (DDA) or Information Dependent Acquisition (IDA) and Data Independent Acquisition (DIA) or SWATH.

DDA/IDA

In this type of data acquisition, MS spectrum is collected on a broad m/z range (e.g. 200 Da-1400 Da) and The analyte peaks are detected and sorted by descending intensity. This procedure is repeated over and over again across the LC gradient. A narrow Q1 isolation window is used to send only that analyte through for MS/MS analysis.

In this procedure there is a high risk of lower level analytes either not being detected in the original MS spectrum or the mass spec running out of time (too slow relative to the complexity of the sample) to capture MS/MS spectra for everything detected in MS mode. This creates gaps in the data.

DDA is usually performed after fractionation of the complex samples and combine all the MS and MS/MS run from all the fractions to generate spectral library for identification of all the proteins expressed in that sample. Fractionation of the samples can be done by different means for example, by offline HPLC or by running a gel and excise several bands from the gel as different fractions before tryptic digestion of the protein samples.

DIA/SWATH

In this type of data acquisition, the mass spec uses a wider Q1 isolation window and steps it across the entire m/z mass detection range. This way, the mass spec collects full MS/MS spectra on every detectable analyte that passes through each Q1 window. The full mass range is interrogated in an LC time frame (short cycle times). This creates a complete MS and MS/MS picture of everything detectable in your sample, without the need for repeated runs or re-analysis. This method of acquisition requires a critical inter-relationship in technology performance: Q1 acquisition window control and MS/MS acquisition resolution at high speed.

Data quality control

The instrument functionality and the data generated in the mass spec are always quality checked before analysis. Instrument quality check is performed by running tuning solution directly to the mass spec. Data quality check is performed by running β-Galactosidase digest run as a calibration standard (Figure 2). In Analyst software, presence of specific peaks with higher than a cut-off intensity is considered to be acceptable for further acquisition of samples. If cell lysate is used as sample, we also run K562 cell lysate digested with trypsin protease and check for TIC intensity and pattern as a function of time to be sure about instrument performance. Then only we can run samples of interest.

The data generated from the Sciex Triple TOF 6600 comes out from the detector as .wiff files. Initial quality check of the data is performed in Peakview software which represents the Total Ion Current (TIC) of the sample run as a function of time. Also, in Peakview, qualitative and quantitative visualisation of the generated DDA and SWATH data are performed (Figure 3).

Data analysis pipelines

After the initial quality check, the raw data files from sample acquisition can undergo data analysis. We are in the process of developing the pipelines for analysing DDA data for spectral library generation and SWATH data for quantitative analyses. Detailed data analysis pipeline is provided as a flowchart in Figure 1 (*Nature Protocols* volume 10, pages426–441; 2015).

Mass spec facility as a support to different projects

The following supports are expected to be provided by our mass spec facility-

- ✓ Experimental design for qualitative and quantitative analysis of samples
- ✓ Generation of spectral library most appropriate and relevant samples in a project
- ✓ Proteomic characterisation of cell models created in different projects. Characterisation of tissue and organoids obtained from solid tumors
- ✓ Patient specific SWATH data acquisition and analysis for differential proteomics in two or more different conditions
- ✓ Rapid identification of prognostic and therapeutic biomarker in patient samples (e.g. Plasma/serum, CSF, Tissue, Bone marrow derived MNCs etc.)

Discussions/ Future plan

- ✓ Trans Proteomic Pipeline (TPP) for analysis of SWATH data is being developed for differential proteomics studies with cell models as well as with patients.

- ✓ Spectral libraries are generated by DDA/IDA run from relevant samples or can be downloaded from previously generated proteome data; DDA spectral libraries are used for quantitative analysis of SWATH data. We are generating most relevant spectral library to represent our samples and generating SWATH data with different project needs for differential proteomics analysis.

- ✓ SWATH data, once generated, will be stored in server re-analysed anytime in future. Depending on the research questions we are asking, we can access the data from server and analysis pipeline will be run depending on the research objectives.

- ✓ Patient-specific SWATH data would be generated and analysed for the purpose of developing personalized targeted therapy and identification of rapid prognostic and therapeutic biomarker.

- ✓ All the pipelines are being standardised based on the research objectives of two types of cancers- Acute Lymphoblastic Leukaemia (ALL) and Gallbladder cancer (GBC).

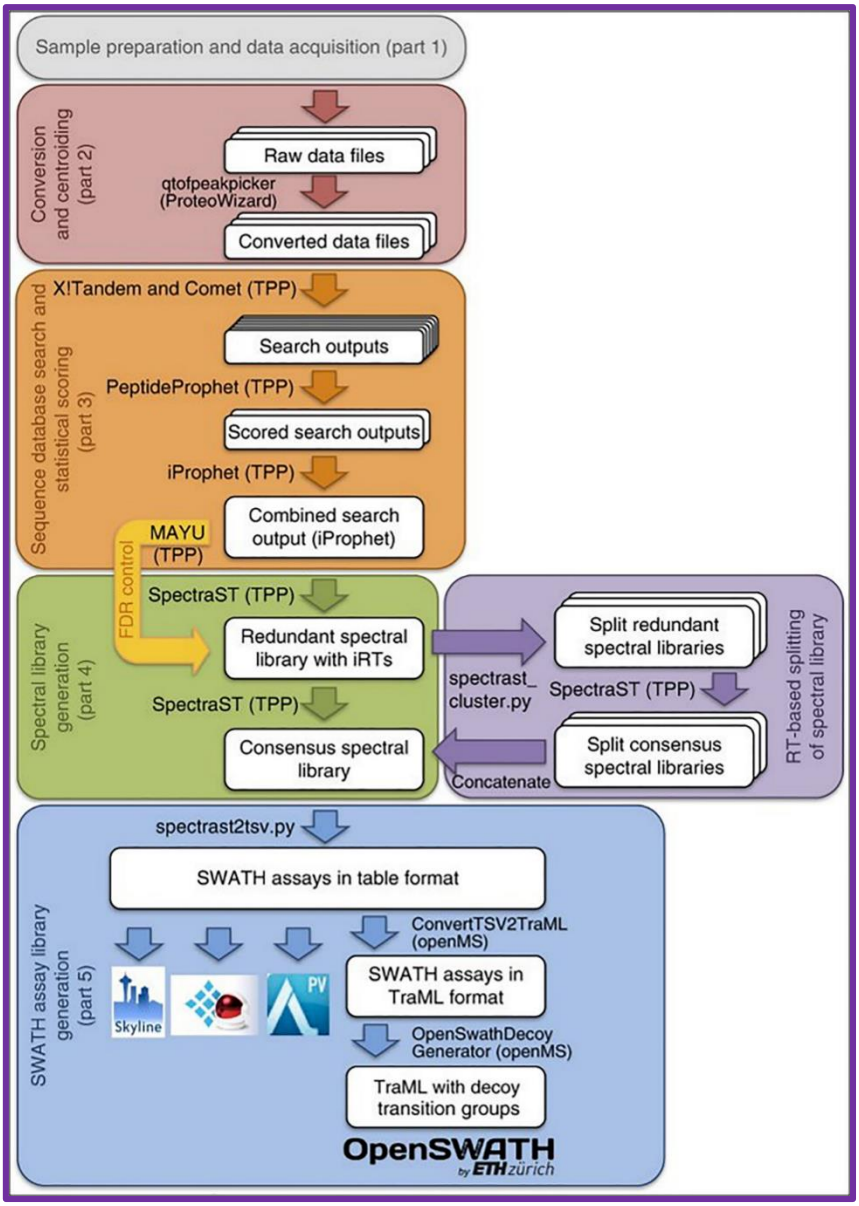
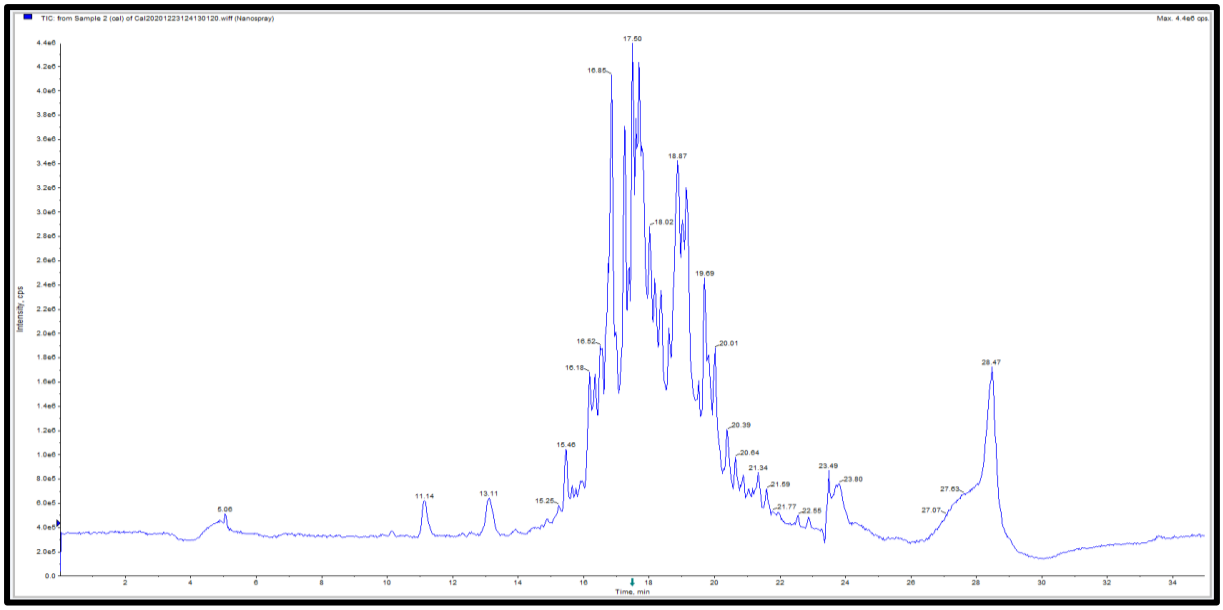


Figure 1 Data analysis pipelines for DDA and SWATH acquisition for preparation of spectral library and quantitation of proteins



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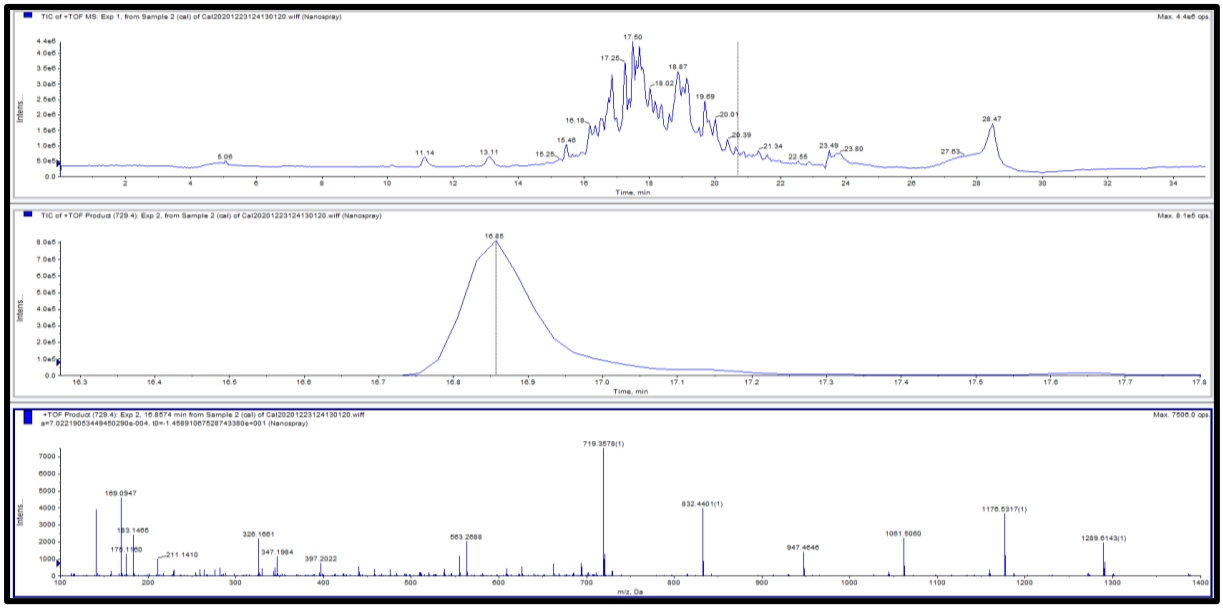
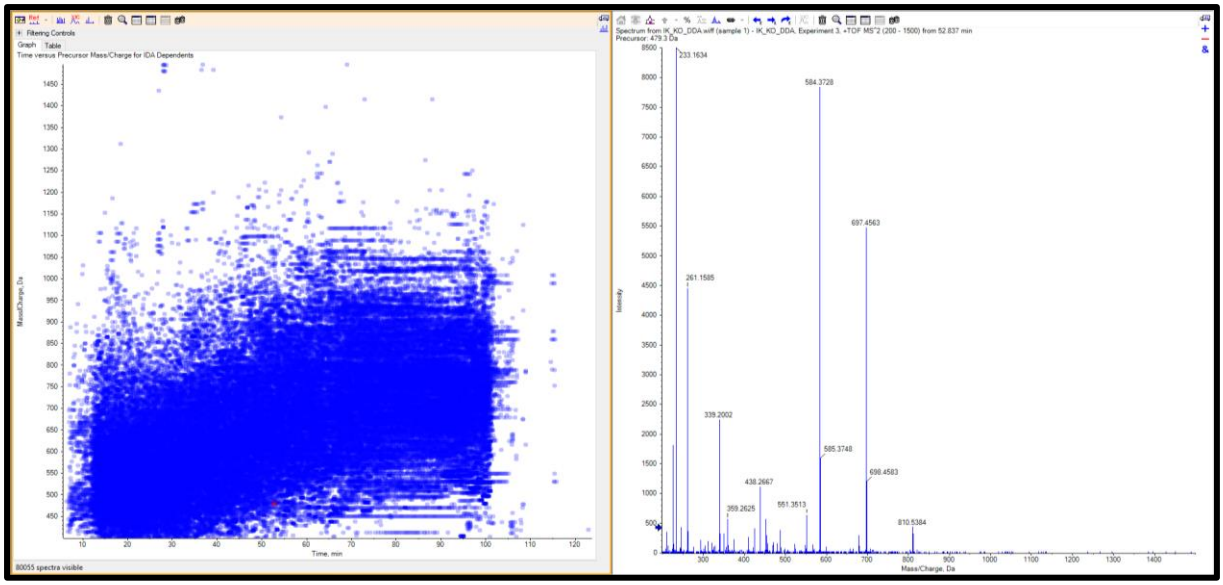


B

Figure 2 A. TIC distribution of DDA run of β-galactosidase digest. **B**. MS spectral distribution and MS/MS fragment spectra of precursor ion 729.4 from β-galactosidase digest



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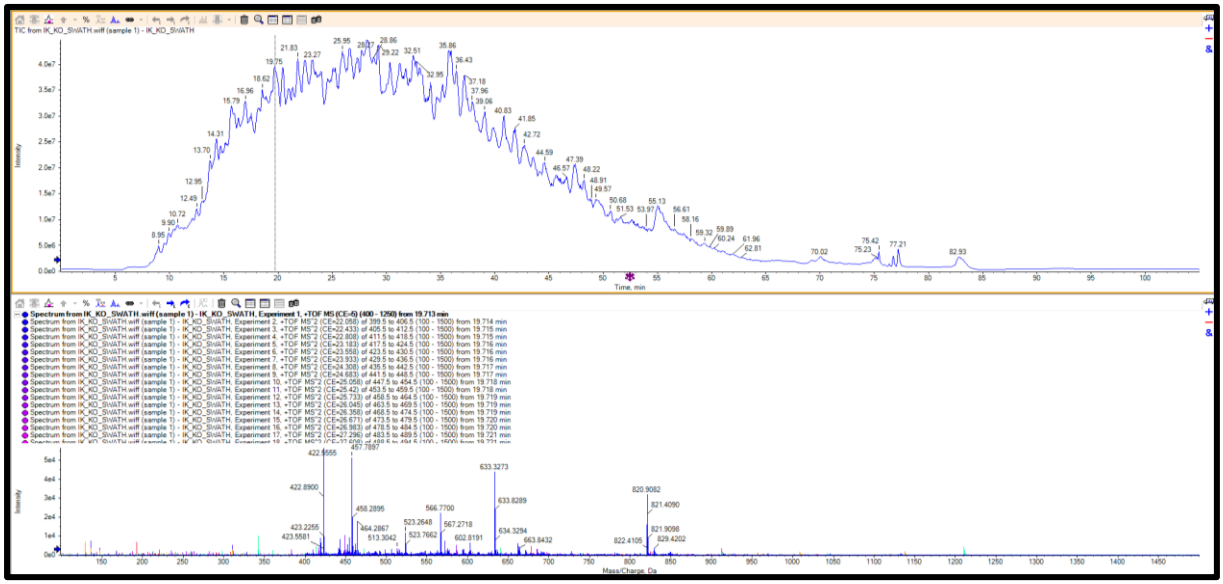

B

Figure 3 A. Visualisation of number of spectra generated and spectral distribution generated from a sample (*IKZF1* knock-out NALM6). **B**. TIC and MS/MS spectral distribution in all time points of the SWATH run for the sample (*IKZF1* knock-out NALM6) distributed throughout the mass range

Cancer Genomics Laboratory

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Team Composition

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Team TMC:

Piyali Biswas, Dr Chumki Bhattacharya and Dr Mayur Parihar

At TTCRC, the Cancer Genomics team is multidisciplinary consisting of highly motivated and well-trained individuals in the wetlab who set up project specific experimental workflows; a team of enthusiastic and skilled bioinformaticians and a supportive bio-banking team. The Clinical Research Unit (CRU) and Cytogenetics department serve as the backbone of this team and working together to provide better care for cancer patients.

