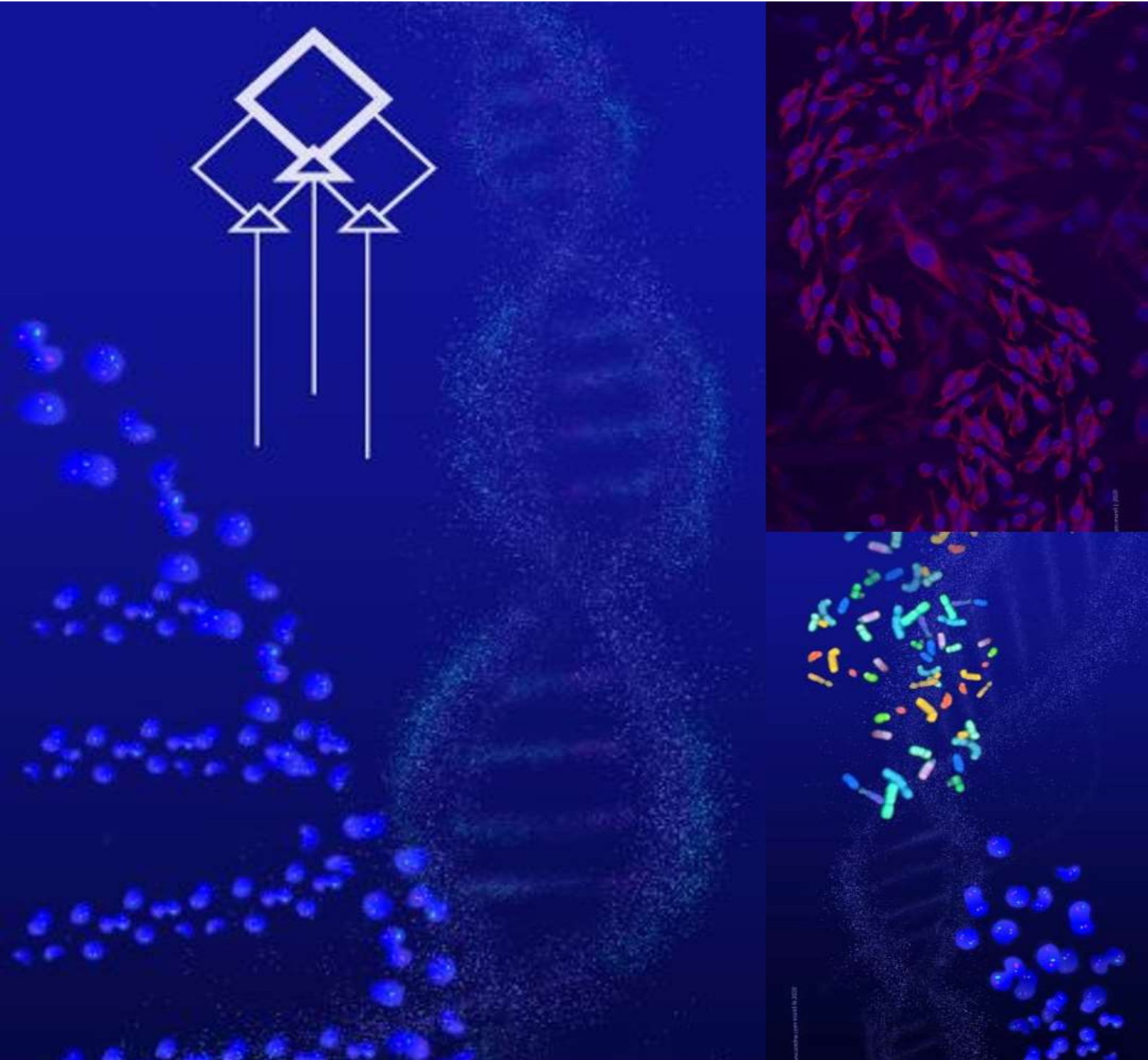




MAZUMDAR SHAW
MEDICAL FOUNDATION

ANNUAL REPORT 2024-25



MAZUMDAR SHAW MEDICAL FOUNDATION

8th Floor, A-Block, Mazumdar Shaw Cancer Center, 258/A, Bommasandra Industrial Area, Anekal Taluk, Bangalore 560 099

www.ms-mf.org

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Message from the Managing Director



Healthcare stands at a decisive inflection point. The traditional architecture of medical practice and diagnostics, largely linear, reactive, and reductionist, is now being reshaped by the mediating power of artificial intelligence. Yet the true significance of AI does not lie merely in augmenting memory, accelerating computation, or deciphering complexity beyond unaided human cognition. Its deeper impact is epistemic: a shift in how we think, imagine, and integrate

knowledge.

AI introduces a new mode of reasoning, one that allows patterns, trajectories, and latent transitions to be perceived before they crystallize into overt disease. Diagnostics are therefore moving beyond isolated molecular markers and static biochemical thresholds toward predictive, phenotype-level modelling of the individual. This enables anticipation of change before classical causality becomes biologically testable, opening a profound new space for early interception, prevention, and delay of disease expression, including genetically mediated disorders.

This transition demands a fundamental rethinking of biomedical research. Health is no longer a static state, nor disease a binary event, but a dynamic continuum shaped by resilience, compensation, and loss of biological redundancy over time. Therapeutics, in this context, are not merely tools for symptom control or maintenance, but instruments for altering trajectories—intercepting chronic disease and modulating risk long before irreversible damage occurs. In this contemporary AI-driven research paradigm, such insights are no longer shaped by the specialist alone, but emerge from close collaboration between domain experts, data scientists, and ethically guided artificial intelligence.

Mazumdar Shaw Medical Foundation (MSMF), with its strong commitment to translational medicine, is deliberately realigning its strategy to this emerging reality. Through its integrated ecosystem, the Mazumdar Shaw Centre for Translational Research (MSCTR), MSMF–Technology Business Incubator, the Advanced Diagnostic Research Centre, and the Mazumdar Shaw Cancer Outreach Program, in partnership with Narayana Health–Mazumdar Shaw Medical Centre—we have created a cohesive scientific enterprise that spans discovery, validation, implementation, and impact.

Our vision is clear: to convert cutting-edge science into real-world solutions that transform diagnostics, accelerate therapeutics, and elevate standards of care. Achieving this requires interdisciplinary fluency, openness to emerging technologies, and the intellectual courage to challenge established boundaries. Equally, it demands deep partnerships with clinicians, scientists, industry, and communities, ensuring that innovation remains ethical, equitable, and implementable at scale.

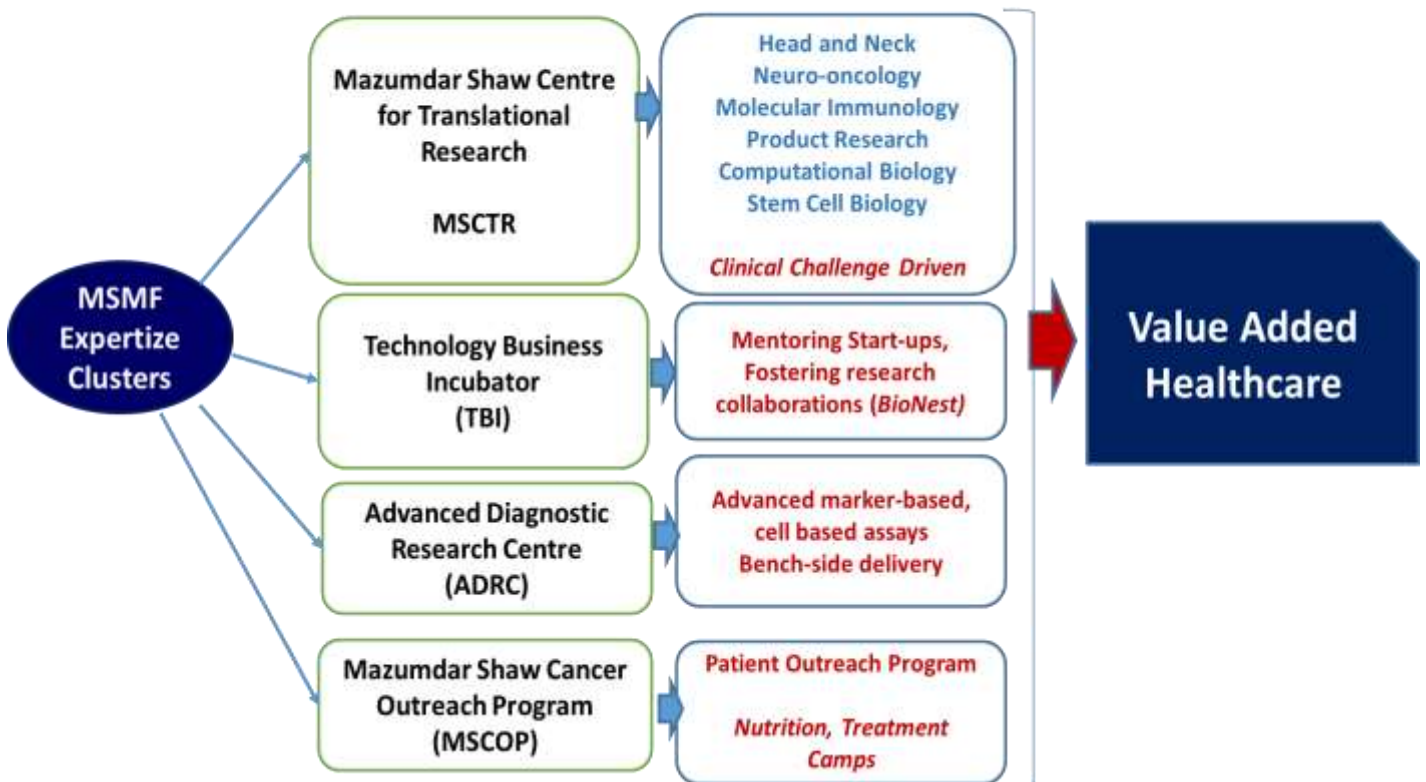
Professor Dr. Paul C Salins
Managing Director, MSMF

MSMF ECOSYSTEM

MSMF is organized into 4 verticals, the research wing is called Mazumdar Shaw Centre for Translational Research comprising research program in multiple disease areas. MSMF caters to broader society including the Advanced Diagnostic Research Center (ADRC), Technology Business Incubator (TBI) and Mazumdar Shaw Cancer Outreach Program (MSCOP).

THE MSMF ECOSYSTEM

Combining research, education and innovation towards improved healthcare



ACHIEVEMENTS

PATENTS

- 3D MODEL FOR TUMOUR MICROENVIRONMENT ANALYSIS”, Patent Application no.: 202241074987
- SYSTEM FOR IN-VITRO MODELLING OF NODAL METASTASIS IN ORAL SQUAMOUS CELL CARCINOMA”, Patent Application no.: 202341042308
- SYSTEM COMPRISING ARTIFICIAL INTELLIGENCE INTEGRATED MOLECULAR CYTOLOGY AND RADIOLOGY FOR TRIAGING OF THYROID NODULES”, application number 2023414045806

GRANTS

- **Repurposing of anti-Icn2 Mab for treatment of lung fibrosis:**
BT/CS0114/06/22: BIRAC: 49L; 15 Jan 2024 - 14Jan 2025; PI Dr Manjula

FELLOWSHIPS

- **Mr Pavan Hallur, PhD Scholar, Integrated Head and Neck Oncology Program**–PM Fellowship (CII; Jai Research Foundation)
- **Dr Durga Prasan, PhD Scholar, Stem Cell Program**–PM Fellowship (FICCI; 64

CONFERENCE RECOGNITION

Integrated Head and Neck Oncology Program

- **Ms Greeshma:** Best Podium Presentation Award for Basic Science Research category (FHNO), 2nd Best Poster (THYROCON), NH Research Day
- **Dr Anela Thomas:** Best Poster-podium Presentation Award (FHNO)
- **Dr Sumsum Sunny:** Narendra Desai Award for Best Podium presentation for Basic Science Research category (FHNO),

MAZUMDAR SHAW CENTRE FOR TRANSLATIONAL RESEARCH

INTEGRATED HEAD AND NECK ONCOLOGY PROGRAM

The Integrated Head and Neck Oncology Program focuses on a multi-disciplinary approach towards addressing the multiple grand challenges of down-staging oral cancer, accurate prognostication and the possibility of reversing treatment resistance in head and neck cancer. The team at MSCTR adopts a systems biology approach, exploring the clinical, cellular, molecular, biophysical and AI-based parameters in tissues, cells and body fluids, such as saliva and blood. Given that over two-thirds of the patients with head and neck cancer present at advanced stages III/IV, with an overall survival rate of less than 20%, early detection is the key. Secondly, about 50% of all head and neck cancers recur after 'curative intent treatment'. As in the majority of solid tumors, once the disease recurs or develops distant metastasis, there are no curative treatment options. *Approaches toward screening and early detection, accurate prognostication, and reversing resistance that integrate AI-based automation are hence an immediate need to enhance accuracy, applicability, affordability and accessibility.* Novel target/drug identification that can lead to chemoprevention and novel therapeutics are a long-term objective.

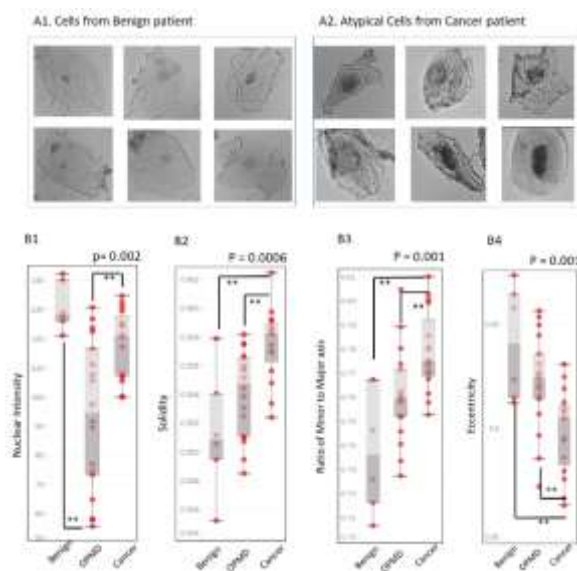
EARLY DETECTION OF ORAL CANCER

Early detection through effective screening programs has shown potential in reducing mortality by identifying oral potentially malignant disorders (OPMDs) and early-stage cancers. However, the current gold standard for diagnosis, biopsy, is invasive and unsuitable for large-scale screening. The team is investigating multiple adjuncts including imaging, cytology, salivary assays and multi-omics based profiling.

The current study addresses the need for a minimally invasive, pathology- equivalent, point-of-care (PoC) screening tool for oral cancer. Cytology is a minimally invasive method that has significantly impacted cervical cancer screening but has shown limitations in diagnosing oral dysplastic lesions due to subjective interpretation and lack of well-defined diagnostic criteria.