Minimal Residual Disease monitoring in childhood ALL- Success, Challenges and Future

The Minimal Residual Disease (MRD) laboratory at TTCRC was established with an aim to offer more sensitive and advanced tools for detecting residual clones in childhood ALL. Though flow-MRD (FCM) is available across all ICiCLe centres offering a rapid turnaround time, interpretation is subjective and the technique requires viable cells for analysis. So, clonotypic Ig/TCR based genomic PCR-MRD testing was established at our centre to address the problems of reproducibility, sensitivity and sample portability. This has enabled clinicians to take decisions on appropriate therapy for patients based on the depth of response to therapy.

Our experience suggests PCR-MRD complements FCM in identifying high-risk patients more precisely. PCR-MRD has a greater sensitivity of 10^{-5}, which is a log higher than that of FCM. Comparing the sensitivities of FCM vs PCR-MRD for the discordant cases where FCM reported negative at the level of 10^{-4}, and PCR-MRD was either positive or positive but not quantifiable, about 20% were in the range between 10^{-3} and $5*10^{-4}$ and 80% lies beyond the range of 10^{-4}, which is the assay limiting sensitivity of FCM. Therefore, PCR-MRD has been able to successfully identify low MRD positivity in 45% patients, where FCM reported negativity at $<10^{-4}$.

Here, we report an exemplar of discrepancy between PCR and FCM-MRD. Figure 3, shows the MRD kinetics of a relapsed patient at longitudinal time-points. As depicted, MRD by PCR was high at end of induction (FU1) and consolidation (FU2), but undetectable by FCM. The patient was further treated using a Blinatumomab-based modified therapy which resulted in achieving molecular remission at subsequent time-points by both PCR and FC-MRD.

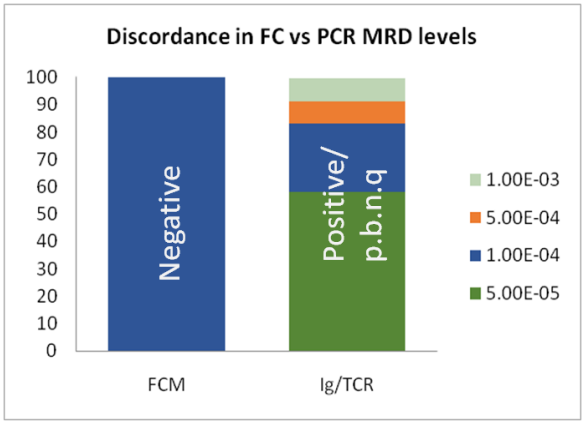

Figure 2. Bar plot showing discordance between FCM negativity and PCR-MRD positivity at levels ranging from 10^{-3} to 10^{-5}.

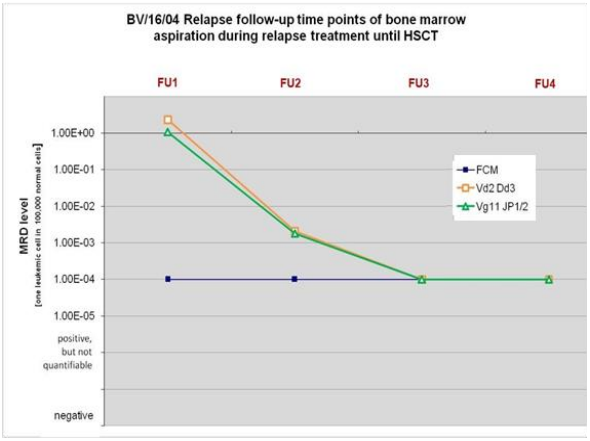

Figure 3. MRD Kinetics of relapsed patient showing levels assessed by FCM and PCR-MRD at serial follow-up time points during treatment.

Though PCR-MRD is sensitive, robust and reproducible, the current workflow is labour-intensive and time-consuming. With the available manpower and resources, we are able to offer testing in 5 patients per month at our hospital, which is clearly insufficient for our needs. Moreover, there are technical challenges with samples having borderline leukemic blasts <30%, resulting in loss of a significant proportion of patients with non-informative markers (~30%), who are lost to follow-up tracking.

Transitioning to NGS-based MRD clonal marker identification

To overcome the present challenges, we intend to make a transition to high-throughput sequencing based clonal marker identification, which would allow for multiplexing patient samples at lower turnaround times. Currently, we are in the process of standardizing the NGS-based MRD workflow, which is adapted from the protocol developed by EuroClonality-NGS Consortium. As illustrated in Figure 4A, it involves a two-step library preparation. In the first step, the clonal targets (TRB, TRG, TRD, IgK, IGH) are amplified using different multiplex PCR reactions, followed by a second round of PCR, which allows for dual indexing of patient samples for multiplexing in the sequencing run. We have successfully been able to standardise the first round of PCRs using positive controls like cell-lines and patient samples. (Figure 4B).

By end of 2021, we propose to optimise the library and sequencing protocols for marker identification using Illumina-based platform. We are hoping that this would increase our throughput for screening to atl east 4 times more than our current monthly output with standard PCR-based workflow.

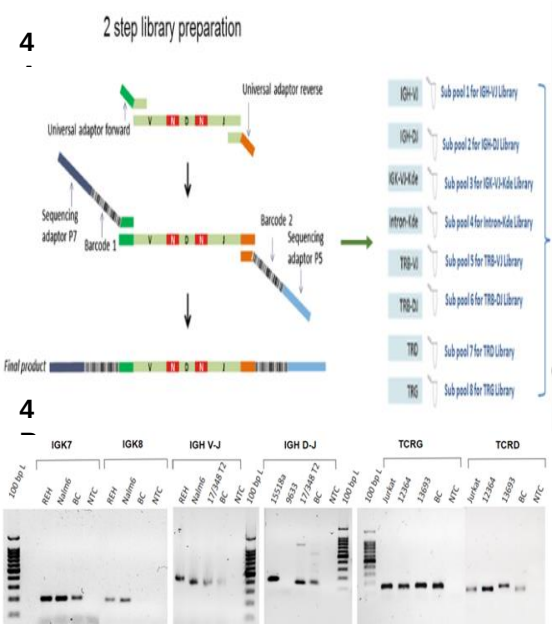

Figure 4. **A** Schematic workflow of NGS-based MRD marker identification developed by EuroClonality-NGS group, showing the 'two-step' library preparation approach. **B** 'First round PCRs' in Ig/TCR loci (TRG, TRD, IgK, IGH) showing amplification with positive controls and buffy coat (BC) DNA. No amplification seen in 'No template control' (NTC).

In addition to this, we have collaborated with DKMS who are developing an alternative approach for marker identification and MRD quantification using unique molecular identifiers (UMI) (Figure 5). Sequencing is initially being standardized using Illumina and would later be done using the Oxford Nanopore technology, MinION.

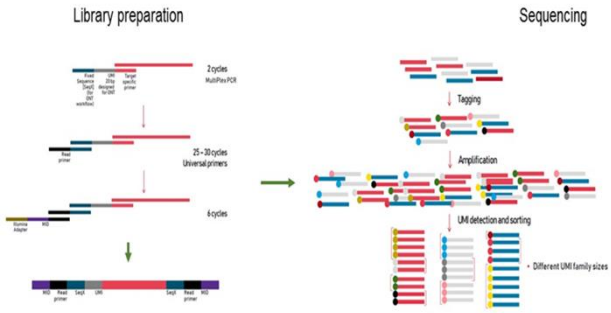

Figure 5. Schematic workflow of the UMI-based NGS assay developed by DKMS for MRD marker identification and MRD quantification in ALL.

Going forward, we wish to adapt the EuroClonality-NGS workflow on MiNION using the dual-pore R10 flow cells and compare our findings with that of Illumina for both the approaches. MinION-based sequencing will not only lower the costs of sequencing significantly but also provide greater flexibility in terms of multiplexing samples at reduced run-times. We are optimistic to develop this in collaboration with DKMS, which would allow for wider access to smaller centres, who lack expertise and resources to set up a sequencing facility.

Genetic Characterisation of ALL and Gall Bladder Cancer

We have studied a cohort of total 57 high-hyperdiploid (HeH) BCP-ALL patients included from the ongoing multi-centric clinical trial (InPOG-ALL-15-ICiCLe-ALL-14; CTRI 2015/12/006434) between 2015 to 2019 of ALL patients in Tata Medical Center (TMC), Kolkata. As HeH subtype is characterized by gain of chromosomes, a high-density SNP array analysis (using CytoScan HD platform, Affymetrix) was also performed to get additional information on the copy number alterations (CNA) in these patients which further revealed the

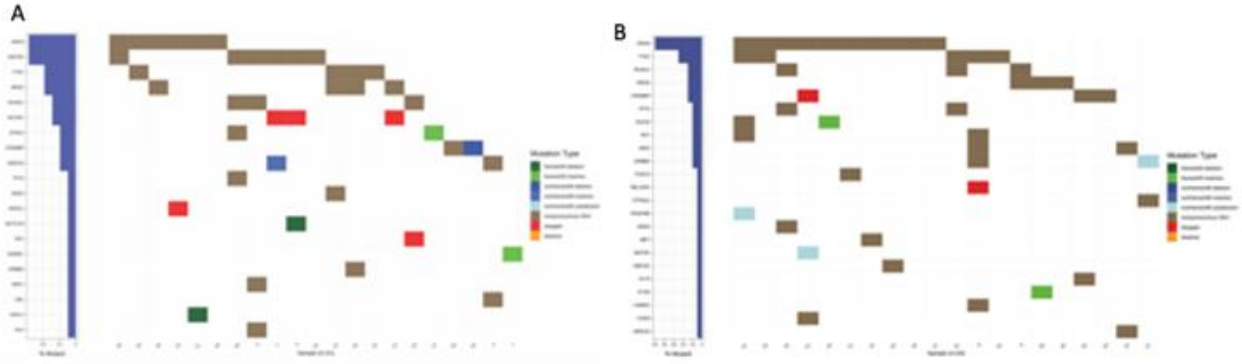

Figure 6. Waterfall plots of UPD (A) and non-UPD (B) sample cohort.

presence of whole chromosomal uniparental disomies (wUPDs) within a subgroup of patients (44%). We previously reported our mutational findings in HeH patients based on the Targeted Sequencing Panel. Genes involved in RAS signalling pathway (*KRAS*, *NRAS* and *TYK2*) as well as genes which act as chromatin modifiers (*KMT2D* and *CREBBP*) were mutated in almost 69% of samples. Further analysis on the mutation signatures between the UPD and non-UPD patients revealed that mutations in *KRAS*, *TYK2* and *ERBB2* genes were more frequent in nUPD patients whereas genes like *KMT2D*, *NRAS* and *ARID1A* harbor more mutations in UPD patients.

We have also performed the whole transcriptomic profiling of 28 HeH patients to identify the differentially expressed genes in UPD (n=14) vs nUPD (n=14) cohort. A tSNE analysis showed four distinctive clusters in patients based on presence or absence of UPD samples.

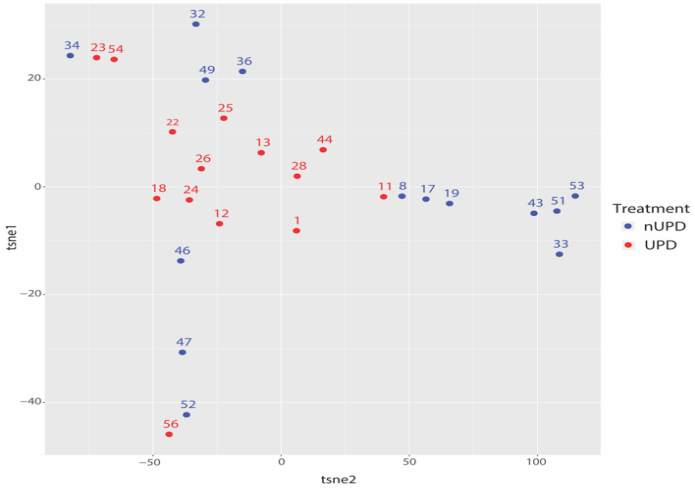

Figure 7. The tSNE plot of 1000 most variable genes derived transcriptomic data of 14 UPD and 14 non-UPD.

Different combinatorial approaches were considered to identify the differentially expressed genes within our sample cohort. Consensus predictive methods determined 40 upregulated and 11 down-regulated genes in UPD and nUPD patients. The identified genes were further considered for their functional analysis. The pathway enrichment analysis shows their probable involvement in signal transduction, transcription regulation, protein metabolism, transport mechanism and disease related pathways. However, cellular response to stress, cell cycle regulation, apoptosis, programmed cell death and regulation of immune systems were found to be upregulated only in UPD patients.

In the coming year, we are also embarking into the genetic characterisation of B-Other ALL which represents one of the most heterogeneous and complex molecular subtype of BCP-ALL. Lack of reliable prognostic markers often interfere with risk stratification and therapeutic interventions in these patients which

further leads to poor treatment response and relapses. Hence we aimed to characterize the genomic landscape of “B-others” using whole genome SNP array (CytoSNP 850K) and mRNA sequencing approach to improve prognosis and disease management.

Integration of genetic information like copy number alterations (CNAs) and single nucleotide polymorphisms (SNPs) with treatment response in patients and exploring the novel fusions and gene-expression through transcriptome sequencing may improve the clinical outcome in these patients.

We are also establishing a genomic pipeline in TTCRC to better characterize gall bladder cancer (GBC) based on two high-throughput approaches – 1) whole exome sequencing (100X) of GBC tumour samples to explore the somatic mutational profile and 2) m-RNA sequencing of GBC tumour and tumour-derived organoid samples.

Computational Biology

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Lead - Bioinformatics

Tushar Mungle

Clinical Informatician

Sangramjit Basu

Bioinformatics technologist

The computational biology group at TTCRC investigates the complexity in cancer biology by integrating large data sets generated by different experimental conditions. These include identification of genomic variants, e.g somatic copy number variations, single nucleotide variations, differential gene expression patterns, protein expression and the putative impact on cancer. The department is currently equipped with high-end computational facilities which include sophisticated tools and techniques in-terms of computational power and storage.

The TTCRC computational biology group works on multi-omics data. This includes identification of patient-specific biological markers using genomic and transcriptomic profiling of sample cohorts. solid and liquid tumour studies. High throughput sequencing data derived from Illumina and Oxford Nanopore platforms provide data on genomics and transcriptomic data. Proteomics data is generated from samples analyse on a Triple TOF and Imaging data from a high throughput confocal microscope.

Structural Variance and Single Nucleotide Variation Detection

Computational approach provides an in-depth understanding in determining the chromosomal structural variance from whole genome analyses. Sequencing data derived from a 95 gene panel across the sample cohort provided a better understanding in detecting the mutational burden across the sample cohort. To minimize manual intervention, the data were processed through a standardized multi-layered workflow. Each step accounts for processing of data through rigorous filtration criteria, leading to identification of pathogenic variants.

Transcriptomic analysis and Fusion gene identification

Transcriptomic data processed through in-house multi-layered automated analysis

pipeline respectively. The process ensures prediction of high-quality reads derived from protein coding region. Differential gene expression analysis is done from normalized reads counts and multiple statistical programs. This provides a basic understanding in the change in gene expression patterns among the different experimental groups. RNAseq data are processed to determine the probable fusion transcripts within the sample cohort using our multi-layered robust in-house pipeline. Fusion transcripts are identified with high confidence with experimental validation. Additionally, mutation detection derived from RNAseq data provides an addition layer of filters in validating the somatic variants determined from the gene panel sequencing data.

Functional characterization of differentially expressed gene sets

Downstream analyses lie in investigating the potential biological effects of genes expressed differentially in the sample cohorts. Differentially expressed genes were considered for pathway discovery. The approach used key differentially expressed genes, likely to be involved in disease processes. This process is known as Functional Gene Set (FGS) analysis.

High-throughput microscopy image analysis

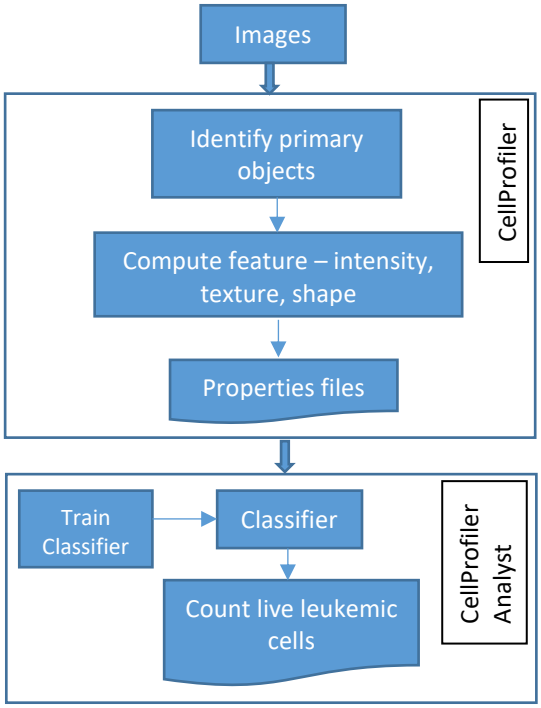


Figure 1: Overview of image analysis pipeline for live leukemic cells quantification.

Imaging based drugs screening process involves treating primary ALL cells in co-culture with several drugs in different log concentrations. Images are then acquired and analysed for population of live leukemic cells. CellProfiler and CellProfiler Analyst software is used to quantify the live leukemic cells from the images. Primarily, all the objects are identified from the images. Different features related to cells such as intensity, shape, and texture are computed that is followed by training the classifier based on the features for live leukemic cells as positives and the rest as negatives. The trained classifier classifies the cells from the set of images to give live population of leukemic cells for respective drug treatments. Figure 1 provides an

overview image analysis workflow developed for the work.

High throughput Proteomics analysis

Proteomics analysis rely on data acquisition process in terms of both Data Dependent (DDA) and Data independent (DIA) acquisition mode. The DDA analysis is a multi-step process which includes combination of multiple tools and PeptideShaker. Initially file formats are converted and most intense 250 peaks are obtained for downstream analysis. The selected peaks are searched against human proteome (Uniprot database) using multiple algorithms like Xtandem and MSGF+. Results are merged at 0.01 FDR with PeptideShaker. Obtained results are used to create a sample group specific spectral library which is in turn used to quantify the elucidated proteins from the SWATH (DIA run) traces. This analysis is executed in Skyline. Both PeptideShaker and Skyline are application with intuitive graphical user interface that helps to both visualize the data as well perform data Quality Check.

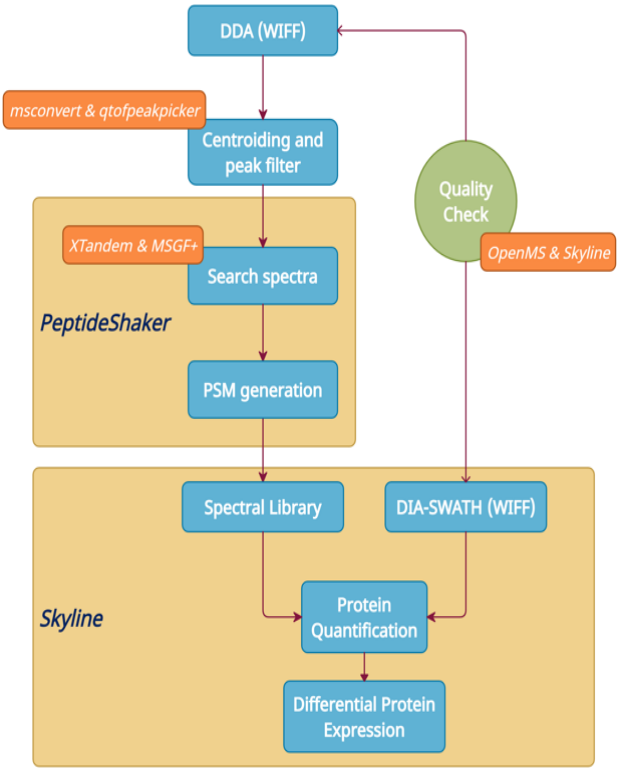


Figure 2: Schematic representation of proteomics analysis pipeline used for data acquisition and interpretation respectively.

India Alliance Fellows

Arunabha Chakraborty

IA Early Career Fellow

The role of the IK6 isoform of IKZF1 in childhood acute lymphoblastic leukaemia

My research goal is to investigate the mechanisms by which the imbalances in *IKZF1* isoform expression promotes leukaemic cell survival under cytotoxic stress. Understanding the impact of *IKZF1* deletion isoforms, particularly IK6, on cell survival after chemotherapy and the mechanisms of drug resistance in leukemic clones with the deletion.

Hypothesis:

IKZF1, in association with other transcription factors (e.g. *PAX5*) restricts the supply of glucose and energy to pre-B cells to initiate differentiation. Wild-type *IKZF1* (IK1) is transported to the nucleus and functions as a dimer. It is a transcription factor and acts both as an activator and a repressor. The IK6 (Δ4-7) isoform lacks the DNA binding domain and nuclear localising signal. It does not enter the nucleus and cannot function as a transcription factor. It retains the carboxyl zinc finger interactive domain, which could

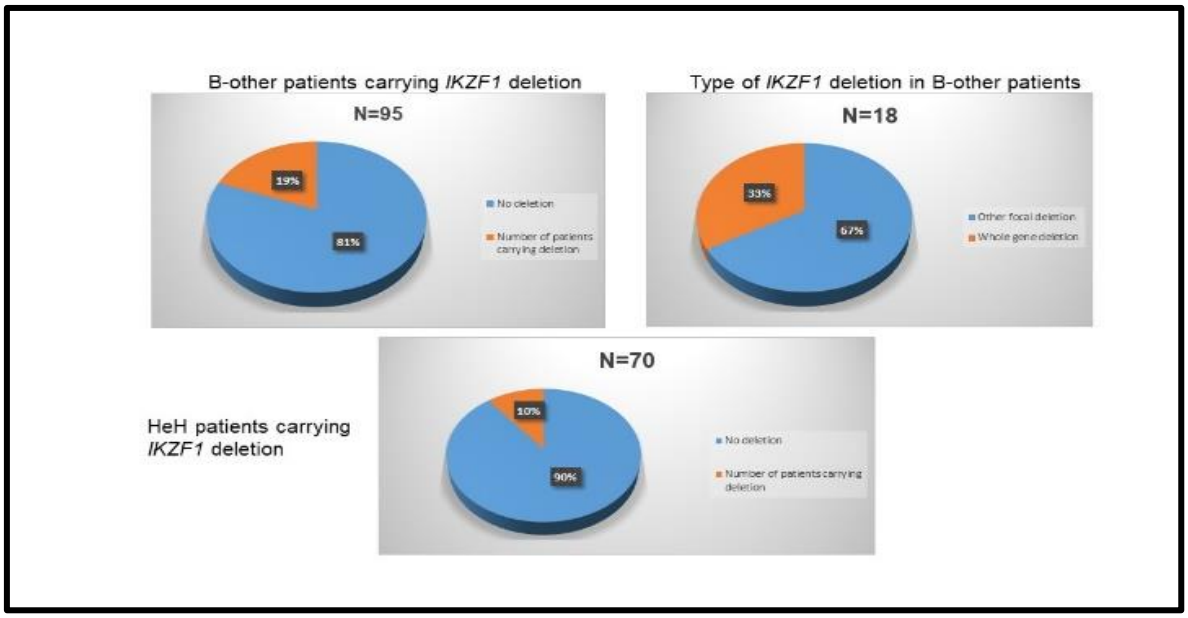


Figure 1. Screening of BCP-ALL patients for *IKZF1* deletion revealed the highest propensity of deletions found in B-other BCP-ALL (19%). 10% of the HeH patients were found to carry a deletion in *IKZF1*. Deletions were either a whole gene deletion or focal deletions. Δ4-7 was found to be the most prevalent among all the focal deletions in our patients

impede IK1 entry into the nucleus due to heterodimerisation. in the cytoplasm to prevent its tumor suppressor function. I hypothesize that, IK6, at least in part, is responsible for the metabolic adaptation of the leukemic cells with its microenvironment. This promotes survival. I also hypothesize that clones carrying an Ikaros deletion, are more adhesive and invasive in nature. This allows these cells to migrate from the bone marrow to other organs.

Why is this study important?

A. This study will establish the pathways through which IK6, the deletion isoform of Ikaros, implements its role towards leukaemic cell survival and resistance of the leukaemic clones against chemotherapeutic drugs.
B. Novel functions of IK6 will be identified.

Current findings/expected outcome:

Patient screening for *IKZF1* deletion

Screening of BCP-ALL patients at Tata Medical Center to identify presence of *IKZF1* deletions in different cytogenetic subtypes. This has been done using multiplex PCR based approach specific for *IKZF1* gene (Fluorescent PCR); followed by fragment analysis, Multiplexed Ligand-dependent Probe Amplification (MLPA) which analyses 9 genes including *IKZF1* and Cytoscan HD (Affymetrix) which a genome wide SNP array analysis.

Patient screening data suggested that propensity of *IKZF1* deletion is maximum in the B-other cytogenetic subtype of BCP-ALL (19%) (Figure 1) and it is seen in 10% of paients with High Hyperdiploid (HeH) (Figure 1). In our patients, deletion of *IKZF1* in exon 4-7 (Δ4-7), which expresses the IK6 isoform is the most prevalent of all the focal deletions found in *IKZF1*.

CRISPR-Cas9 based knock-out of *IKZF1* in leukaemia cell line NALM6

A CRISPR-Cas9 mediated knock-out of *IKZF1* (IK-KO) has been performed in leukaemia cell lines NALM6. IK-KO clones were sorted using GFP expression and propagated in several passages. Absence of IKAROS expression was confirmed by western blot analysis. Five different IK-KO clones were selected and propagated

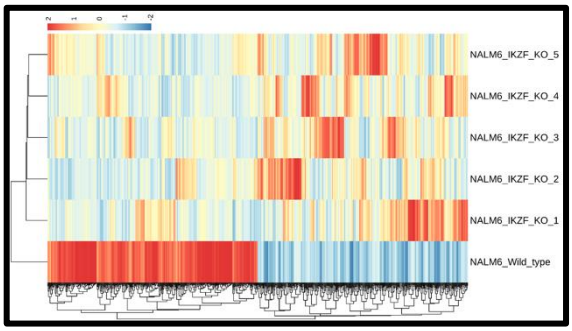


Figure 2. Heat-map of differential gene expression in five *IKZF1*-ko NALM6 cell lines compared to the NALM6-wt cell lines

in culture. These IK-KO cell lines were used further for differential gene expression and compared to that of the NALM6-wt cells.

Transcriptomic analysis of the *IKZF1*-KO NALM6 cell line compared to the NALM6 wild type (NALM-wt) cell line

We performed RNA-sequencing (RNA-seq) to compare the transcriptome profile of the *IKZF1*-KO NALM6 cells (five different single cell clones) as well as NALM6-wt cell line. Gene expression profile (GEP) of both the cell lines revealed that there are distinct GEP of the knock-out cells compared to that of the wild type cells (Figure 2).

Pathway analysis of the top 350 up- or down-regulated genes in the *IKZF1*-ko NALM6 cells revealed that genes involved in important pathways related to leukaemia were found to be differentially expressed in the *IKZF1*-ko NALM6 cells compared to the NALM6-wt cells (Figure 3).

Gene set enrichment analysis (GSEA) with the differentially expressed genes in *IKZF1*-ko NALM6 cells showed number of genes enriched in the gene sets ALL cell proliferation and glucose metabolism.

Further analysis of the *IKZF1*-KO NALM6 cells using SWATH proteomics is ongoing for a better understanding of pathways and proteins altered in the *IKZF1*-ko NALM6 cells compared to the NALM6-wt cells. After the proteogenomic analysis is established and candidates are identified to be involved in the disease process, validation will be performed with samples from BCP-ALL patients.

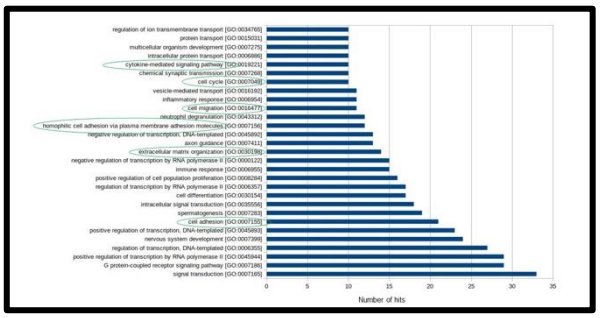


Figure 3 Major pathways represented by top 350 up- and down-regulated genes in IK-KO NALM6 cell line compared to NALM6-wt

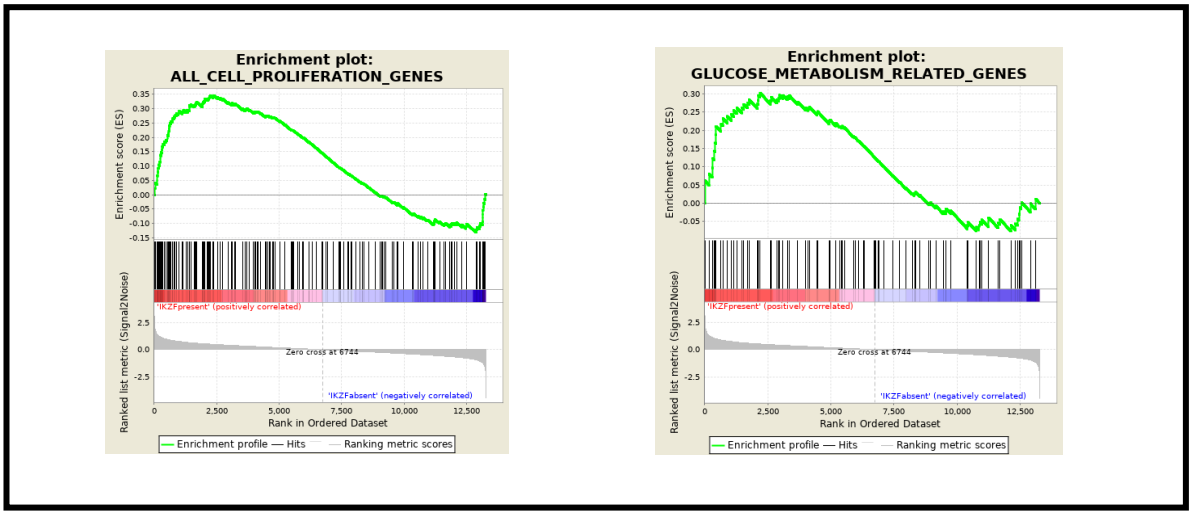


Figure 4. Gene set enrichment analysis for genes involved in ALL cell proliferation and glucose metabolism

in progress:

Characterisation of the cells with different Ikaros status are being performed using several functional studies under different types of stress (e.g. chemo stress, glucose deprivation, serum deprivation) in hypoxia and normoxia; with respect to cell viability/proliferation, cell cycle, apoptosis. A IK-KO is being created in the RS 4;11 ALL cell line as well to validate the findings from NALM-6 cell line models. Lentiviral transduction of IK6 into the IK-ko cell lines has already been done to generate IK6 overexpressed NALM6 cell lines. Re-introduction of IK1 to study whether cells are going through rescue from IK6 effects is the next plan in near future.

Proteogenomic characterization of cell lines as well as patient samples with different Ikaros status are ongoing for development of rapid identification of biomarkers.

Jasmeet Sidhu
IA Early Career Clinical Fellow

Developing strategies for acute lymphoblastic leukaemia patients with poor therapeutic response

Summary: Therapeutic options for patients with poor treatment response or patients with relapse/refractory acute lymphoblastic leukaemia (ALL) are limited. *Ex-vivo* drug screening has a positive correlation with clinical patient response. High-throughput phenotypic drug screening can identify alternate sensitive agents for patients with difficult-to-treat or poor response ALL and can help design personalised effective therapies for these patients.

Background: Childhood ALL is characterised by prognostically significant genetic subtypes. Genotype based risk stratified chemotherapy cures >85% of patients in the west [1,2]. Within all prognostic subcategories, the most significant determinant of outcome is the minimal residual disease (MRD) burden after induction therapy. The current understanding is that chemo-resistant subclones survive induction and cause MRD and ultimately, lead to relapse [3]. In India, a risk-adapted MRD strategy is used in the national clinical trial for childhood ALL (ICiCLe-ALL-14; CTRI/2015/12/006434). Post-induction intensification of therapy in those with MRD levels $\geq 10^{-4}$ improves outcome[4]. But still, ~20% of patients relapse and have limited therapeutic options. A better understanding of the factors that contribute to MRD in children on the ICiCLe-ALL-14 protocol is required for further optimisation of therapy to improve outcomes.

Hypothesis: Automated agnostic phenotypic high-throughput drug screening can identify alternate therapeutic agents for patients with difficult-to-treat ALL (MRD ≥0.01% or relapsed refractory disease).

Aims: Decreasing the MRD burden can be achieved in ICiCLe-ALL-14 by identifying alternative induction agents in genetic subgroups prevalent in Indian children.

Research objectives:

1. High-throughput imaging-based *ex vivo* drug screening to identify anti-tumour drug combinations in real time
2. Transcriptomic studies to identify drug survival mechanisms using an *ex vivo* model of MRD

Methodology:

Cell culture and reagents: Immortalised human bone marrow cell line, hTERT, was cultured in DMEM (Invitrogen) with 10% foetal bovine serum (FBS).