Label-Free Deep UV Microscopy in Oral Cytology:

Oral cancer remains a significant global health challenge. Early detection is essential for improving prognostic outcomes, yet current diagnostic practices are hindered by the invasive nature of biopsies and the reliance on staining methods. This study presents a low-cost, label-free deep ultraviolet (UV) microscopy system, integrated with artificial intelligence (AI), for analyzing unstained cytology specimens. Leveraging the absorption properties of nuclei under UV light, this technology produces high-resolution molecular images, enabling real-time, automated, and objective analysis of cellular and nuclear



Prominent nuclear features using UV imaging. UV cytology image of cells (cropped) from benign (A1) and atypical cells from cancer patients (A2). Nuclear features extracted from cells (mean value of each patients) were depicted B1-B4. Features significantly separated benign, OPMD and cancer patients. ** $p < 0.005$

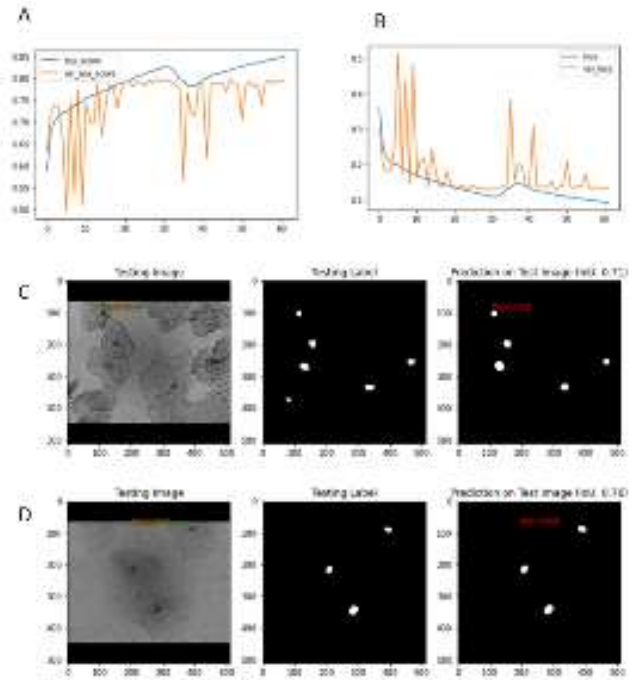
morphology. Forty patients with oral lesions—spanning benign, oral potentially malignant disorders (OPMD), and oral squamous cell carcinoma (OSCC)—participated in this study. Cytology nuclei were segmented using a deep learning-based U-Net architecture, and key nuclear features, including intensity, solidity, eccentricity, and axis ratio, were extracted and analyzed. These features demonstrated high sensitivity (>80%) and specificity (>79%) in distinguishing diagnostic groups. Furthermore, unsupervised clustering based on these features effectively classified patient cohorts, underscoring its potential for early diagnosis. The proposed method eliminates the need for staining, reduces processing time, and minimizes environmental impact, making it particularly suited for primary healthcare settings. By integrating advanced imaging with AI, this scalable approach addresses critical gaps in early oral cancer detection, offering significant potential to improve patient outcomes. Validation in larger and more diverse cohorts is required to enhance its clinical utility.

Oral Potentially Malignant Lesion Atlas Project: Validating the efficacy of novel, point-of-care diagnostics and developing an integrated multidimensional, prognostic nomogram

In this study we aim to evaluate the efficacy of various point-of-care (PoC) early detection platforms in terms of their efficacy, positioning in the different healthcare systems, and surveillance. These assays will be integrated with novel molecular signatures to develop an AI-based prognostic nomogram. The multi-dimensional comprehensive atlas of OPMD for disease progression and malignant transformation, thus developed will be converted into an open-source data-centric platform resource that facilitates future collaborative projects in the field. The primary objective of this project is to accomplish comparative assessment and precise positioning or deployment of PoC assay systems in the national healthcare systems that will enable accurate screening, detection, and prognostication of patients with OPMD. The primary objectives of the proposal include i) To evaluate the efficacy of multiple point-of-care systems for the detection of oral potentially malignant disorders (OPMD) ii) Comparison of multiple point-of-care platforms in the early detection of oral cancer to validate their positioning in different levels of healthcare systems. Iii) Assessing the effectiveness of multimodal point-of-care tests in monitoring the progression of oral potentially malignant lesions (OPML) and iii) develop a prognostic model combining clinical/auto-fluorescence images, saliva markers, cytology, histology, multi-omics, and microbiome data.

The secondary objectives include i) To design and develop a clinical, pathological, and multi-omics data warehouse to provide tangible benefits to patients and research cores by detecting and treating cancer early ii) Assessment of the PoC systems in the oral cancer surveillance and progression of OPMD as a part of a longitudinal study iii) To assess the efficacy of the prognostic nomogram in assessing malignant transformation iv) To validate the molecular markers identified by high-throughput profiling in an independent cohort of patients.

A total of 265 participants have been recruited for the study with the images/samples collected for imaging, cytology, and saliva assays. For multiplex cytology and salivary assays, the laboratory validation is completed and for regulatory strategy, discussion with MedTech Mitra has been initiated. Early-stage validation (TRL5-6) will be completed in 1-2 months once the approval is obtained. The study is currently ongoing



Segmentation of nucleus. The figure demonstrates the performance of the U-Net model in nucleus segmentation. It presents the Intersection Over Union (IoU) and total loss curves during both training and validation phases (A, B), highlighting the model's optimization over time. Additionally, examples of segmentation results are shown in (C, D), where the predicted nucleus overlays are compared with the ground truth for images achieving a mean IoU above 0.70

in terms of the assay validation for the different settings (imaging, cytology and saliva). The data for the prognostic model is also currently being collected.

HEAD AND NECK CANCER; PROGNOSIS, THERAPY

The team works on multiple challenges in head and neck cancer prognosis including i) identifying markers of therapy resistance to enable prediction of treatment outcome ii) develop 3D organoid-based models that can enable personalized assessment of treatment resistance iii) improve the detection accuracy of malignant nodules in USF-guided FNAC of thyroid nodules iv) explore the landscape of nodal metastasis and identify markers/novel PoC methods for peri-operative prediction/detection of the metastatic status and v) validation of novel targets and development of novel therapeutics for head and neck cancer.

INDETERMINATE NODULE IDENTIFICATION IN THYROID CANCER

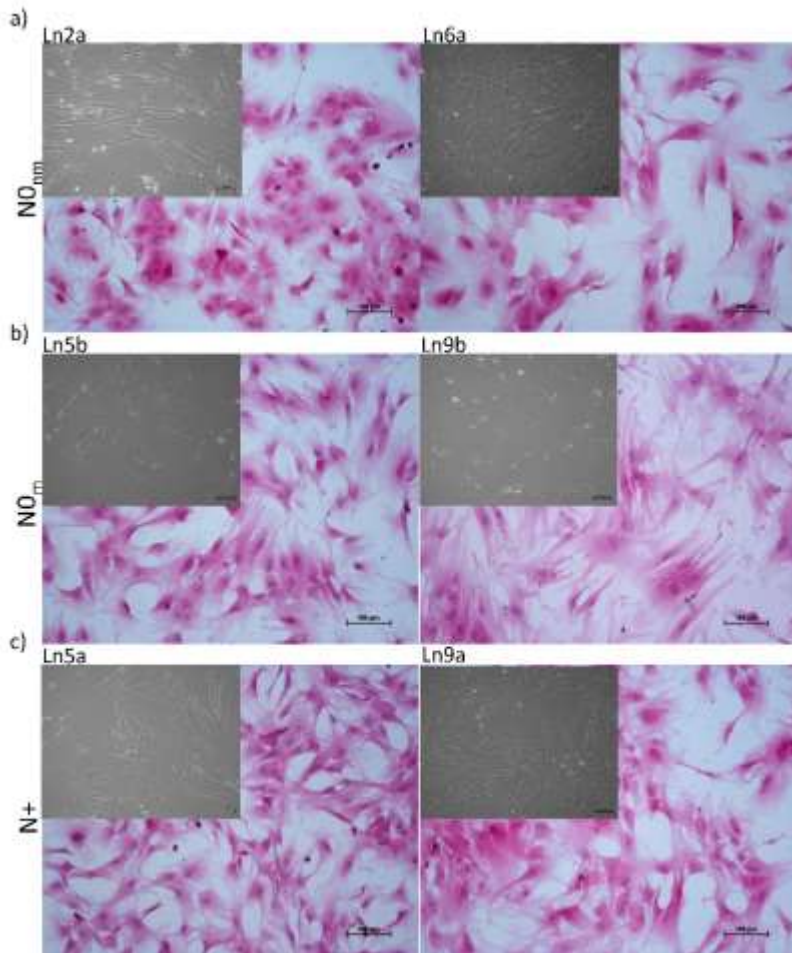
Ultrasound-guided fine needle aspiration cytology (FNAC) is the preferred method of identifying malignancy in palpable thyroid nodules using the Bethesda reporting system. However, in around 30–40% of FNACs (Bethesda categories III, IV, and V), the results are indeterminate and surgery is required to confirm malignancy. Out of those who undergo surgery, only 10–40% of patients in these categories are found to have malignancies, thus proving surgery to be unnecessary for some patients or to be incomplete in others. While molecular testing on thyroid FNAC material is part of the American Thyroid Association (ATA) guidelines in evaluating thyroid nodules, it is currently unavailable in India due to cost constraints.

A systematic review and meta-analysis assessed the diagnostic performance of immunocytochemical markers in differentiating benign from malignant thyroid lesions in FNAC samples. The diagnostic performance of the markers in delineating indeterminate thyroid nodules (Bethesda categories III, IV, and V) was also analyzed. HBME-1 and Gal-3 showed comparable diagnostic efficacy in these categories, with HBME-1 having a DOR of 11.19 and AUC of 0.88, and Gal-3 having a DOR of 14.46 and AUC of 0.86. In conclusion, accurate preoperative discrimination of benign and malignant thyroid nodules is crucial for appropriate surgical management. Despite limitations in FNAC-based cytology interpretation, the identified markers, particularly TPO, CK-19, HBME-1, Gal-3, and CD56, demonstrated significant potential in improving diagnostic accuracy. The meta-analysis provides a comprehensive evaluation of these markers, supporting their use in clinical settings to enhance the preoperative differentiation of thyroid nodules. The markers are currently under evaluation for their efficacy in distinguishing benign and malignant by IHC as well as in FNAC samples with a grant from Endocrine Society of India (ESI).

PROFILING IN NODAL METASTASIS: REFERENCE GENE EVALUATION

MODELING THE LYMPH NODE STROMAL CELLS IN ORAL SQUAMOUS CELL CARCINOMA: INSIGHTS INTO THE STROMAL CUES IN NODAL METASTASIS

The study explores the development and characterization of lymph node stromal cell cultures (LNSCs) from patients with oral squamous cell carcinoma (OSCC), highlighting the importance of understanding tumor-node cross-talk for effective prognostic and therapeutic interventions. Herein, we describe the development and characterization of primary lymph node stromal cells (LNSCs, N=14) from nodes of metastatic and non-metastatic OSCC patients. Primary cultures were established by the explant method from positive (N+; N=2), and negative nodes (N_{0m}; N=4) of the metastatic patients (N=3) as well as negative (N_{0nm}; N=8) nodes from non-metastatic (N=4) patients.



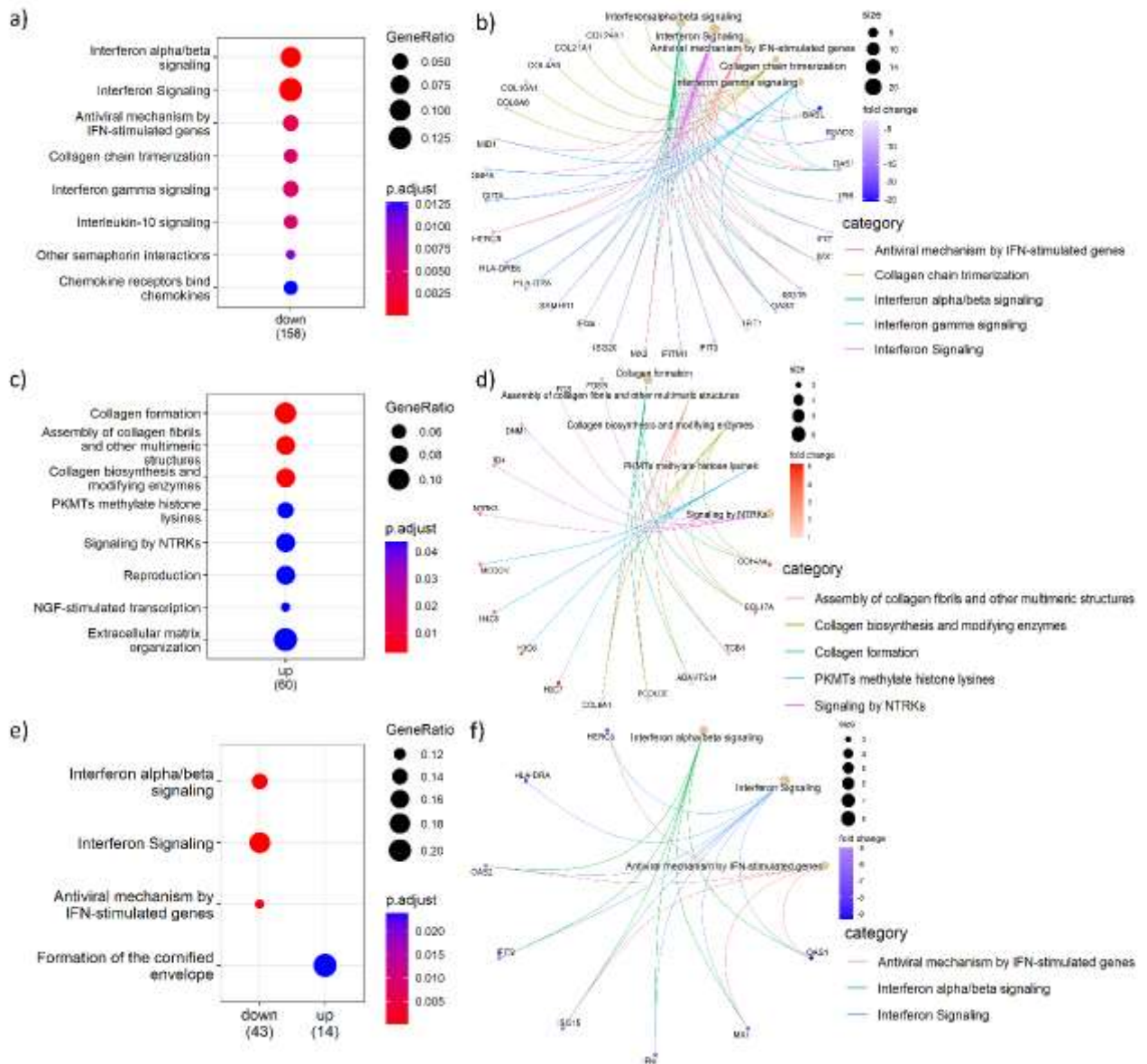
Morphology and growth

characteristics of the primary

cultures: The lymph node explants LNStCs from the NO_{nm} (a), NO_m (b), N+ (c) groups were cultured for approximately 4-6 weeks, trypsinized, expanded, and freezes were made at the early passages (passage 1-10). The H&E staining was done on cells cultured on coverslips overnight. The cells showed varied morphology with stellate, reticular and fusiform shaped cells. The images were taken at 10X magnification and the scale bar represents 100µm. Abbreviations: H&E: hematoxylin and eosin, LNStCs: Lymph node stromal cells, NO_{nm}: Negative node from non-metastatic patient, NO_m: Negative node from metastatic patient, N+: Positive node from a metastatic patient, Ln2a, Ln6a, Ln5b, Ln9b, Ln5a, Ln9a represent the codes of the primary cell lines

STR profiling confirmed the purity and novelty, while characterization by immunocytochemistry/flow cytometry revealed heterogeneous cell populations consisting of fibroblastic reticular cells (CD31-Gp38+) and double negative cells (CD31-Gp38-).