Cytotoxicity and viability assays: Drug responses were assessed in primary ALL cell cocultures on hTERT-immortalized primary bone marrow mesenchymal stromal cells (MSCs) (**Figure 1**). MSC (2.5x10^3 cells/well) were plated in 384-well plates (Greiner) in 30µL serum free medium (AIM-V., Life Technologies). After 24h incubation at 37°C, 5% CO2, 2.5 x 10^4 viable leukaemia cells suspended in 30µL medium were added and incubated for an additional 24h followed by addition of drug solution. Drug stock solutions were prepared in dimethyl sulfoxide (DMSO; stored at -20°C). Six serial log dilutions (10 µL per well) were used in triplicates for screening. Optimal concentration rages were calculated based on the frequency distribution of IC50 values per each drug and as reported previously. After 72h of incubation with compounds, live cell numbers were evaluated using CyQUANT (Life Technologies) live cell staining (7µL per well) and incubated for 1 hour at 37°C, 5% CO2. Automated imaging was performed using the ImageXpress microscope (Molecular Devices) with 10x Plan Fluor objective (Nikon) (covering 70% of the well surface). Images were processed and analysed using Metaexpress (Molecular Devices). Drug response quantification was performed using curve-fitting non-linear regression on

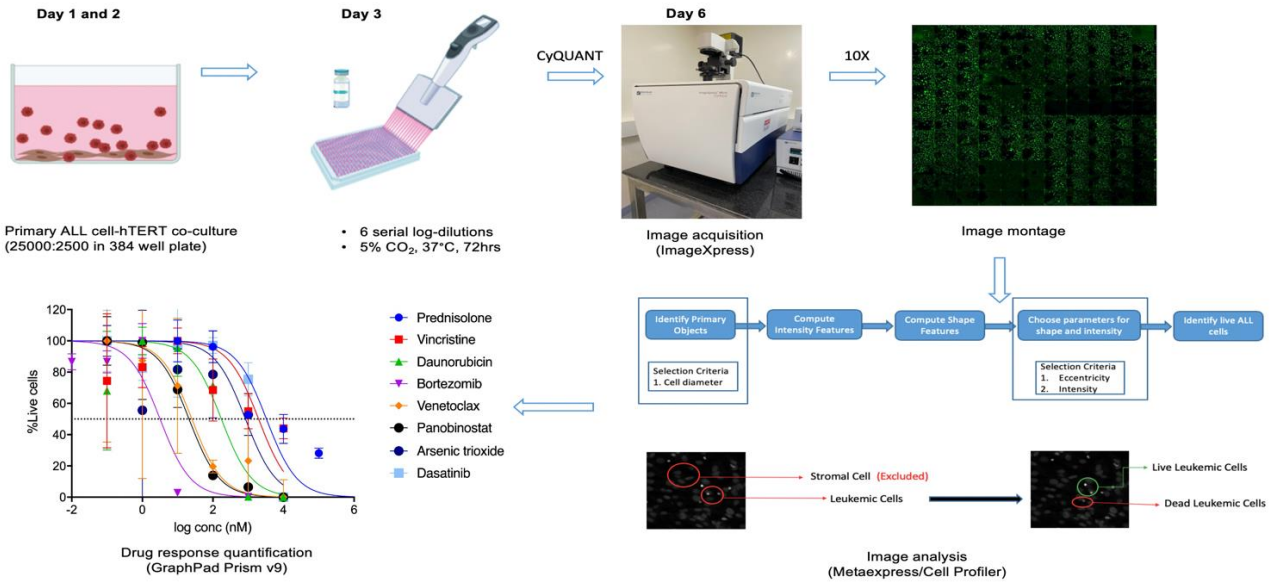


Figure 1: Schematic representation of high-throughput drug screening pipeline

ALL, acute lymphoblastic leukaemia, CO_2, carbon-dioxide

Table 1: Patient characteristics

	N
Age (years)	
Mean	8
Range	3 - 18
Sex	
Male	11
Female	6
Immunophenotype	
Precursor B	11
T	6
Risk (frontline patients)	
SR	3
IR	2
HR	9
Cytogenetics	
ETV6-RUNX1	2
HeH	3
BCR-ABL1	0
KMT2Ar	1
TCF3-PBX1	3
B-others	1
TAF15-ZNF384	1
Unknown/T	6
<0·01%	8
≥0·01%	4
Pending	2

data normalized against untreated samples (GraphPad Prism version 9).

Drug resistance profile: A drug resistance profile was made for each patient by combining the results in *ex-vivo* sensitivity to induction drugs (prednisolone, vincristine, daunorubicin and asparaginase). For each of 4 induction drugs except prednisolone, patients were classified into 3 groups as sensitive (33% lowest IC50 values), intermediately sensitive (33% intermediate IC50 values), or resistant (33% highest IC50 values) [5]. For prednisolone, these 3 groups were defined using cut-off values of 1µM and 64µM as previously reported [6]. Sensitivity toward a drug was scored as 1, intermediate sensitivity was scored as 2, and resistance was scored as 3 for each individual drug. Combining the separate scores of 4 induction drugs of each patient resulted in an individual PVAD score that varied between 4 (sensitive to all three drugs) and 12 (resistant to all three drugs).

Results: Total of 17 ALL (11 BCP ALL and 6 T ALL) patients were profiled with *ex-vivo* drug screening using cryopreserved pre-treatment diagnostic samples (ICiCLe-ALL-14 study cohort). Patient characteristics are in **Table 1**. The mean viability of the recovered ALL cells was 69% after thawing (determined using Trypan

blue exclusion assay) with mean blast percentage 78%. Median PVAD score in patients with MRD <0.01% and MRD ≥0.01% was 6 and 8 respectively. But there was no statistically significant correlation of PVAD score with MRD (Spearman correlation coefficient: r=0.6, P=0.057). This could be due to a smaller number of patients screened till now.

Drug screening was performed for an average of 7 drugs (range 4-9) per sample (**Figure 3**) and identifies different ex-vivo drug sensitivity response pattern in patient with low and high MRD. In samples of patients with MRD≥0.01% or relapsed/refractory patients, a group of drugs was found to be sensitive in drug screening (**Figure 4a**). These include venetoclax (*BCL-2* inhibitor), bortezomib (proteosome inhibitor) and panobinostat (histone deacetylase inhibitor). Dasatinib was found to be additionally sensitive in a subset of T-ALL patients (**Figure 4b**). It has been previously reported by our group that patients with T ALL having high *SRC* expression are sensitive to dasatinib[7].

Future plan:

<u>Short-term goals:</u>

- Refining and launching cell profiler-based image analysis pipeline

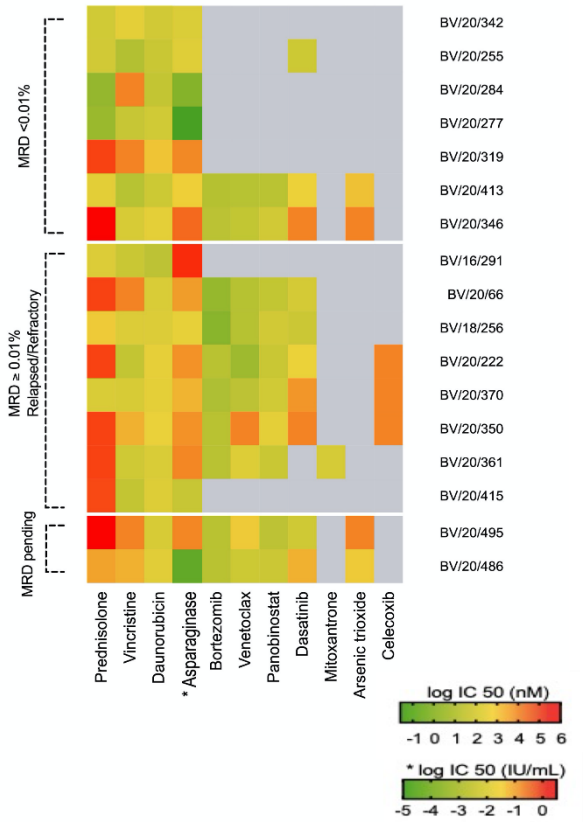
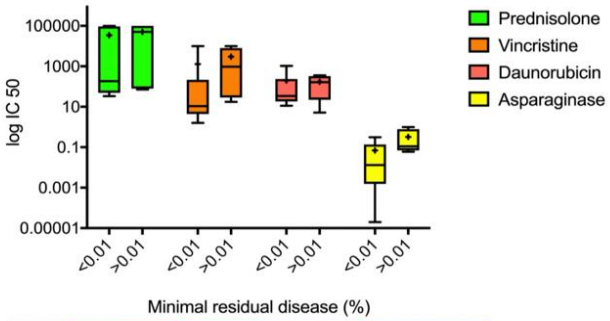


Figure 2: Heatmap showing relative ex-vivo drug response (log IC50) to 9 drugs screened across primary ALL cells of varying genomic subtypes and MRD response (N = 17). Grey boxes represent drug(s) not tested for patient. log, logarithm, MRD, minimal residual disease, IC50, half-maximal inhibitory concentration, nM, nanomolar

- Merging the image analysis pipeline with drug response quantification
- Widen the panel of drugs used for screening (use automated liquid handling system)
- Use of synergy-finder tools to identify sensitive drug combinations
- Use of multi-drug screening to identify & isolate "MRD" cells – understand mechanism of drug resistance

<u>Long-term goals</u>

- Systematic evaluation of DRP as potential strategy for HR patients in frontline therapy



	Prednisolone		Vincristine		Daunorubicin		Asparaginase	
MRD (%)	<0.01	>0.01	<0.01	>0.01	<0.01	>0.01	<0.01	>0.01
Median	0.2 µM	50 µM	11 nM	955 nM	34 nM	163 nM	0.01301 IU/mL	0.1117 IU/mL
IQR	0.05 – 93 µM	0.08 – 100 µM	4 – 216 nM	29 – 7962 nM	18 – 236 nM	22 – 329 nM	0.0015 – 0.07 IU/mL	0.07 – 0.78 IU/mL

Figure 3: Positive association of *ex-vivo* drug response to induction therapy drugs and end-of-induction MRD.
(**A**) Boxplot representation of log IC50 values for prednisolone, vincristine, daunorubicin and asparaginase against MRD categories (<0.01% and >0.01%) (N = 11). Boxes represent interquartile ranges, whiskers encompass values between the 5th and 95th percentile, horizontal bars and '+' within boxes indicate median and mean values respectively, (**B**) Inset table denotes IC50 values (median and IQR) in MRD <0.01% and >0.01% groups [Log, logarithm, MRD, minimal residual disease, IC50, half-maximal inhibitory concentration, IQR, inter-quartile range, µM, micromolar, nM, nanomolar, U/ml, units per millilitre]

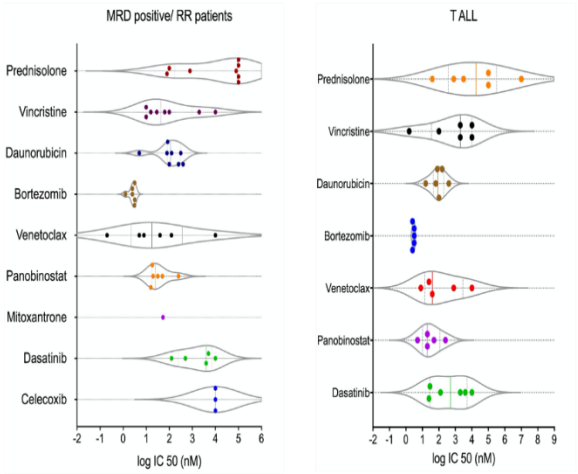


Figure 4: Distinct drug activity patterns detected for individual patients and sub-groups of interest.
(**A**) Violin plot represents drug response as log IC50 (nM) of primary relapsed/refractory and MRD >0.01% ALL patients (n = 8) tested using banked diagnostic bone marrow samples. Data represents persistent resistance to standard chemotherapy and individual sensitivity to alternate drugs. Each dot represents a patient. The vertical bars inside each violin plot denotes median (solid line) and inter-quartile range (dotted line). (**B**) Scatter plot representation of drug response of T ALL patients to alternate therapies [log, logarithm, MRD, minimal residual disease, IC50, half-maximal inhibitory concentration, nM, nanomolar, RR,

- Potential pre-treatment drug screen platform to develop phenotypic personalized therapy

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IA Early Career Fellow
Leukaemia Cell Biology

Welcomed 2020 on a high-spirited note. I had identified that ALL cells with *TP53* deletion were resistant to anthracyclines, most likely by downregulating expression of p53 direct targets involved in apoptosis (e.g. *FAS*, *TNFRSF10B*) and cellular stress (*TP53INP1*, *ZMAT3*) (Annual Report 2019). Excitement of returning to TTCRC and an increased vigour to maximise my academic time at Alderley Park marked my final months at University of Manchester. And then the world came to a standstill (literally!).

Self-isolation, post my return to Kolkata, was followed by an urgency to help set up the COVID-19 testing centre at Tata Medical Center. The p53 project seemed like a fanciful thought. While most of the team members were working from home, a few of us trickled into the offices and lab to work out the transition from "work-from-home" to "work-on-site" for the rest. Those were difficult 4 months, with more to learn than any experimental failure or success could have ever taught us.

Come August, with the team members back on site (some of who were new faces for me), we resumed lab work. Much to my delight, the p53 project became a reality again. The project welcomed a new member, Arko Bhowal. Two young interns, Ananya Mahadevan and Amrita Roy, courageous souls with a desire to expand their technical prowess joined the p53 bandwagon. While Amrita focused on validating results (Figure 1A) from the transcriptomic profiling of p53WT (wild-type) and p53KO (knockout) clones performed in University of Manchester in 2019, Ananya got busy establishing wild-type

TP53 in a lentiviral backbone (Figure 1B) to rescue the effects of p53 loss on downstream signaling.

While at Alderley Park, I had the opportunity to use the Agilent Seahorse extracellular flux analyser and assess the mitochondrial activity of p53WT and p53KO clones under steady state conditions (Figure 2A). We hypothesised that chemoresistance results from an altered metabolic state; a shift from glycolysis to oxidative metabolism. Evidence is mounting in favour of this hypothesis [1-5]. Exposure to sub-lethal doses of mitoxantrone revealed a small population of viable p53WT cells with enhanced mitochondrial activity (Figure 2B). The data indicates that p53KO cells are driven by oxidative phosphorylation without or with stress, whereas, some p53WT cells can switch from glycolysis to oxidative metabolism under conditions of cytotoxic stress. This metabolic plasticity implores further investigation.

Much awaits 2021. Ananya is optimising her protocol for site-directed mutagenesis to establish p53 mutants (p.G245S/R and p.R248Q/W) and introduce these in p53KO cells. Amrita plans to cross-examine the transcriptomic profile with the proteomic profile of unstressed and stressed p53WT versus p53KO and/or p53 mutated cells. Our aim is to identify pathways enriched in cells lacking functional p53 that can explain the chemoresistant phenotype of p53 altered cells. Arko faces an uphill task. He has to demonstrate that increased

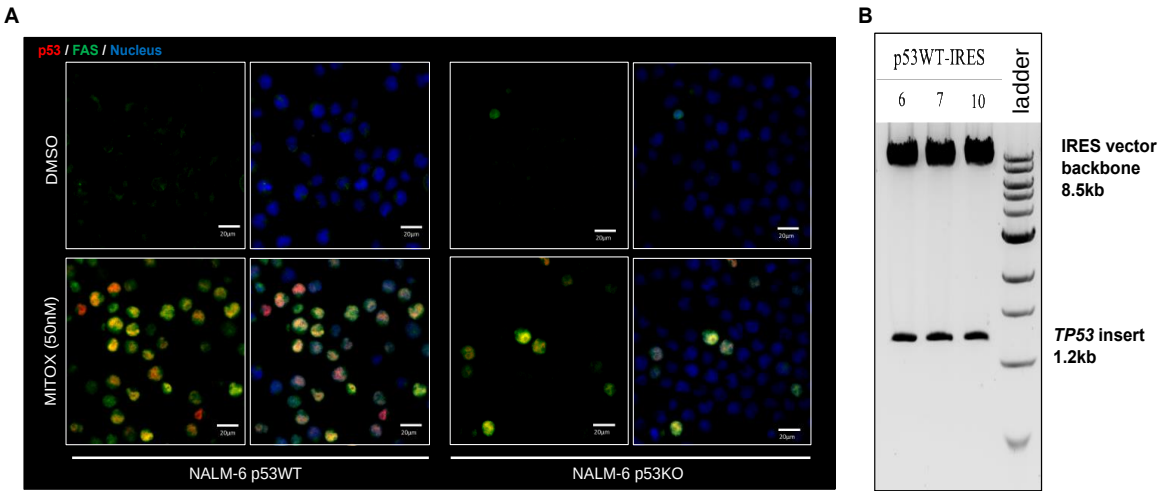

Figure 1: Establishing tools to study p53's role on stress adaptation.
A: p53 was deleted in ALL cells with wild-type p53 (NALM-6) using CRISPR-Cas9. Mitoxantrone-treated p53WT cells co-expressed FAS and p53. p53KO cells failed to elicit expression of both FAS and p53, validating the loss of *TP53,*
B: Wild-type *TP53* was cloned into IRES lentiviral backbone. Clone #7 will be used to rescue the effect of p53 functions. WT, wild-type; KO, knockout; MITOX, Mitoxantrone.

mitochondrial activity marks chemoresistant cells. His aim is to identify a common mechanism of stress adaptation involving mitochondrial respiration. Overall, we aim to establish a p53-regulated expression profile in conjunction with the ability to adapt to stress to identify patients likely to fail conventional chemotherapeutic protocols before starting therapy. We expect our work to identify novel processes of drug resistance with the potential of developing cheaper and less toxic therapies.

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5. van Gastel, N., et al., *Induction of a Timed Metabolic Collapse to Overcome Cancer Chemoresistance.* Cell Metab, 2020. **32**(3): p. 391-403.e6.

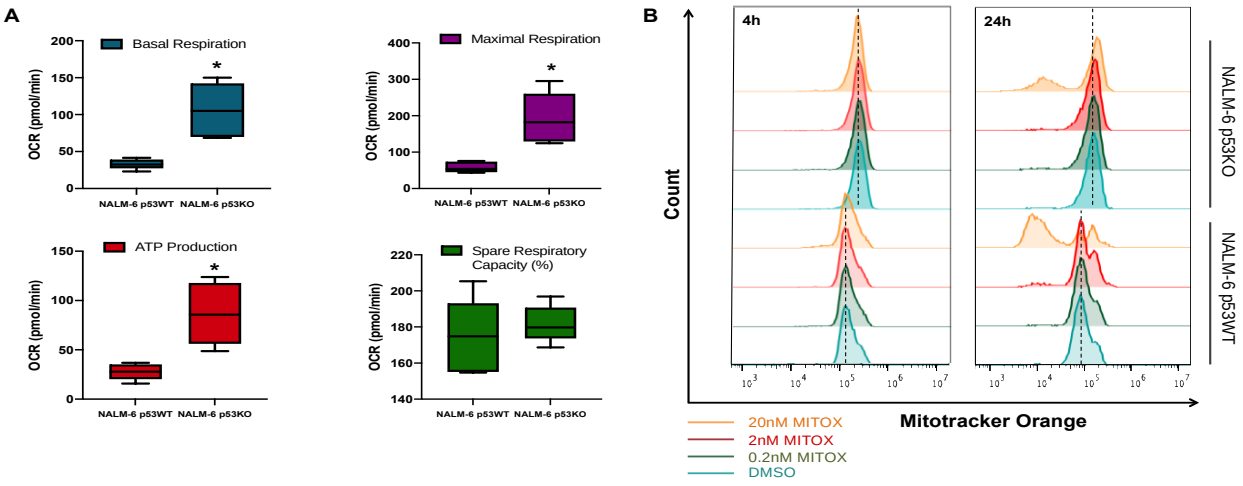


Figure 2: Loss of wild-type p53 increases mitochondrial activity in ALL cells *in vitro*.
A: Under steady-state conditions, NALM-6 p53KO cells exhibit high mitochondrial activity in terms of basal respiration, maximal respiration and ATP production in comparison to p53WT cells,
B: p53KO cells without or with Mitoxantrone treatment demonstrate higher mitochondrial activity (dotted line) in comparison to p53WT cells. Mitochondrial membrane potential (MMP) as a measure of mitochondrial activity was assessed by Mitotracker Orange staining (n = 2, in triplicates). OCR, Oxygen consumption rate; WT, wild-type; KO, knockout; MITOX, Mitoxantrone. * denotes p = 0.05.

TCS at TTCRC

Amit Saxena
Head
Genomics and Translational Research

Anju Goel
Head
Translational Research Platform

Binuja Verma
Principal Investigator
Genomics and Translational Research

TCS is contributing to accelerate research initiatives by deploying platform and solutions for Translational Research. TCS is also collaborating with TTCRC on projects related to Knowledge Graph based insight generation and Imaging Analytics. TCS solutions also support multi-center clinical trials and analytics of data from EMR and other systems.

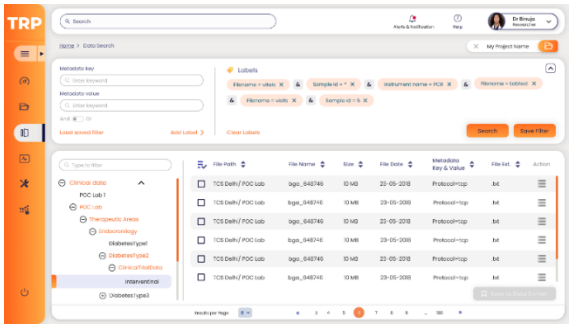
The Translational Research Platform has undergone a technology refresh. It is now cloud based with new and improved features. The UI is more intuitive to the needs of scientists and researchers. Scalability of the platform is enhanced for large volumes of data storage and processing. Some of the key features include Project management, Metadata based Data Search, Data Corner, Tools Repository and Analytics Corner.

Translational Research Platform Features:

Data Search

Users will be able to search for files based on metadata key value pairs e.g., file type, name, owner, Ext. etc. using the platform feature. Users can access files based on hierarchy/folder structure in data search.

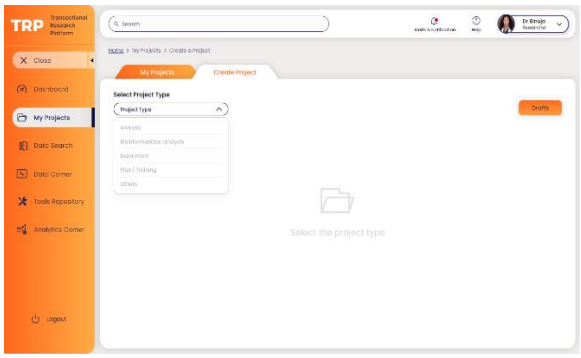
Data Corner



Users will be able to view & select platform files and save them into Saved Data tab to be used further. Users can upload his/her own files in My data for processing and further analytics.

My Projects

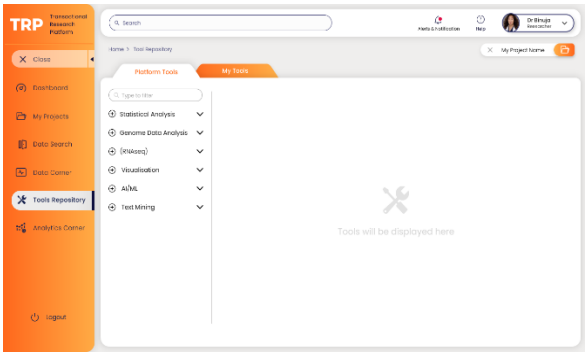
Users can define projects and capture project related information. Users will be



able to access My Projects in the platform to organize and manage the data files and perform related analysis within a workspace. Each workspace can have multiple projects in it.

Tool Repository

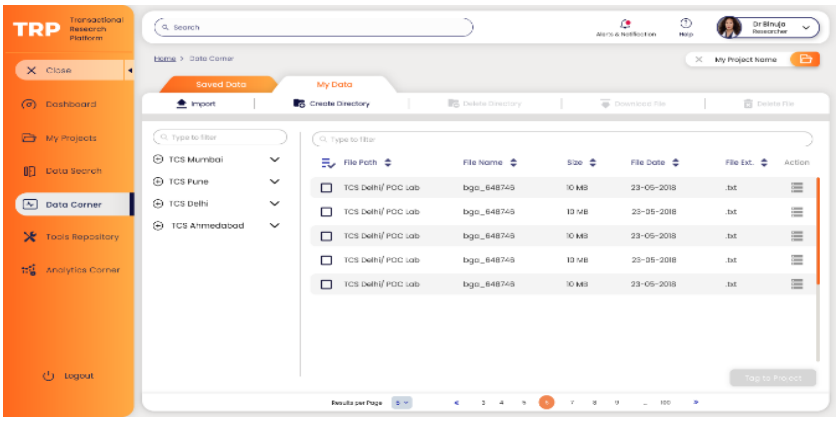
Users will be able to view and select tools for Analysis based on roles/permissions.



Analytics Corner

Users will be able to create workflow/pipelines in Analytics Corner in the platform to perform analysis using CLI (Command Line Interface) tools. Users can launch Notebook in Analytics Corner for coding in R/ Python.

Fig: Translational Research Platform – Data Corner



Projects and Initiatives:

High-throughput imaging-based ex vivo drug screening to identify anti-tumour drug combinations in real time

We have initiated an Imaging Data Analytics project with the Researchers at TTCRC. The project aims to develop Imaging Data Analytics workflows and algorithms to analyze high throughput images generated for ex vivo drug screening to identify anti-tumour drug combinations in real time in ALL patients. Aim is to develop an image processing application which is able to detect the live cells present post drug infusion into the culture. These cultures are imaged on different days to understand the efficacy of various drugs on the cancer cells. The amount of data which gets generated per patient is quite huge (around 20GB per patient) as different drugs are tried on the culture in high-throughput drug screening machine. Current image analysis software in use does not have the necessary accuracy and is not robust as it is using intensity and shape features only.

Use of Knowledge Graphs for Exploratory Analysis

Assess comparative effect of chemotherapy on patients with and without UPD in high Hyper- diploid ALL patient's Initial analysis dataset has 25 UPD patients and 33 non-

UPD patients. Out of this, RNA-sequencing has been performed for 28 patients (13 UPD and 15 non-UPD patients). Top 97 upregulated and 80 downregulated genes in patients with UPD were identified by PI. Our primary objective is to use knowledge-graph based approach to identify significant gene-disease relationships in these patients for prioritizing expressed proteins as probable targets. Some of the public databases used for creation of the knowledge graph include data from UCSC, Uniprot and Reactome among others.

ICiCLe Trial website development:

The ICiCLe ALL-14 Trial Website was developed to reach patients and their families, health care professionals, researchers, and the public on a wider scale so that they can have easy access to information on the study.

The website focuses on all the aspects of the treatment protocol being used to treat the patients with ALL and therefore helps us to understand the benefits of this multicenter randomized trial. This study website also answers many of the queries which are being frequently raised by the patients and other people and moreover gives us a glimpse about the collaborating centers as well as the funding bodies associated with this trial.

The website can be accessed via the TTCRC homepage at https://icicle.ttcrc.org/

Pretrial Cost Analysis:

Evaluation of impact of risk stratified therapy on direct treatment costs in patients with ALL treated at the hospital. Calculation and Analysis of Direct Medical Cost of Treatment on ICiCLe Protocol - Assessment in the Pre-trial cohort of Tata Medical Center Kolkata. Some of the data extracted include:

1. IP Cost, OP Cost, Overall Cost as per various categories of billing.
2. Length of stay, ICU Admissions, IP Admissions, Emergency ward admissions data.
3. Discharge summary data, First admission and discharge dates for patients, Bifurcation of each category and subcategories of billing.

Integrated Data Management for ICICLE trial:

ICICLE is the first clinical trial created on IDM for TTCRC. This is a multicenter trial to create treatment strategy for Acute Lymphoblastic Leukaemia (ALL), which is the most common cancer of childhood. This clinical study will help to improve outcome of clinical treatment. Clinical DB is set up as per complex requirements to collect, review and analysis of data for patients enrolled for study. We have supported to resolve technical challenges faced by users and to improve user experience. There is a data for 2000+ patients entered in IDM and DB is capable

to handle data with stability. We will support to meet upcoming clinical study milestones.

The Consolidated dataset (consisting of more than 300 columns) was created by combining data related to Registration, Risk Stratification, Study Consent forms along with details of End of Induction, End of Consolidation, Randomization 1, Eligibility for SR, Randomization 2 as well as Death, Relapse and Trial Withdrawal forms from CTMS. Since this complex report consists of information of multiple forms combined, it makes easy for clinicians to analyze the data in a consolidated manner rather than looking across data separately for each of those forms.

r-ALL1 on IDM

This is the second clinical study built on IDM. This study will assess the feasibility of a uniform strategy to manage first relapse ALL and evaluate event free survival with this protocol. This study is built on IDM. There were additional complex requirements added by the study team after study build to reduce errors and to generate quality data for patients enrolled. We have collaborated extensively with programming team to explain, plan, and implement changes in the database. These approaches will help to get clinical data generated with high accuracy and reduce cycle time for review and analysis of data.

Translational Study in Breast Cancer: Markers and tools for the prediction of response to radiation therapy /or sensitivity

Collaborators: Dr. Sanjoy Chatterjee, Dr. Rosina Ahmed

The ongoing project is a part of **HYPORT Trial** which aims to develop markers and tools for the prediction of response to radiation therapy /or sensitivity in breast cancer patients undergoing Hypo-Fractionated Radiotherapy Schedule of 35GY in 10 Fractions in advanced incurable Breast Cancer

Summary

As radiation therapy is a key modality in the treatment of cancer, it is of tremendous importance to increase our understanding of the molecular pathogenesis of radiotherapy toxicity. This will lead to find ways of predicting those patients likely to suffer with long term side effects and to develop new approaches for their management. The field of radio genomics is expanding with evidence of genetic polymorphisms underlying inter-individual differences in radiotherapy responses. The effective response to ionizing radiation (IR) exposure is complicated by biological heterogeneity, as certain patient tumors may be inherently more insensitive to a given dose of IR. We are working in developing markers and tools for the prediction of response to radiation

therapy/or sensitivity in breast cancer patients undergoing a specific protocol of Radiation therapy. This is a retrospective study design using bio banked Fresh Frozen and FFPE samples, with the aim to identify the genetic markers of clinical toxicity and investigate the clinical response of breast cancers to hypo fractionated course of radiation therapy. Currently exome sequencing data is being generated in a pilot set of samples (pre and post treatment) which would be analyzed for potential genetic alteration that could be correlated to clinical toxicity and outcome of therapy. We would also attempt to build a pan cancer analysis of possible molecular and cellular mechanisms contributing to radiation toxicity and response. This is to gain a deeper understanding of mechanisms of radiation response and thereby the clinical outcome as it is hypothesized based on the contribution of different factors including genetic aberrations, epigenetic alterations, changes in the response to cellular signaling, metabolic alterations, and beyond. This can be done using publicly available data like from TCGA, IGCA etc. integrating multi-omics data comprising of whole exome sequencing, transcriptome, epigenome and proteomics.

Current Status

We have initiated the genome sequencing project with the objective to analyze and identify the genetic variations associated with clinical toxicity and treatment response. The pilot phase of the study is being completed. In this phase we have standardized and established the experiment and analysis pipeline for exome sequencing using DNA extracted from a subset of FFPE study samples (N=12/fine needle biopsy samples). The SOPs and protocols for the wet lab methods have been developed. Currently bioinformatics pipelines for analyzing WES data is being standardized.

NGS data Analysis

A. Variant Calling

NGS analysis for variant calling (SNVs/indels/CNVs) have been completed.

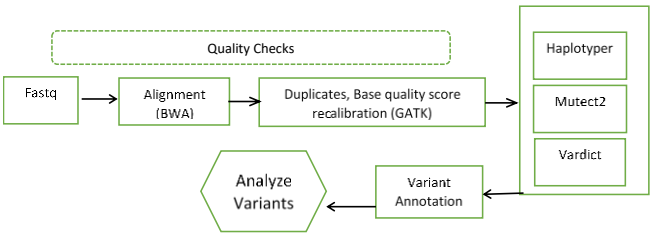


Fig1: Overview of Variant calling pipeline

B. Variant Annotation and filtering

Method is being finalized.

Next Steps

To complete the data Analysis

Correlate genetic variation with clinical data (clinical outcomes)

System Medicine Cluster (SyMeC)

Geetashree Mukherjee
Senior Consultant
Histopathology

ORAL CANCER RESEARCH

The project is in collaboration with the National Institute of Biomedical Genomics (NIBMG), Kalyani, and funded by the Department of Biotechnology, Govt of India, New-Delhi.

PI Geetashree Mukherjee, CO-PI Vivek Radhakrishnan, Co-Investigators: Deepak Mishra, P. Arun and Joydeep Ghosh.

The study investigates the relationship between genomic alterations and tumor immune microenvironment in oral squamous cell carcinoma – gingivo buccal (OSCC-GB) with the aim to identify prognostic and predictive biomarkers. The Primary Objective is to determine whether the burden of genomic/epigenomic alterations in the tumor correlates with immunological diversity in treatment naïve, OSCC-GB patients.

Methodologies being used at Tata Medical Center (TMC) are a) Immunohistochemistry (IHC) and b) Flow Cytometry (FACS).

IHC: On 124 cases have been performed for 40 markers.

FACS: 40 samples (Tissue) & 40 samples (Blood) have been performed till date. Rest of the samples could not be processed or were incomplete due to inadequate number of cells. Experiments are ongoing with more samples.

RESULTS TILL DATE - LIKELY TO CHANGE AS THE STUDY IS ONGOING. SEQUENCING IS BEING DONE AT NIBMG, THE RESULTS OF WHICH WILL BE INTEGRATED.

Summary till date :

- SCC-GB - Hot or Altered Immune (98.38%)
- Consistent expression of PDL-1 (87.096%)
- Over all picture is that of “Exhausted T lymphocytes”.

Probable mechanism of immune escape of tumor cells is predominantly by expressing PDL-1.

Other possible mechanisms of immune escape:

- IDO & COX2 } High IDO-1 and COX-2 expression in the tumour cells are thought to facilitate T cell anergy and immune escape.
- Hypoxia - The HIF 1 α expression in tumour cells was consistent in each sub-group of CD8. (both IM & CT); provide a motivation to observe the HIF 1α association with PDL-1 expression at metabolomics and RNA Seq level.

There is a good level of concordance betweee Flow data and IHC data.