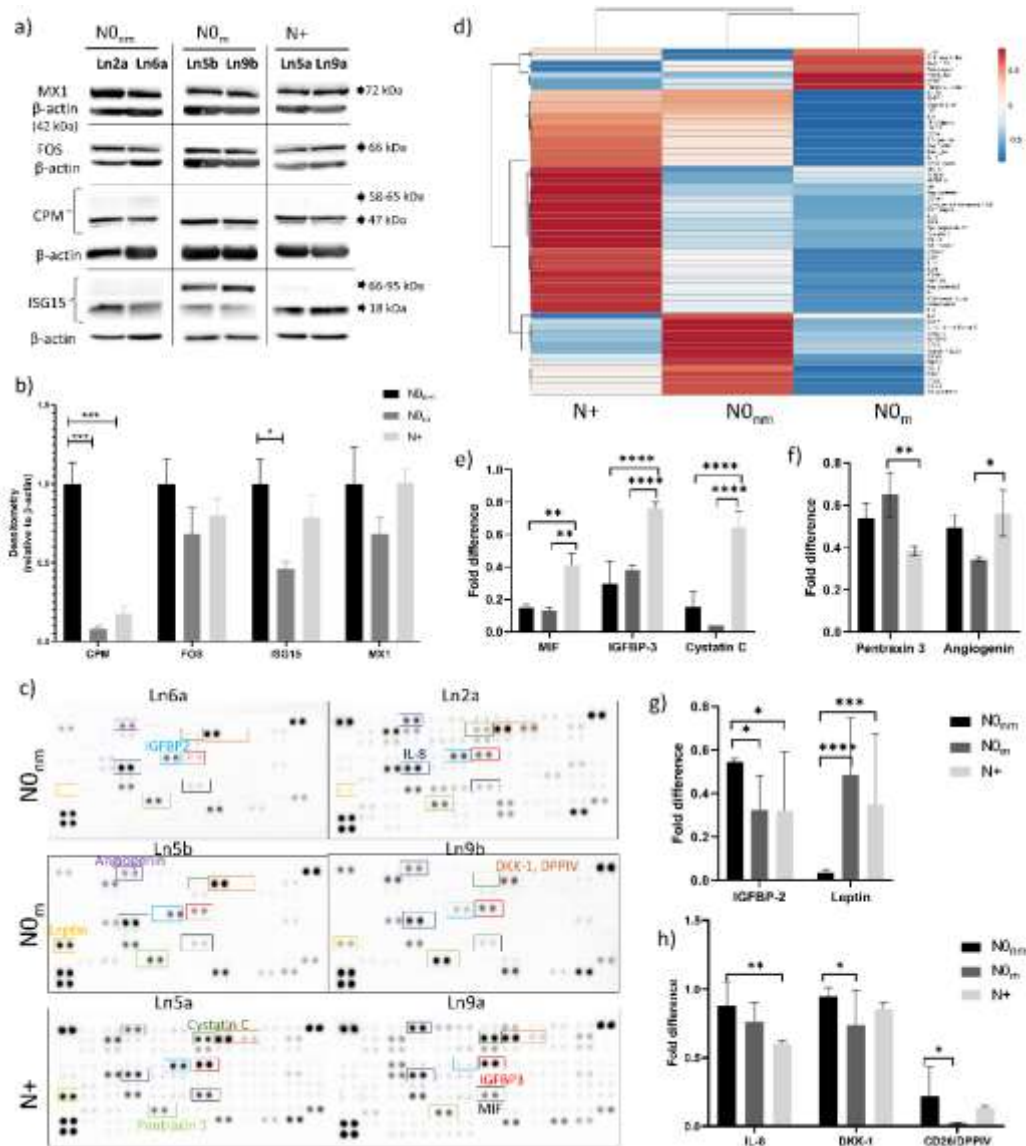
Transcriptomic profiling indicated molecular alterations in the cells based on the non-metastatic (NO_{nm}), the pre-metastatic (NO_m) or metastatic (N+) status of the nodes, pro-inflammatory, matrix remodelling, and immune evasion being the primary pathways (**Figure 2**). Assessment of the protein levels for five selected markers (MX1, ISG15, CPM, ITGB4 and FOS) in the cell lines revealed that CPM levels were significantly reduced in the N+ and NO_m nodes whereas ISG15 levels reduced in NO_m. Significantly, the profiling also provided insights into possible glycosylation of CPM (NO_{nm}) and ISGylation of ISG15 (NO_m) (**Figure 3a-b**). Cytokine profiling indicated release of chemokines/anti-proliferative cytokines from the negative nodes, while angiogenic/pro-metastatic cytokines were released from the nodes of metastatic patients (**Figure 3c-h**). The lymph node stromal cell models established in the study with distinctive transcriptomic/cytokine characteristics will be invaluable in delineating the processes underlying nodal metastasis



Pathway enrichment for different comparison groups. The enriched pathways from the differentially expressed genes were identified using Cluster Profiler and represented with dot plots and corresponding cnetplots for different comparisons; N0_m vs N0_{nm} (a, b) N+ vs N0_m (c, d) N+ vs N0_{nm} (e, f). Abbreviations: N0_{nm}: Negative node from non-metastatic patient, N0_m: Negative node from metastatic patient, N+: Positive node from metastatic patient

Protein expression of MX1, ISG15, FOS, ITGB4 and CPM were evaluated using western blot analysis for the selected genes along with the control β -actin. Densitometric analysis showed significant lowered expression of CPM (58-65kDa) in premetastatic and metastatic node groups and ISG15 (18kDa) in premetastatic group (Figure 6 a-b). The cytokines secreted by the cells grouped into N0_{nm} (Ln2a, Ln6a), N0_m (Ln5b, Ln9b) and N+ (Ln5a, Ln9a) are profiled by cytokine array. Each blot contains three reference spots and a negative control in duplicates. The heatmap was generated for the cytokines with differential profile across the three groups N0_{nm}, N0_m & N+ (Figure 6 c-d). The bar graphs represent the fold difference of the significant cytokines (calculated w.r.t. the pixel density of the cytokines against the reference spots; $p < 0.05$) overexpressed by the metastatic nodes in comparison to the non-metastatic nodes from the N0_{nm}, N0_m groups include MIF, IGFBP-3 & Cystatin C. Pentraxin 3 and angiogenin showed significant expression difference in the N0_m and N+ groups. IGFBP-2 and Leptin showed significant difference in expression in

comparison to the $N0_m$ and $N+$ groups. DKK1 and CD26 expression show significant difference between the $N0_{nm}$ and $N0_m$ groups whereas IL8 expression is significantly downregulated in the $N+$ group when compared to $N0_{nm}$ (Figure 6 e-h).