Publications:

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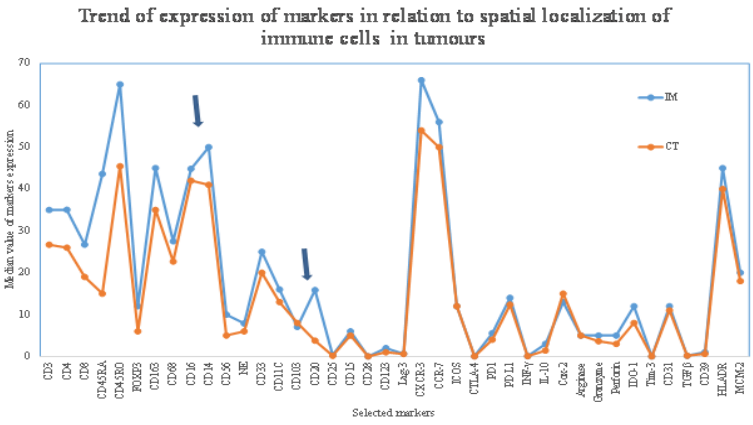
Clinical and translation study on cervical cancer

Tata Medical Center is the clinical nodal center of this consortium with NIBMG, IICB, IISER, Bose Institute and ISI and is funded by Department of Biotechnology (DBT) from 2017 till 2021.

SyMeC cervical cancer screening study (CSS)

Aims and Objectives: Identify biomarkers for HPV persistence in screened positive women and help develop a triage strategy for colposcopy and treatment for precancerous lesions.



A screening cohort of 2502 women was recruited from Jan 2018 - Sept 2019 by primary HPV testing and Qiagen HC2 Hybrid Capture II test detected 253(10%) women positive for HPV infection. These women were further evaluated by colposcopy to detect precancerous lesions caused by HPV. In women (89%) who underwent colposcopy and directed biopsy, we identified 46% women with no HPV related lesions, 44% women with low grade HPV infection – koilocytosis and CIN 1, and 9.2% women with high grade infection – CIN 2 & 3. To help formulate a triaging strategy after primary HPV screening, women with low grade lesions were followed after 1 year with a repeat HPV test; women with CIN2 were followed for 6 months before undergoing treatment and women with CIN3 underwent treatment immediately. This protocol would identify women with persistent HPV infection and those with progression of CIN2 lesions. These clinical and biomarkers parameters will provide information that will help stratify colposcopy referrals in order to improve detection of high-grade lesion and prevent overtreatment of low-grade lesions. The clinical parameters with regards to cervical biopsy and high-risk HPV genotypes of the HPV positive women have been generated (Table 1&2). The follow-up of these patients is ongoing to identify women who have "persistent" HPV infection and those who have "cleared" the HPV infection on subsequent visits. We intend to analyze further the cervical scrapes and blood of these women to identify the reason for persistence and clearance of HPV infection which plays an important role in the development of cervical cancer.

Screen and treat approach	No. of colposcopies	Normal	K'cytosis	CIN1	CIN 2&3	PPV HSIL	PPV for all lesions
HPV primary screening	253	95	28	73	21	8.3%	48.2%
HPV primary screening + HPV 16/18 triage	86	31	11	25	10	11.6%	53.4%
HPV primary screening + HPV 16/18/31/33/45/52/58 triage	129	47	17	38	12	9.3%	51.9%

Table 1: Stratifying colposcopy referrals

HPV genotype	Number of women with HPV subtypes	Normal	Koliocytosis	CIN1	CIN2	CIN3	CIN2& CIN3	PPV CIN2/3
ANY HPV	253	95	28	73	17	4	21	8.30%
HPV 16	54 (21.3%)	20	6	15	5	1	6	11.10%
HPV 18	37 (14.6%)	13	5	11	4	1	5	13.51%
HPV 31	11 (4.3%)	5	2	2	1	0	1	9.09%
HPV 33	7 (2.7%)	0	2	3	0	0	0	0
HPV 35	4 (1.5%)	1	0	2	0	0	0	0
HPV 39	4 (1.5%)	2	1	1	0	0	0	0
HPV 45	10 (3.9%)	5	1	3	0	1	1	10%
HPV 51	22 (8.6%)	8	0	4	2	2	4	18.18%
HPV 52	14 (5.5%)	3	1	7	0	0	0	0
HPV 56	20 (7.9%)	11	1	2	4	0	4	20%
HPV 58	27 (10.6%)	9	4	8	2	1	3	11.10%
HPV 59	9 (3.5%)	5	0	1	3	0	3	33.33%
HPV 68	39 (15.4%)	12	4	17	0	0	0	0
HPV 16 & OTHERS	22 (8.6%)	10	0	8	2	0	2	9%
HPV 18 & OTHERS	11 (4.3%)	2	3	4	1	1	2	18.20%
Non 16/18 HPV TYPE	21 (8.3%)	9	3	3	2	0	2	9.50%
UNDETERMINED	67 (26.4%)	25	8	18	4	0	4	5.90%

Table 2: HPV genotypes and cervical biopsies

SyMeC translational cervical cancer study (TCS)

Aims and Objectives: Identify biomarkers of treatment failure to standard chemo radiation therapy, identify possible biomarkers and radio sensitizers that can reduce this failure and recurrence of cervical cancer.

A cohort of 190 women with cervical cancer were recruited to facilitate translational work at NIBMG and IICB to identify genomic and immune signatures/biomarkers that would be correlated to their outcomes to treatment and survival status. The analysis is ongoing and will be available next year. A subset of these cancer patients will have their functional imaging by MRI and PET CT to analyze the parameters such as ADC texture, diffusion and metabolic parameters. This is likely to help with improved diagnostic performance for assessing high- grade cervical carcinomas, parametrial invasion, lymph node metastasis, stages III–IV, and recurrence relative to the performance of using ADC values. This analysis and follow-up of patients is ongoing till 2021-22.

Team Composition:

PI: Dr Mammen Chandy ; Co-PI: Dr Jaydip Bhaumik, Dr Sanjay Bhattacharya, Dr Geethashree Mukherjee, Dr Divya Midha, Dr Santam Chakraborty , Dr Saugata Sen, Dr Aditi Chandra, Dr Sumit Mukhopadhyay, Dr Soumendranath Ray, Dr Jayanta Das; Project Consultant: Dr Sonia Mathai;Project Staff: Shrabanti Sarkar Ghosh, Barnali Ghosh, Anuradha Biswas, Manali Mukherjee, Ajit Mukhopadyay, Anamika Palit, Kasturi Das, Sona Chowdhary, Thumpa Das, Priya Hati, Rama Gupta, Shyamali Mondal, and Dr Ratnaprabha Maji.

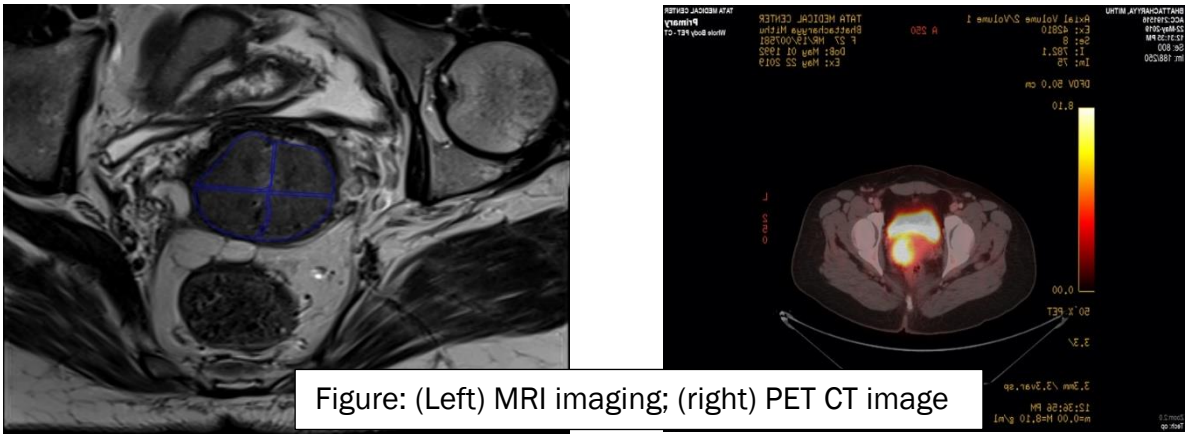


Figure: (Left) MRI imaging; (right) PET CT image

Clinical Hematology Oncology and HCT

Vivek Radhakrishnan

Senior Consultant

Clinical Hematology and BMT

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Dr. Saurabh Bhave *MD, PDF*

Dr. Jeevan Kumar Garg *MD, DrNB, PDF*

Dr. Arijit Nag *MD MRCP(UK) DM PDF*

Ongoing Investigator Initiated Translational Projects

1. Acute Myeloid Leukemia, ALTITUDE Study

- Peer Reviewed Grant funding by Tata Education and Development Trust
- Joint Institutional Collaborators: Laboratory Hematology, Molecular Pathology, Cytogenetics and Microbiology
- PI: Dr. Vivek Radhakrishnan
- To establish a Precision oncology work platform at Tata Medical Center in patients with Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome with excess blasts (MDS-EB). Multimodal-omics based comprehensive genomic Characterization of a uniformly treated cohort of AML patients,

accompanied by MRD assessments.

- and SOPs. The enrollment of the patients is ongoing, and as for now 30 AML patients were screened, out of which 19 were recruited in the study. Biobanking is being carried out for Bone marrow aspirate (mutational profile and MRD) and faecal-oral microbiome samples at different time points (as per the study protocol).
- For the gene mutation profiling and MRD assessment, targeted sequencing panel and cancer database are being developed. Standard Bioinformatics pipeline for data analysis has been developed and is undergoing validation. With the in-principle approval of a related grant, the immune cell profile at defined timepoints will be assessed by two distinct methods of estimating the immunoscore viz., immunohistochemistry (IHC) with Digital Image Analysis and Nanostring Digital Spatial Profiling using Tissue Microarray.

2. **CLARION Project: Academia Industry Collaboration to establish a Cellular Immunotherapy Program for Cancer patients.**

- **We have established the** infrastructure, manpower, protocols
- Peer-reviewed Grant funding approved in-principle: Department of Biotechnology, BIRAC
- Industry partner: Intas Pharmaceuticals, Ahmedabad
- Study Chair: Prof. Mammen Chandy
- Principal Investigators: Dr. Vivek Radhakrishnan (TMC) and Dr. Lakshmikanth Gandikota (Intas)
- The goal of this study is to establish a clinical grade Cellular Therapy (specifically CAR-T Cell manufacturing) and a clinical administration facility at Tata Medical Center Kolkata, and further facilitate the clinical development of indigenous CAR-T cell and other cellular immunotherapies.
- Infrastructure development ongoing: This will establish a and commission a cGMP facility is ongoing.
- After full funding received equipment and clinical trial/regulatory submissions will begin

3. Immuno-Oncology: GIFT Study

- Peer-reviewed Grant funding through Department of Biotechnology Systems Medicine Cluster project for cancers of Cervix

and Oral cavity (Gingivo-buccal sulcus)

- PI: Dr. Geetashree Mukherjee
- Co-PI: Dr. Vivek S Radhakrishnan [Immuno-oncology component]
- Genomic Immune profile of Tumour-Excavating the relationship between genomic alterations and tumor immune microenvironment in oral squamous cell carcinoma – gingivo buccal (OSCC-GB) to inform immunotherapy.

Ongoing Investigator Initiated Prospective Clinical Trials

1. **PRIME STUDY:** Effect of Pomalidomide Bortezomib- Dexamethasone induction on MRD status in patients with newly diagnosed Multiple Myeloma.

- PI: Dr. Vivek Radhakrishnan/ Dr. Jeevan Kumar
- To determine the activity of a combination of Pomalidomide-bortezomib dexamethasone as initial therapy in NDMM, by assessing response using MRD assessment.
- Patient recruitment ongoing.

2. **R-BED Study**- Phase II study of Bortezomib, Etoposide, Dexamethasone combination therapy, with or without Rituximab, in Adult Relapsed or Refractory, B-cell Acute Lymphoblastic Leukemia who are transplant ineligible.

- PI: Dr. Vivek Radhakrishnan/ Dr. Arijit Nag
- To determine the safety and activity of a combination therapy containing Bortezomib, Etoposide and Dexamethasone, with or without Rituximab, in relapsed refractory adult patients with B-ALL.
- Patient recruitment and analysis ongoing

3. **RIC-FT10***:* Reduced Toxicity and Reduced Intensity conditioning regimen using Fludarabine and Treosulfan for high-risk hematological malignancies undergoing allogenic hematopoietic cell transplantation.

- PI: Dr.Vivek S Radhakrishnan/ Dr. Saurabh Bhave
- To evaluate the toxicity profile of Fludarabine and Treosulfan conditioning regimen as reduced intensity and reduced toxicity conditioning therapy in high risk hematological malignancies. To determine the 100 day regimen related toxicity.
- Patient recruitment ongoing.

Ongoing Investigator Initiated Registry Studies and Projects

1. National Lymphoma Registry Project- Database formation of details of lymphoma patients in ONCOCOLLECT software. [PI: Prof. Reena Nair]

2. National CML Registry Project- Database formation of details of CML patients in ONCOCOLLECT software. [PI: Dr. Vivek Radhakrishnan]

3. Institutional Acute Myeloid Leukemia and MDS Clinical database and cost-analysis outcomes project [PI: Dr. Vivek S Radhakrishnan]

4. International T-cell Lymphoma Project v2.0 [PI: Prof. Reena Nair]

5. CRIMSON Project- Database formation of details of cancer patients receiving immunotherapy and precision medicine in Tata Medical Center [PI: Dr. Vivek S Radhakrishnan]

6. CIBMTR Registry [CIBMTR (Center for International Blood & Marrow Transplant Research)], Hematopoietic Cell Transplantation and Cellular Therapies) [PI: Dr. Vivek S Radhakrishnan]

7. National IMAGE Study- Multiple Myeloma [PI: Dr. Jeevan Kumar].

Ongoing Pharma Sponsored Registry Studies:

1. Lymphoma: RITUXIMAB generic (Reditux):- Promise Registry to compare Effectiveness, Safety, and Resource Utilization of Reditux (Rituximab) vs. the reference Medicinal product to treat Diffuse Large B –Cell lymphoma and Chronic Lymphatic Leukemia in Routine Clinical Practice . The enrolment of patient for this study is completed and follow-up ongoing. [PI: Prof. Reena Nair]

2. Lymphoma: RITUXIMAB generic (Mabtas) :- A multi-center, observational, data collection registry study to monitor the routine clinical use of MABTAS in Indian patients". The enrolment of patients for this study is ongoing. [PI: Dr. Saurabh Bhave]

Ongoing Pharma Sponsored Clinical Trials: Ongoing/ Approved

1. A Phase 1 Study(SPARC): to Determine Safety, Tolerability, Pharmacokinetics, and Activity of K0706, a Novel Tyrosine Kinase Inhibitor (TKI), in Subjects with Chronic Myeloid Leukemia (CML) or Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia (Ph+ALL) Protocol No.: CLR_15_03 (Dr. Vivek S Radhakrishnan).

2. A phase 3(BOSTON): randomized, controlled, open label study of selinexor, bortezomib, and dexamethasone (svd) versus bortezomib and dexamethasone (vd) in patients with relapsed or refractory multiple myeloma (rrmm) karyopharm. Protocol No.: KCP-330- 023 (Dr. Jeevan Kumar).

3. Clinical Outcomes of CLL and MCL patients treated with Ibrutinib: An Observational retrospective medical chart review from India that may require exchange of certain information that is confidential and proprietary in nature. (Dr. Vivek S Radhakrishnan).

4. DARZALEX: A Prospective, Single-Arm, Multicenter, Pragmatic Phase-IV Trial Investigating Safety and Effectiveness of

DARZALEX (Daratumumab)In Indian Subjects With Relapsed and Refractory Multiple Myeloma, Whose Prior Therapy Included a Proteasome Inhibitor and an Immuno modulatory Agent. (Dr. Vivek S Radhakrishnan).

5. A randomized, double-blind, placebo controlled phase III multi-center study of azacitidine with or without MBG453 for the treatment of patients with intermediate, high or very high risk myelodysplastic syndrome (MDS) as per IPSS-R, or Chronic Myelomonocytic Leukemia-2 (CMML-2).

6. Clinical Outcomes of CLL and MCL patients treated with Ibrutinib: An Observational retrospective medical chart review from India that may require exchange of certain information that is confidential and proprietary in nature. (Dr. Vivek S Radhakrishnan).

Closed/Completed Studies:

1. A Phase 2, Open-Label Randomized Trial Evaluating the Efficacy and Safety of Two Dosages of Once Daily Oral CA-170 in Patients with Selected Relapsed Advanced Tumors (ASIAD). Protocol No.: CA-170-201. (Dr. Vivek S Radhakrishnan).
2. A Randomized, Double-blind, Multicenter, Multi-national Trial to Evaluate the Efficacy, Safety, and Immunogenicity of SAIT101 Versus Rituximab as a First-line Immunotherapy Treatment in Patients with Low Tumor Burden Follicular Lymphoma Protocol No.: AGB002. (Dr. Vivek S Radhakrishnan).
3. A Phase 2b Open-Label Study of Selinexor (KPT-330) in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma. Protocol No: KCP-330-009. (Dr. Vivek S Radhakrishnan).
4. Safety and efficacy study of Azadine® (Azacitidine): in treatment of myelodysplatic syndrome in indian patients. Protocol No.: 484-14. (Dr. Vivek Radhakrishnan).