Protein expression and Cytokine profiling of the $N0_{nm}$, $N0_m$ & $N+$ groups: Protein expression was profiled by western blotting of MX1, ISG15, FOS, ITGB4 and CPM (a), and densitometric analysis (b). Profiling by cytokine array (c) and analysis by heatmap (d) as well as differential profiling indicated the significant cytokines in the metastatic node $N+$ nodes (e), in the $N0_m$ and the $N+$ nodes (f-g) and in the $N0$ nodes (h). Abbreviations: $N0_{nm}$: Negative node from non-metastatic patient, $N0_m$: Negative node from metastatic patient, $N+$: Positive node from metastatic patient. The error bar represents the standard error of mean. The p value significance is represented by * ($p < 0.05$), ** ($p < 0.005$), *** ($p < 0.0005$) & **** ($p < 0.0001$)

GRANTS

1. Oral Potentially Malignant Lesion Atlas Project: Validating the efficacy of novel, Point-of-Care diagnostics and developing an integrated multidimensional, prognostic nomogram (ICMR; A multi-centric 5-year grant to develop PoC technologies for Oral Cancer Early Detection)
2. A point-of-care Artificial Intelligence (AI)-based screening tool for oral cancer (Ministry of Education; Indian Institute of Science)
3. Triaging of indeterminate thyroid nodules combining radiomics, molecular cytology and mutational profiling - a multi-centric study (Endocrine Society of India)
4. Multimodal intraoral imaging system for oral cancer detection and diagnosis in low resource setting (Collaboration project with Narayana Health, NIH)
5. 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 (In collaboration with Narayana Hrudayalaya, HNCOG) NCG 2018-2025

PUBLICATION

- James BL, Zaidi SN, Aiswarya RK, Shetty V, Vidya Bhushan R, Dokhe Y, Naveen BS, Pillai V, Dhar SK, Kuriakose MA, Suresh A. Modeling the lymph node stromal cells in oral squamous cell carcinoma: insights into the stromal cues in nodal metastasis. *Hum Cell.* 2025 Jan 6;38 (2):41. doi: 10.1007/s13577-024-01166-8. PMID: 39760828.
- Kekatpure V, Subramaniam N, Sunny S, Nambiar S, Sarah T, Vasudevan V, Rao A, Murali A, Kolar T, Krishnamurthy A, Kantharia R, Nair SV, Thankappan K, M N B, Kumar R, Balasubramanian S, Toprani R, Agrawala S, Battoo AJ, Bakshi J, Babu S, Shah S, Trivedi N, Selvam S, Kannan R, Kumar A, Suresh A, Pillai V, Chaturvedi P, Iyer S, Kuriakose MA. Two by Two Factorial Design using Metformin and Curcumin for Second Primary Head and Neck Cancer Prevention Trial. *Asian Pac J Cancer Prev.* 2024 Jun 1;25(6):1935-1943. doi: 10.31557/APJCP.2024.25.6.1935. PMID: 38918654; PMCID: PMC11382851.
- Gurushanth K, Sunny SP, Raghavan SA, Thakur H, Majumder BP, Srinivasan P, Thomas A, Chandrashekhar P, Topajiche S, Krishnakumar K, Gurudath S, Patrick S, Linzbouy L, Edith AKA, Jha S, Srivatsa G, Shetty A, Suresh A, Kuriakose MA, Birur PN. Holistic Approach for the Early Detection of Oral Cancer: A Comprehensive Training Module. *J Maxillofac Oral Surg.* 2024 Aug;23(4):816-823. doi: 10.1007/s12663-024-02198-1. Epub 2024 May 18. PMID: 39118933; PMCID: PMC11303606
- James BL, Zaidi SN, Bs N, R VB, Dokhe Y, Shetty V, Pillai V, Kuriakose MA, Suresh A. Reference gene evaluation for normalization of gene expression studies with lymph tissue and node-derived stromal cells of patients with oral squamous cell carcinoma. *Oncol Lett.* 2024 Sep 6;28(5):540. doi: 10.3892/ol.2024.14673. PMID: 39310029; PMCID: PMC11413728.

PATENTS

Granted

1. Pharmacological formulation comprising Curcumin and Metformin for Head and Neck Cancer (Granted; #462241)
2. Anti-CXCR4 inhibitor in reversing resistance to chemoprevention and Chemotherapy (Granted; #449011)
3. Molecular Marker based cytology for detection of oral potentially malignant and malignant lesions (Granted; #391264)
4. Salivary Protein markers for diagnosis and prognosis of oral cancer (Granted; #408050)

Filed (2024-2025)

- 3D MODEL FOR TUMOUR MICROENVIRONMENT ANALYSIS", Patent Application no.: 202241074987
- SYSTEM FOR IN-VITRO MODELLING OF NODAL METASTASIS IN ORAL SQUAMOUS CELL CARCINOMA", Patent Application no.: 202341042308
- SYSTEM COMPRISING ARTIFICIAL INTELLIGENCE INTEGRATED MOLECULAR CYTOLOGY AND RADIOLOGY FOR TRIAGING OF THYROID NODULES", application number 2023414045806

CONFERENCES

1. Foundation of Head and neck Oncology (FHNO) 2024, 18th - 20th October 2024, in Mumbai
 - Artificial Intelligence Integrated Molecular Cytology for Objective Triaging of Thyroid Nodules – Presenter: Greeshma **(Received Best Podium Presentation Award for Basic Science Research category)**
 - Clinical validation of inhouse salivary ELISA-based assay with S100A7 and S100P for early detection of oral potential malignant lesions (OPML) – Presenter: Ankita P
 - Enhancing Pathologist Consistency: Evaluating Inter-Observer Concordance to Develop Automated Diagnostic Tools for Oral Epithelial Dysplasia- Presenter: Anela Thomas **(Received Best Poster-podium Presentation Award)**
 - Tumor-lymph node stromal cell cross talk in OSCC: insights into the tumor and stromal cues in nodal metastasis- Presenter: Bonney Lee James
 - Transcriptomic profiling of oral potentially malignant disorders: Presenter: Gangotri S
 - Label Free Cytology for Early detection of oral cancer in Low Resource Setting- Presenter: Dr. Sumsum P S **(Received Narendra Desai Award for Best Podium presentation for Basic Science Research category)**
2. Indian Association of Oral & Maxillofacial Oral Pathologists, PG Convention 2024 15-16th June, Pune
 - Quantifying Inter-Observer Variability in Oral Epithelial Dysplasia Grading: A Path towards AI-Assisted Consistency - Presenter: Dr. Anela Thomas
3. THYROCON held at Bangalore on Dec 1 2024
 - Artificial Intelligence-driven Support for diagnosis and management of Thyroid Nodules in resource constraint settings – Dr. Anela Thomas
 - Artificial intelligence integrated molecular cytology for objective triaging of thyroid nodules – Greeshma P **(Received Second position for Best Poster)**
4. IACR 2024
 - Perioperative biomarkers for nodal metastasis in oral squamous cell carcinoma Presenter: Madhumati

TEAM

PRINCIPAL INVESTIGATOR: Dr Amritha Suresh

ORAL CANCER CONTROL PROGRAM: Dr Sumsum Sunny (Research Scientist)*, Dr Bhargabi Paul Majumdar (Oral Medicine Consultant)*, Dr Anela Thomas (Oral Pathologist)*, Shivani M (JRF). Ankita P (JRF). Sowmya CN (Core Facility), Keerthi J, Sai Lakshmi (Core facility)*, Uma M*, Srinivas*, Saraswathi *
CHEMOPREVENTION: Mr Ramdev (Project Manager), Sreelakshmi PK*, Nanditha

CELLULAR/ MOLECULAR DIAGNOSIS/ PROGNOSTICATION OF HEAD AND NECK CANCER: Bonney L James (PhD Student, MAHE), Madhumati HK (ICMR SRF), Pavan Hallur (ICMR SRF, PM Fellowship), Gangotri Siddappa (PhD Student, RGUHS), Greeshma P (SRF),

NH CLINICAL TEAM

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DEPARTMENT OF ENDOCRINOLOGY: Dr Subramanian Kannan

DEPARTMENT OF PATHOLOGY: Dr Nisheena Raghavan, Dr Shaesta Naseem, Dr Vidya Rao

COLLABORATORS

MSMF: Dr Ravi Sirdeshmukh, Dr Sujan Dhar, Dr Smitha PK,

National: KLE institute of Dental Sciences, IISc, Biocon Foundation, HBCH Varanasi, NCI Chandigarh, EMC, Kochi, SRMC, Chennai

International: Roswell Park Cancer Institute, University of Arizona, University of Illinois

NEURO-ONCOLOGY RESEARCH PROGRAM

The focus of the Neuro-Oncology Research Group is mainly on Glioblastoma – its tumor heterogeneity, microenvironment, and therapy-resistance at cellular, molecular, and histological levels using clinical specimens, established cell lines, tumor-derived cells, 3D culture system, multi-omics analysis, and computational approaches. The broad objectives of our group are described below.