Ex vivo models to dissect pathogenesis and improve outcomes in gallbladder cancer

Anindita Dutta
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This project was conceptualised in April, 2019. The aim is to understand why certain patients get gallbladder cancer and identify alternative therapeutic modalities. Due to its rarity in most part of the world, there is a lack of a representative model to study gallbladder cancer pathogenesis. In 2019, the team trained at the University of Cambridge in developing *ex vivo* organoid models. Subsequently, a dedicated research facility at TTCRC has developed patient derived organoid models of gallbladder and gallbladder cancer. The focus is on developing robust, representative, reproducible *ex vivo* model systems for fundamental research and high throughput drug discovery.

TMC Team Members

Manas Roy	(Surgery)
Sudeep Banerjee	(Surgery)
Saugata Sen	(Radiology)
Paromita Roy	(Pathology)
Mohandas Mallath	(GI)
Joydeep Ghosh	(Medicine)
Shrikant Atreya	(Palliative)

Past Member

Jaydeep Das

The Team: This is a multidisciplinary collaborative programme of research. At

the Tata Medical Centre, the clinical team includes the Hepato-biliary Surgeons, Digestive Disease, Medical Oncology, Palliative Care Unit, Radiology and Pathology. CRU works with the clinical and research team to follow up and track patients reporting to the clinic and undergoing treatment. TiMBR collects and processes samples from patients consented for the study. At TTCRC, DGS, SC and AkD are involved in processing clinical materials and developing *ex vivo* models. MP is engaged in creating resources to understand the molecular mechanisms of disease pathogenesis. AkD is in a PhD programme, jointly supervised by TTCRC and IIT-KGP, focusing on organoids models of gallbladder cancer. Analytical processes include integrated cell biology, genomics and proteomics analysis available at TTCRC. Jaydeep Das, involved in developing biomaterial-based scaffold for GBCa cells, has moved to pursue a PhD with IIT-Bombay and Monash University focusing on biomaterial-based culture of CAR-T cells.

Background:

While gallbladder cancer (GBCa) is rare in most parts of the world, North, East and North-East India with Pakistan have among the highest incidences internationally. It is uncommon in other parts of India. At Tata Medical Center, ~300 patients are diagnosed with GBCa per year. Due to its rare presentation in the high-income countries, limited chemotherapeutic interventions have been tested for GBCa. Outcomes are poor worldwide with a median survival of 6 months after diagnosis.

GBCa is more common in women and obese individuals. Geographical locations suggest a genetic predisposition. Gallbladder (GB) stones are implicated in the pathogenesis, although <3% of patients with GB stones develop GBCa. *Salmonella* spp. colonise the GB, are cytotoxic to human gallbladder cells and have been identified in GBCa samples.

Table 1

Reagents	Purpose
Williams E media without phenol red	Keep tissue moist
Rock inhibitors	Prevent cell death
EGF	Prevent cell death
b-mercaptoethanol	Maintain RNA integrity
Fluconazole	Antifungal
Amphotericin B	Antifungal
Penstrep	Antibiotic
Primocin	Antibiotic

Other risk factors associated with GBCa include type 2 diabetes, deficiency of zinc and selenium, exposure to copper, cadmium and other heavy metals, such as, arsenic.

The majority (>90%) of GBCa is adenocarcinoma. Of the ~1200 mutated genes identified, mutations of *TP53*

(*mutTP53*) are the most frequent. Activating *KRAS* mutations (e.g. KRAS G12D), are regularly (18%) found in Japanese patients, however, less frequent (7%) in Indian patients. Recently mutations in the *ELF3* gene have been identified in Indian patients with GBCa.

Aims:

(i) Develop preclinical models of gallbladder cancer pathogenesis.

(ii) Identify potential prognostic and therapeutic biomarkers.

(iii) Assess novel therapeutic modalities.

Hypothesis:

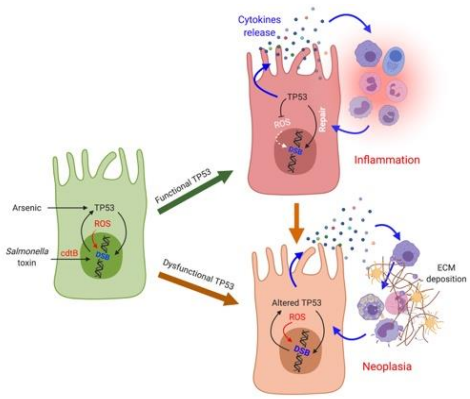


Figure 1. Schematic diagram of proposed model of GBCa pathogenesis.

We postulate that chronic tissue injury from combinations of exposure to biliary cholesterol, trivalent arsenic and salmonella toxin results in generation of oxidative stress in gallbladder epithelial cells leading to DNA damage of the GB epithelium. Stress-induced DNA damage with dysfunctional TP53 promotes neoplastic transformation (Figure 1). Aberrant epithelial cells interactions with stromal and infiltrating immune cells in the microenvironment further favour progression of the disease.

1.1. Establishment of an annotated tissue and organoid biorepository for GBCa

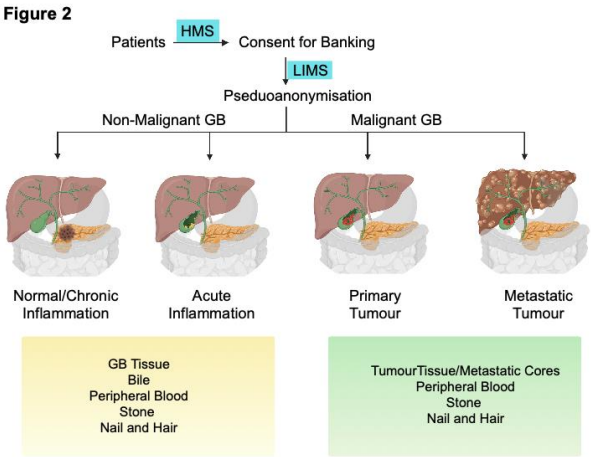


Figure 2. Schematic flow of GB/GBCa samples in the biobank. Non-malignant tissues are categorised as clinically normal or with chronic inflammation and acute inflammation. Malignant tissues are grouped either as primary tumour or tumour with metastasis. Tissue, peripheral blood, bile, stone, nail and hair are collected from respective patients.

Institutional Review Board approval for biobanking and use of biobanked samples was obtained in 2019. Samples are obtained from patients undergoing surgery or image guided biopsy at the Tata Medical Center. Tissues are categorised as normal GB, inflammatory GB (chronic or acute) and tumour GB (primary or metastatic). Transport processes for collecting and banking of high-quality tissue derivatives for downstream studies has been established (Table 1). Samples collected from each patient include primary tissue, peripheral blood, bile, nail and hair for nucleic acid, protein characterisation. Fresh samples are processed for *ex vivo* organoid model generation (described below in 3.1). The customised workflow is shown in Figure 2. Going forward, we aim to improve the conditions for banking of cryopreserved organoids.

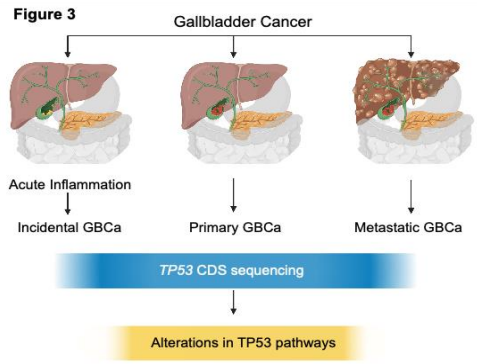


Figure 3. TP53 alterations in GBCa. Formalin fixed paraffin embedded blocks for tumour gallbladder obtained from patients with incidental GBCa, primary GBCa or Metastatic GBCa. Coding region of *TP53* gene sequenced and direct targets of TP53 studied in the corresponding section of blocks with immunohistochemistry.

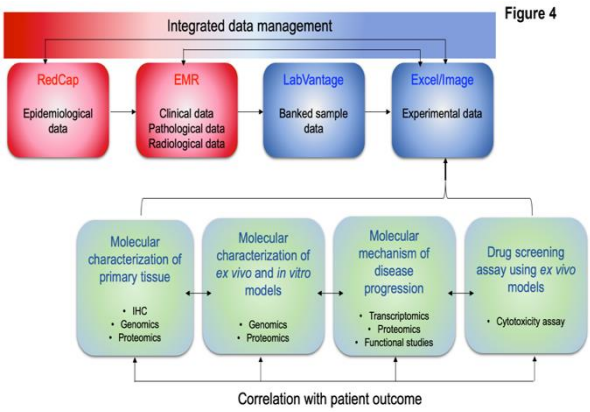


Figure 4. Overview of data integration for the GBCa project

1.2. Molecular and pathological characterisation of GBCa

Our hypothesis is that inflammation and TP53 alterations (genetic and/or epigenetic) contribute to tumour behaviour. To test this hypothesis, we aim to investigate the *TP53* mutation status in GB samples with inflammation (acute or chronic) and early detected (primary GBCa) or metastatic GBCa (Figure 3) along with the alterations in expression of TP53 target genes which regulate cell cycle, proliferation, apoptosis and angiogenesis pathways. Genetically modified cell lines and/or *ex vivo* models are being created to investigate the role of identified*TP53* mutants in disease progression and therapy response.

- TP53 CDS sequencing has been established (see section 4)

- TP53 sequencing of DNA extracted from buffy coats and organoids has been optimised
- Optimisation of DNA extraction and sequencing of *TP53* are ongoing
- All histopathology slides are jointly evaluated with the pathologists to identify degree of inflammation and phenotypic changes in the GB epithelium.

Prospectively we will test for correlations between the different types of TP53 alterations and the degree of inflammation and tumour behaviour in culture.

1.3. Integrated data management

Clinical data linked to each sample are recorded by the surgical team. Pathological and imaging features of the samples are evaluated by the pathologists and radiologists. All data are captured through the hospital EMR. Epidemiological information (including demography, family history, life-style) are entered into RedCap. Pre-analytical variables linked to each sample and downstream analyses of the samples are recorded in Excel. A comprehensive data management system (Figure 4) within the Translational Research Platform (TRP) is being created to integrate and analyse the clinical, epidemiological and research data linked to each sample.

2.1. Establishing a reproducible primary 3D organoid system

Organoids, representing the same basic intrinsic patterning events i.e. organ-like organization, are valuable tools for disease modelling. Development of tissue specific organoids relies on the pluripotent nature of tissue resident adult stem cells (ASCs) or embryonic stem cells. At TTCRC, three approaches have been established to derive organoids from malignant or non-malignant primary gallbladder tissues. Tissue is collected in media containing factors to preserve cell viability and tissue integrity. In specific culture conditions, mature cholangiocytes (COs) (left panels, Figure 5) or ASCs (middle panels, Figure 5) are enriched to generate the organoids from normal gallbladder. Organoids appear as a sphere with a clear lumen at the centre. Mature COs maintain planar cell polarity and are slow growing compared to ASC derived organoids. In a third approach, both ASCs and mature COs are extracted using enzymatic processing and maintained to enrich mature COs to develop organoids (right panels, Figure 5).

In xanthogranulomatous cholecystitis an enrichment of the disease phenotype was observed when mature COs were enriched (left panels, Figure 6). Diseased organoids were morphologically characterised by an irregular shape and darker lumen when compared to normal organoids. Only normal phenotypes were observed when organoids were derived by enriching ASCs (middle panels, Figure 6). A mix of both normal and diseased phenotypes were observed when a mix of ASCs and mature COs were cultured (right panels, Figure 6).

Comparative qPCR data shows enrichment of mature cell markers, *CFTR*, in the mature CO enriched organoids compared to the ASC enriched organoids (p=0.003). Expression of transient amplifying cell markers (*CK19, CK7, SOX9*) are consistently expressed in all

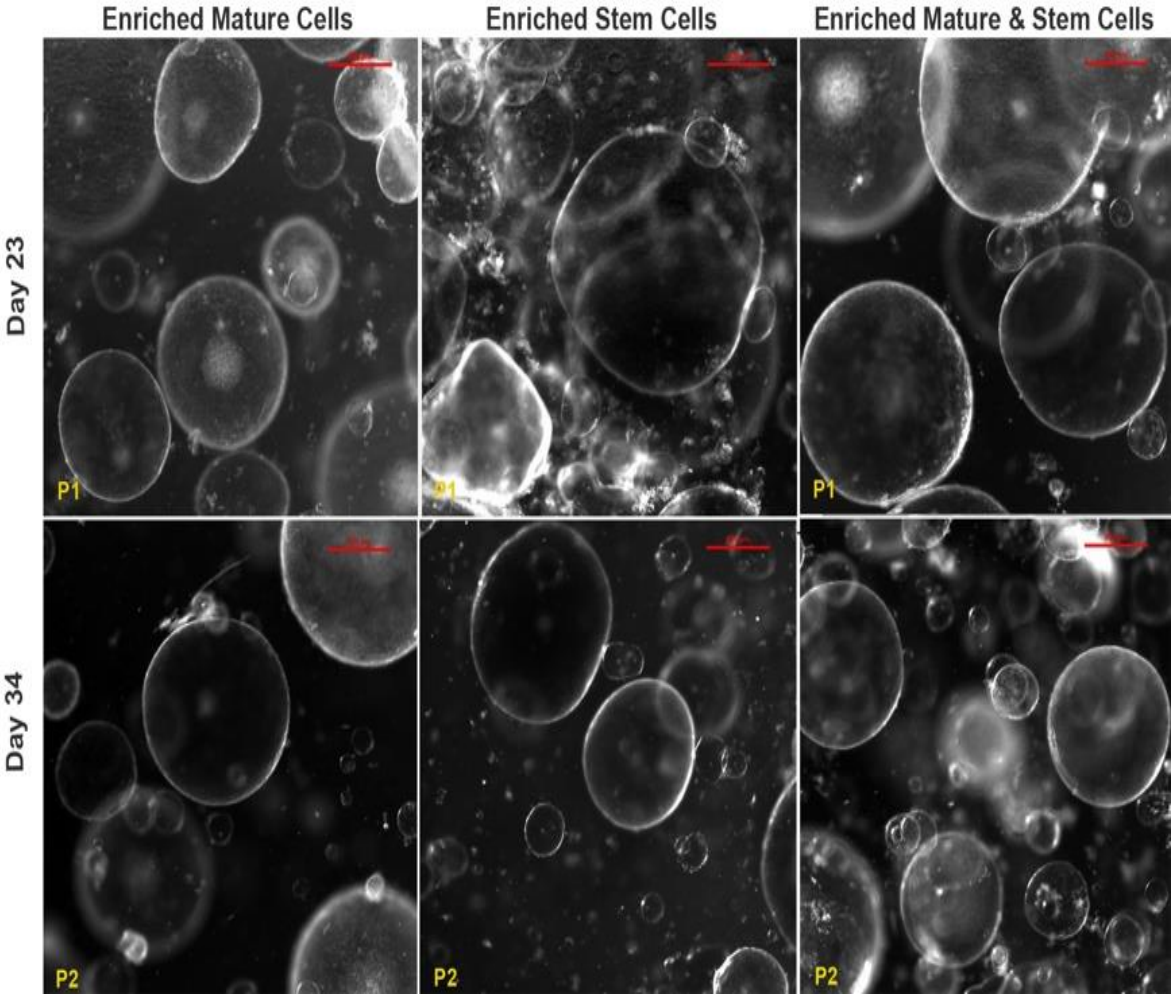


Figure 5. Generation of organoids from normal gallbladder tissue. Representative bright field images of mature cholangiocyte enriched organoids (left panels), stem cells enriched organoids (middle panels) and both mature cholangiocyte and stem cells containing organoids (right panels). Top panels show representative images from 1st passage of the organoids and bottom panels represents the morphology at 2nd passage. Scale bar: 500□m.

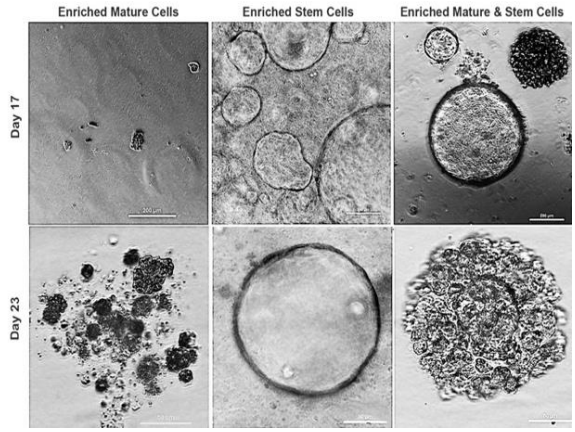


Figure 6. Generation of organoids from inflammatory gallbladder tissue. Representative bright field images of mature cholangiocyte enriched organoids (left panels), stem cells enriched organoids (middle panels) and both mature cholangiocyte and stem cell enriched organoids (right panels) from xanthogranulomatous cholecystitis. Growth and morphology of organoids with different approaches at day 17 (top panels) and at day 23 (bottom panels) after seeding. Scale bar: 200m (top panels); 50m (bottom panels).

three types of organoids (Figure 7). This data

suggests that the two different approaches result in either stemness or planar cell polarity respectively. Expression of *LGR5* (p=0.05) is not significantly elevated in stem cell population. To confirm stem cell enrichment, we will compare the expression of other pluripotent stem cell markers *OCT4*, *NANOG* and *PDX1*. Next steps include proteogenomic characterisation of the different types of organoids and introduction of stromal cells into the current organoid model to more closely mimic the microenvironment.

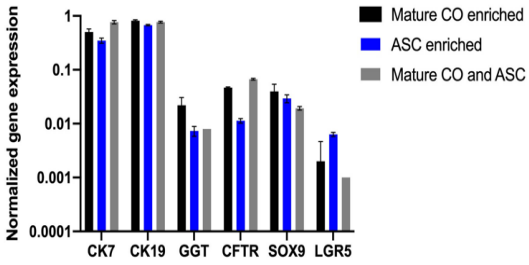


Figure 7. Comparative gene expression of key biliary markers for mature and stem cells. qPCR is performed for all three types of the organoids (mature cholangiocyte enriched: black bars; stem cell enriched: blue bars; both stem and mature cells enriched: grey bars). *CFTR* is a mature cholangiocyte marker. *LGR5* represents stem cells. *CK7, CK19, SOX9 and GGT* are transiently amplified biliary cell markers. Values are normalized against the housekeeping gene *GAPDH* and represented in $\log_{10}$ scale. Error bar: Mean±SD.

2.2 Molecular and functional characterisation of 3D organoid model

Organoids mimic the organ-specific expression of molecular markers and their functional characteristics. We have confirmed expression of CO-specific markers in the organoids with immunofluorescence imaging (Figure 8A). Organoids express Cytokeratin-19 in the cell membrane (left panel). Cytoplasmic expression of Muc5B (middle panel) and Claudin-2 (right panel) in the organoids confirm the characteristics of cholangiocytes, lining the gallbladder epithelium. As gallbladder organoids are derived from ciliated columnar epithelial cells, they are expected to conserve functional epithelial tight junction. Entry of FITC coupled dextran was prevented by the epithelial

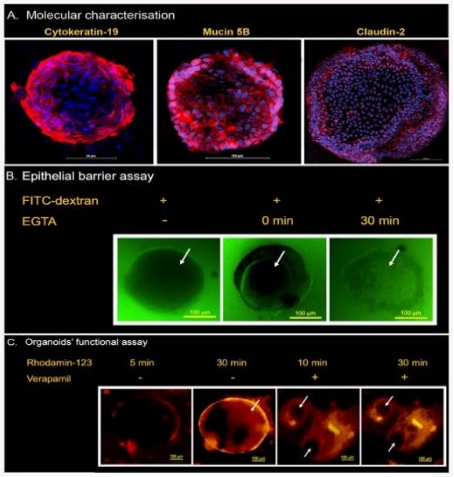


Figure 8. Characterization of the organoids generated from a normal gallbladder tissue. (A) Immunofluorescence images of organoids showing the expression (red) of key biliary markers Cytokeratin-19 (left, scale bar: 50□m), Mucin 5B (middle, scale bar: 100□m) and Claudin-2 (right, scale bar: 100□m). Hoechst-33342 is used to stain the nuclei (blue). (B) Fluorescence images showing tight junction activity of organoids. FITC labelled dextran (green) is used as substrate taken up by the epithelial cells of organoids in the lumen in absence (left) and presence (middle and right panels) of EGTA. Middle and right panels show effect of EGTA at 0 min and 30 min respectively. The arrow indicates the lumen of the organoid. Scale bar: 100□m.(C) MDR pump activity of the organoid cells is measured using rhodamine labelled substrate. Left and right panels show rhodamine uptake at 5, 10 or 30 min in absence (left two panels) or presence (right two panels) of verapamil. The arrow indicates the lumen of the organoid. Scale bar: 100µm.

tight junction of the organoids (Figure 8B, left and middle panels). Disruption of the tight junction by the calcium chelator EDTA, allowed FITC-dextran to enter into the lumen of the organoids (Figure 8B, right panel), confirming the functional epithelial barrier of the organoids. The functional characteristic of the gallbladder cholangiocytes in the organoids were confirmed by evaluating MDR pump activity (Figure 8C). The substrate for MDR pump is labelled with Rhodamine and pumped within the lumen of the organoids (left panel). Blocking the activity of the pump by Verapamil, inhibited the entry of the Rhodamine labelled substrate within the lumen of the organoids (middle and right panels), suggesting active MDR pumps of the organoid forming cholangiocytes.

3. Developing biomimetic platforms for *ex vivo* organoid models

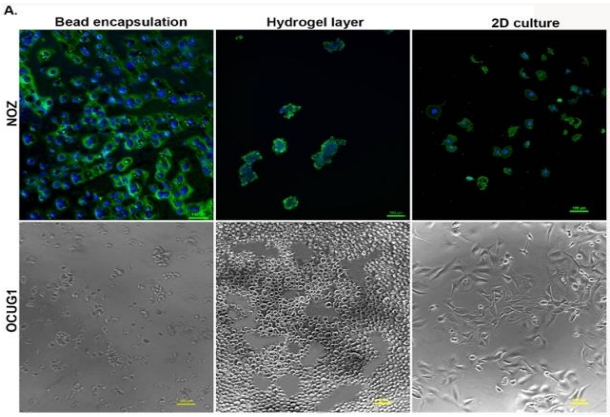


Figure 9A. Morphology of GBCa cell lines grown in different extracellular matrix. GBCa cell lines, NOZ (top panels) and OCUG1 (bottom panels) are grown encapsulated in hydrogel (left panels), on hydrogel layer (middle panels) or on plastic cell culture plates (right panels). NOZ cells are stained with wheat-germ agglutinin (WGA) to visualise the cellular architecture. Hoechst-33342 is used to stain the

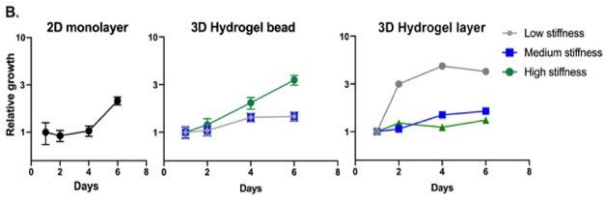


Figure 9B. GBCa cell line growth on matrix with different stiffness. OCUG1 cells were grown in cell culture plastic plate (left panel; stiffness = 2 GPa) or in hydrogels of varying stiffness (low stiffness = 0.4 kPa; medium stiffness = 0.8 kPa; High stiffness = 1.4 kPa). Cells were grown either in hydrogel bead (middle panel) or in hydrogel layer (right panel). Growth of OCUG1 cells were measured on day1, 2, 4 and 6 using WST-1 metabolic assay. All values are normalized by the growth observed on day1 and relative growth is plotted. Error bar: Mean±SD.

Further optimisation is required to create microenvironments which most closely mimic the tissue microenvironment. In collaboration with University of Manchester, we have been developing composite biomaterials to create culture supporting matrices of different stiffnesses and porosity. Alginate-gelatin based biomaterials were synthesised and used to study the growth and survival of GBCa cells. GBCa cells grew in alginate-gelatin hydrogels either encapsulated (left panels, Figure 9A) or used as extracellular matrix (middle panels, Figure 9A). On decreasing the stiffness of the hydrogel, proliferation of GBCa cell line OCUG1 is enhanced (Figure 9B). We will next evaluate the suitability of these hydrogels to grow primary gallbladder cells.

4. Generation of *wt* and *mut TP53* cell lines of gallbladder cancer

We hypothesise that altered TP53 transactivation contributes to the transformation of GB cells. Restoration of wild type TP53 activity/signalling could hinder progression of oncogenesis in stressed GB cells. To test this hypothesis, GBCa cell lines are being generated to express either *wt* or *mut TP53*. The cell line, OCUG-1 (JCRB) has a R267W gain-of-function mutation. TP53 is active and localised within the nucleus of resting cells (Figure 10A). *TP53* will be deleted in this cell line and the *wt TP53* reintroduced. In the GBCa cell line NOZ, there is a Q331V missense mutation in TP53 leading to a truncated TP53. In NOZ cells, the truncated TP53 is expressed at

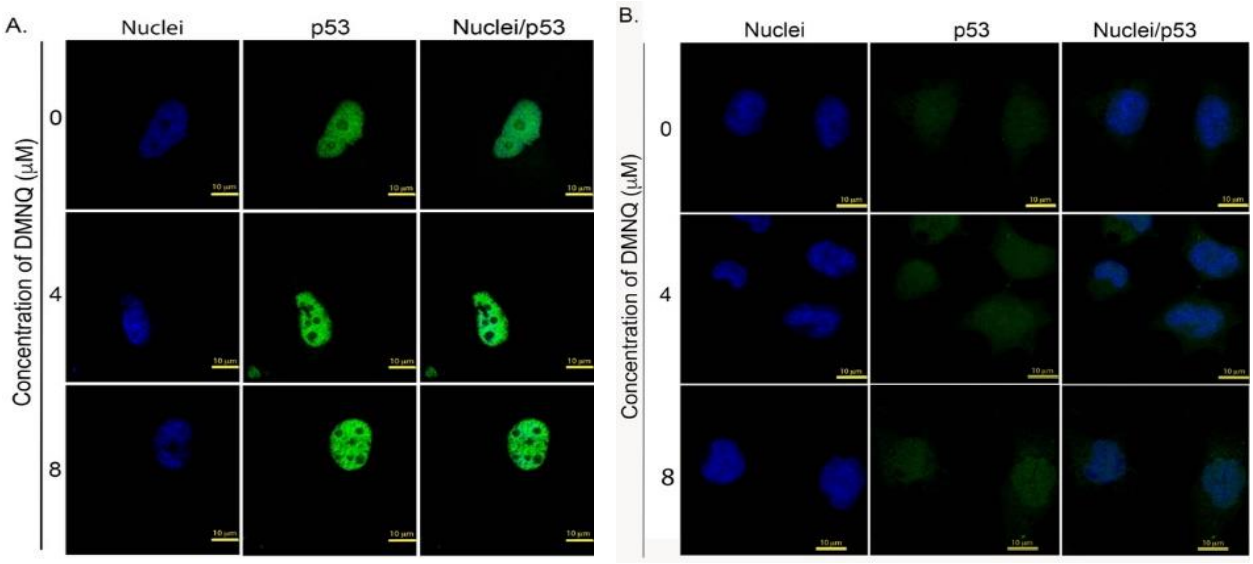
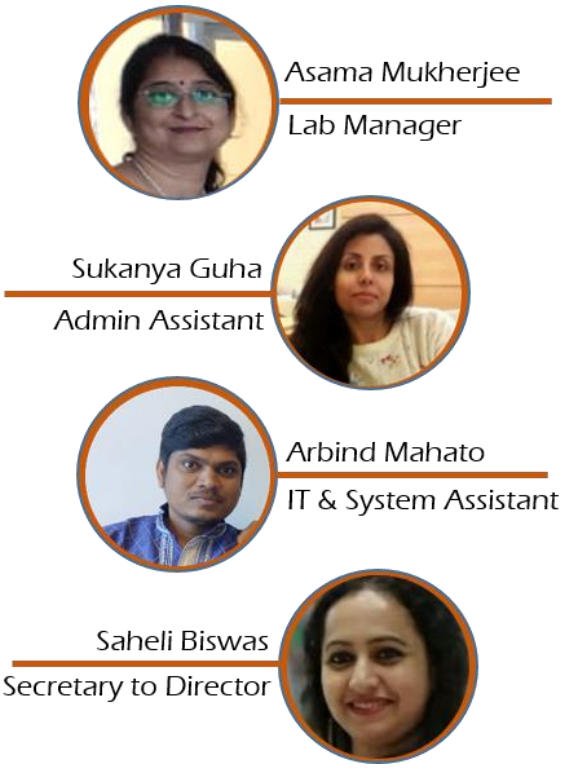


Figure 10 A. Immunofluorescence images of TP53 localisation in OCUG-1 cell line. OCUG-1 cells treated with 0 (top row), 4□M (middle row) and 8□M (bottom row) □M DMNQ for 48 hours. Localisation of TP53 is probed with the Alexa-488 tagged antibody (green). DAPI is used to stain the nuclei (blue). Scale bar:10µm. **B.** Immunofluorescence images of TP53 in NOZ cell lines. NOZ cells treated with 0 (top row), 4 (middle row) and 8 (bottom row) □M DMNQ for 24 hours. Expression and localisation of TP53 is observed using Alexa-488 tagged antibody. DAPI is used as counterstain. Scale bar:10µm.

low levels and localised to the cytoplasm in resting cells (top panel, Figure 10B). There was no change in TP53 expression upon exposure to stress (ROS) (bottom panels, Figure 10B). Ongoing analyses will investigate the role of these different TP53 mutations to disease progression and therapy.

Future Plans: In the coming year, histopathology and proteo-genomic characteristics of the non-malignant and malignant organoids will be correlated with their respective primary tissue counterparts. Organoids derived from normal or inflamed GB will be exposed to environmental stresses to study the pathogenesis of gall disease. Culture conditions of inflammatory gallbladders will further be optimised by co-culturing the immune cells with the organoids.

Administration



Team Members:

The year 2020 brought a wave of disruption in the way of our normal functioning. In spite of several challenges we had been very adaptive with plans for work from home while continuing to support essential services in CRU, biobank and other lab activities. We have used virtual platforms for internal meetings, external talks as well as for candidate interviewing process. We have adopted safe practices and implemented guidelines as the team started to move back to work with the relaxation of lockdown.

Currently TTCRC has over 40 members including PhD student and interns. Tushar Mungle has completed his degree through our collaborative PhD program with IIT Kharagpur while Ankita Dutta was enrolled in this year. We have also started a well-structured internship program for MSc/M.Tech students. The administration extends their support to this growing team to enable them perform their day to day tasks by liaising effectively with the TMC departments of HR, Finance, IT, Materials and Estates. We manage the general administrative responsibilities along with lab operations by working in tandem with the research laboratories and the core facilities.

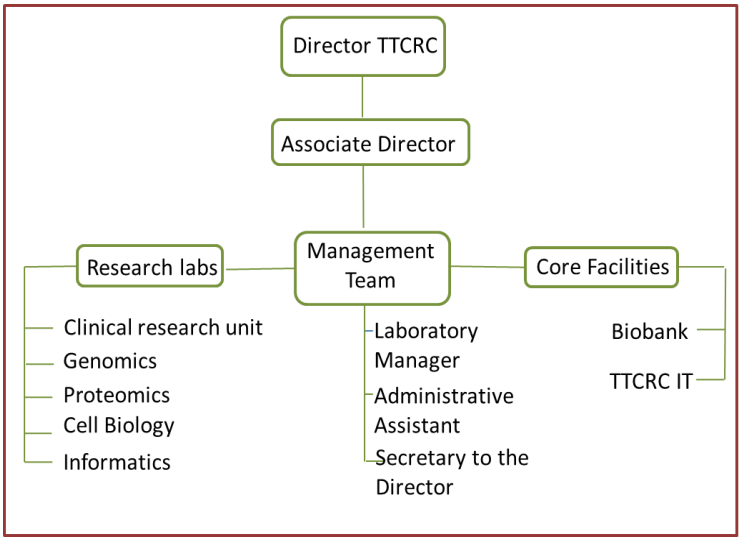


Figure 1. Organizational structure of TTCRC

To increase the visibility of our research in this year we have taken a step towards

launching the TTCRC website https://ttcrc.org. Email services has migrated from the tmckolkata.com address to ttcrc.tmckolkata.org to allow improved file sharing, increased mailbox capacity, security filtering and device compatibility. A 100TB storage server has been installed for data storage. TTCRC has also achieved email migration from. We continue to work to support the laboratories operate to the highest standards of academic and translational research practice.

The team participated in The Annual Review (2020) process conducted between January 15-16, 2021, with great enthusiasm. We have observed oral and poster presentation sessions by our team members along with participation from TCS. We are grateful to Prof. Anindya Dutta for his insightful presentation on this occasion.

Invited Presentations

1. 'In vitro models or avant-garde molecular cuisine' by Dr Annalisa Tirella, University of Manchester (9th May 2020).
2. 'Lessons from developmental disorders: Specificity of KMT2D mutations determine the resultant phenotype' by Dr Siddhartha Banka, University of Manchester (3rd June 2020)
3. 'The tumour suppressor P53; the story unfolds' by Dr Patricia Muller, Cancer Research UK, Manchester Institute (12thJune 2020).
4. 'Development of integrated platform for biomarker and drug target discovery using proteomics' by Prof Anthony Whetton, University of Manchester (17th June 2020)
5. 'Architecture of phosphhoinosidine signalling systems' by Dr Raghu Padinjat, NCBS Bangalore (July 29th).
6. 'Improved restratification in childhood ALL' by Dr. Anthony V. Moorman, Newcastle University (3rd September 2020).
7. 'Experiences with Primary Cell Culture' by Dr Cornelia Eckert - Charité, University Medicine Berlin (17th and 28th September 2020).
8. 'Cholangiocyte organoids for clinical applications' by Dr Fotios Sampaziotis, University of Cambridge (6th November 2020).
9. 'Developmental origins of infant ALL' by Dr. Anindita Roy, Department of Paediatrics University of Oxford (18th November 2020).
10. 'Novel aspects of genomic instability as they impact on cancers: extrachromosomal circles of DNA and DNA repair gene mutations' by Prof. Anindya Dutta (15th January 2021)

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