1. Continue a deeper understanding of the pathophysiology of GBM in order to develop newer, clinically feasible biomarker assays for prognosis, treatment surveillance, and other application
2. Understanding tumor heterogeneity and therapy resistance and exploring newer therapeutic strategies including tumor-specific protein variants as targets or immunotherapy
3. Engineer 3D cell culture models with tumor-derived cells to mimic the glioblastoma microenvironment that best reflects the disease and is useful for studying new therapies.

The ongoing efforts, directed towards the above goals are briefly described below. These projects have been undertaken during this academic session.

1. DEVELOPMENT OF AN INTEGRATED GLIOMA PATIENT-DERIVED CELLULAR MODEL THAT CAPTURES TUMORIGENIC FEATURES & CHEMORESPONSE FOR PRECISION THERAPY

In vitro cellular models are important tools in cancer research to understand the disease biology and therapy resistance observed frequently in cancer. Especially, the scarcity of naïve brain tumour tissues and follow-up tumour samples is the biggest challenge for studying drug response and therapy resistance, which necessitates the development of *in vitro* cellular models. Therefore, our aim is to develop an integrated cellular model using patient-derived short-term primary cultures, spheroids, and tumoroids for chemo-response prediction and therapeutic target identification across the various WHO grades (2021 classification) adult diffuse gliomas.

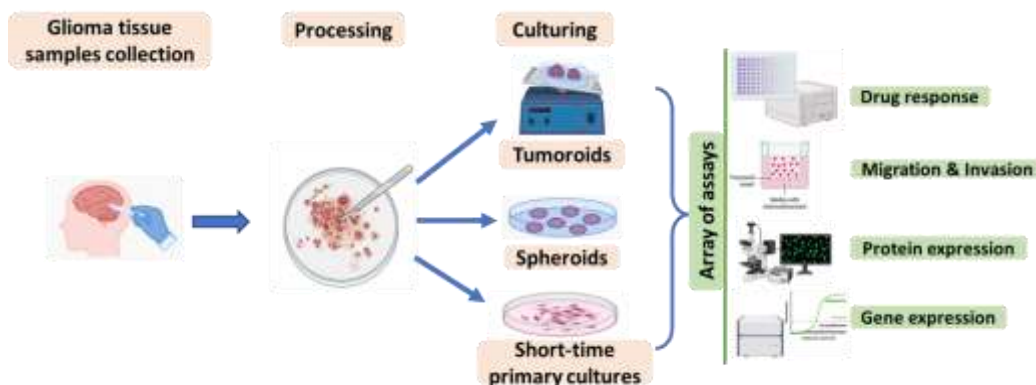


Fig. 1: Working model to develop an *in vitro* cellular platform for capturing tumour heterogeneity and evaluating drug response in gliomas.

Freshly resected adult diffuse glioma tissue samples will be collected and processed for single-cell suspension, followed by developing short-term primary cultures, spheroids, and tumoroids (from tissue chunks) (**Fig. 1**). We shall analyze cell morphology, cell proliferation, migration/invasion, and temozolomide (TMZ) response. Immunofluorescence and qPCR will be performed to evaluate the expression of several lineage-specific, GSC, and EMT markers.

Currently, we have successfully developed 2 LGG (low-grade glioma), 1 HGG (high-grade glioma), and 4 GBM cell lines as adherent cultures. The cellular and molecular characterization is underway. In addition,

these cells are also being grown as spheroids, and the TMZ response is being evaluated. Interestingly, we are also able to grow them as tumoroids (one from each grade). These tumoroids retain the histological features as seen in the corresponding patients (evaluated by a neuropathologist). Therefore, we anticipate that our integrated *in vitro* cellular model will capture glioma-specific tumour heterogeneity and will be a useful tool for chemo-response prediction towards precision medicine and novel therapeutic targets identification for glioma management.

2. IDENTIFICATION OF BIOMARKERS BASED ON IMMUNOSUPPRESSIVE CHARACTERISTICS OF GLIOBLASTOMA

Despite the clinical success of immunotherapy in other cancers, GBM remains non-responsive to immunotherapy due to its cellular and molecular heterogeneity, along with an immunosuppressive tumor microenvironment. Thus, there is an urgent need to identify biomarkers based on the immunosuppressive features of GBM for better disease prognosis and immune-therapy response prediction. The study aims to identify a set of biomarkers based on immunosuppressive behavior of GBM using the bulk RNA-seq data.

Immune cell deconvolution was performed on in-house GBM bulk RNA-seq data (n=13) and TCGA GBM dataset (n=175), followed by identification of differentially expressed immunosuppressive genes. Immune profiling and clustering of bulk RNA-seq data revealed two distinct clusters: Cluster-1 (immunosuppressive) and Cluster-2 (immune-favorable). Cluster-1 showed an abundance of Tregs and M2 macrophages, while Cluster-2 was enriched with T and B cells. Interestingly, progression-free survival for Cluster-1 (~5 months) was significantly lower ($p < 0.05$) than Cluster-2 (~8.5 months). HISGATLAS, followed by STRING analysis, resulted in 12 hub genes. Survival and expression analyses using the TCGA GBM dataset identified four genes—CXCL8, IL7R, CCL18, and S100A8—as linked to poor prognosis and higher expression in Cluster-1. Further, several independent GBM cohorts confirmed IL7R, CCL18, and S100A8 as poor prognostic markers. Additionally, high expression of IL7R, CCL18, and CXCL8 was also found in the non-responder group in an immunotherapy-based clinical trial dataset (SRA PRJNA482620) in GBM.

Our future aim is to establish their role in GBM immunosuppression using *in vitro* cellular assays, followed by evaluating their therapeutic roles.

3. CLONING AND EXPRESSION OF N-TERMINUS GPR56 AND STUDYING ITS CELLULAR FUNCTIONS VIA LIGAND BINDING

Using multi-omics approaches, our earlier published work (Ganesh et al. *Frontiers in Oncology*, 2022) explored the importance of GPR56 in GBM and showed its association with mesenchymal phenotype. Interestingly, a lower level of GPR56 and higher TG2 (cellular ligand of GPR56) is associated with the MES subtype of GBM. To further extend our knowledge of GPR56 in cancer biology, we have chosen cervical cancer (CC) as another cancer model, where its expression (using the TCGA dataset) is significantly higher than in normal tissues (**Fig. 2**).

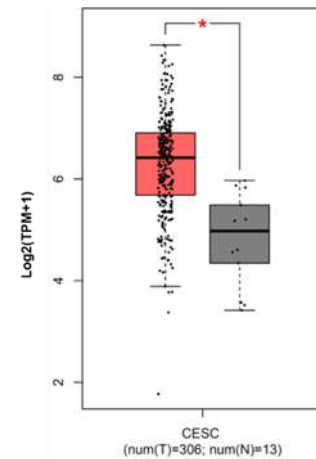


Fig-1: GPR56 expression analysis in CESC using TCGA data.

The prognosis of CC patients remains poor, especially in recurrent and metastatic settings. High GPR56 expression has been shown to be associated with poor survival in CC. Therefore, interfering with GPR56 activity in CC has a strong potential as a therapeutic strategy. Further, GPR56 exerts its functions through N-terminus extracellular receptor interaction with specific ligands. However, its ligand in CC is not known. Therefore, our aim is to identify ligand(s) using soluble N-terminus receptor (GPR56-Nt-Fc) fusion protein and understanding its role in the downstream molecular and cellular processes in CC using cell lines and patient-derived histocultures.

We have already cloned the GPR56-Nt with Fc and expressed it in HEK cell lines followed by purification. Currently, we are characterizing it and also cloning TG2 (the known ligand in GBM context) for further biochemical and cellular assays.

4. SPLICE VARIANTS AS BIOMARKERS AND TARGETS IN GLIOBLASTOMA

Background: Glioblastoma multiforme (GBM) remains the most aggressive primary brain malignancy with a devastating prognosis, characterized by extensive genomic and proteomic heterogeneity that contributes to therapeutic resistance. While traditional genomic and transcriptomic approaches have identified key molecular alterations and enabled subtype classification, a critical gap persists between genomic changes and their functional protein consequences, limiting the translation of molecular findings into effective treatments.

Methods: We applied an optimized proteogenomics pipeline to GBM tissues, integrating transcriptome assembly, custom database generation, and advanced mass spectrometry analysis to identify novel protein variants. Our methodology incorporated dual transcript assembly methods using Trinity and SPAdes algorithms, database optimization through TransDecoder and three-frame translations, and stringent peptide-spectrum match validation through manual inspection and integrated quality metrics. The approach was designed to overcome previous analytical bottlenecks including low confidence in variant identifications and inadequate annotation frameworks.

Results: We identified and characterized over 800 high-confidence peptides, encompassing both canonical and non-canonical sequences derived from GBM tissues. Through comprehensive annotation, these peptides were mapped to diverse genomic features including coding sequences, exonic and non-exonic regions, splice junctions, and pseudogenes. Several peptides displayed sequence attributes indicative of novel translational events, single amino acid variants (SAVs), and alternative splicing patterns. Variant peptides were systematically evaluated for their roles in cancer hallmark pathways, surfaceome profiles, and associations with clinical outcomes including patient survival. Structural modeling of protein isoforms, exemplified by GFAP variants, revealed how exon skipping and novel exonic insertions can significantly alter protein conformation and functional properties.

Conclusions: This study demonstrates the analytical rigor and clinical potential of integrative proteogenomics in GBM research, successfully bridging the gap between genetic variation and functional proteome diversity. Our findings identify putative biomarkers and therapeutic targets that emerge specifically from proteogenomic integration, offering new possibilities for precision oncology approaches in glioblastoma. The methodological innovations and biological insights presented establish a robust analytical framework adaptable to other malignancies characterized by extensive genomic heterogeneity, potentially contributing to improved therapeutic strategies and patient outcomes in neuro-oncology.

Keywords: Glioblastoma multiforme, proteogenomics, protein variants, mass spectrometry, precision oncology, biomarkers, alternative splicing, single amino acid variants

5. IDENTIFICATION AND EVALUATION OF PROGNOSTIC BIOMARKERS FOR AGGRESSIVE PITUITARY ADENOMAS

Pituitary tumours are mostly noncancerous (benign) growth (termed as 'adenomas'), showing the 2nd most common intracranial tumours (10-15%) after gliomas. Generally, they remain in the pituitary gland, but sometimes local spreads are seen in the surrounding tissues, creating physical pressures leading to aggressive and adverse clinical symptoms. 20- 35% of pituitary adenomas (PAs) are invasive and infiltrating in nature. Despite conventional treatment with maximum resection and chemotherapy (TMZ)/radiotherapy, approximately 10% of PAs with the characteristics of invasive and high proliferation rate exhibit early and frequent recurrence. They are clinically termed 'aggressive PAs'. Therefore, there is an unmet need to identify and characterize aggressive PAs for stratifying patients with an increased risk of early recurrence so that a better treatment strategy can be opted for.

In this project, we aim to identify prognostic biomarkers for aggressive PAs that can be integrated into clinical settings for better prognosis. Based on a literature survey, we have selected 5 proteins – CD44, CD15, CD147, CXCR4, and CXCL12 that are highly associated with invasiveness, stemness, and recurrence in PAs. However, their prognostic value is not well explored using the Indian cohort. We then went ahead to evaluate the expression of these proteins in retrospectively collected PAs FFPE blocks (n=56) using an immunohistochemistry (IHC) assay. We prepared a TMA block having 26 samples and performed the IHC. Our preliminary data suggest that strong CD15 expression is more common in aggressive and functional adenomas. Further, CXCR4 is found to be expressed in 70% of aggressive tumors. However, a study with larger samples is needed to explore its prognostic significance, which is underway.

6. VALIDATION OF A MOLECULAR PANEL OF POST-TREATMENT SURVEILLANCE BIOMARKERS BASED ON THE MESENCHYMAL PROPERTY OF GLIOBLASTOMA

Large-scale transcriptomic studies have identified molecular subtypes of GBM, namely proneural (PN), classical (CL), and mesenchymal (MES). The mesenchymal subtype, which is one of the more prevalent subtypes, has been found to be associated with more aggressive, invasive, angiogenic, hypoxic, necrotic, inflammatory, and multitherapy-resistant features with the worst prognosis. Although the median survival of GBM is short, there is a need to develop a panel of post-treatment surveillance biomarkers for better GBM management. Importantly, the MES transition of GBM is also associated with the recurrence. Therefore, one aim is to find out a potential panel of MES-associated proteins that can be used as post-treatment surveillance biomarkers.

Earlier, we identified and created a potential list of 22 genes/proteins (MES-associated) as post-treatment surveillance biomarkers using several datasets, followed by coming down to 12 proteins (based on their plasma levels). We further tested these genes' expression after hypoxia treatment in two GBM cell lines (U251 and LN229) by qPCR and discussed the data during 2023-24. The preliminary data suggested EFEMP2, VCAM1, SERPINH1, SERPINHE1, and SPP1 upregulation (>1.5 fold) in hypoxic conditions.

With this, we plan to test these proteins in GBM plasma during pre-OP, post-OP, and follow-up conditions. After the IEC approval, we initiated the recruitment of patient blood samples. During the last year, we collected 15 glioma blood samples and processed them for plasma and PBMC isolation. Out of 15, we have 10 samples as pre-OP GBM. Our current effort is to collect the follow-up samples, followed by mass spectrometry-based protein identification.

PUBLICATION

1. Ahuja, S., Gupta, P., Ajay, G., Ghorai, A*. (2025). Hypoxia-Induced DNA Damage Response and Genomic Instability Dictate Cancer Treatment Response. In: Mukherjee, S., Kanwar, J.R. (eds) Hypoxia and Tumor Microenvironment. Springer, Singapore, pages 47-76. https://doi.org/10.1007/978-981-96-1016-7_4 (Invited book chapter)
2. Ghorai A, Singh B, Dutt S (2024) Biphasic DNA damage and non-canonical replication stress response govern radiation-induced senescence in Glioblastoma. *J Cell Sci* 137 (24): jcs.261844.
3. First person – Atanu Ghorai. *J Cell Sci* 15 December 2024; 137 (24): JCS263715. <https://doi.org/10.1242/jcs.263715>
4. Ghorai A, Saha S, Rao BJ (2024) PARP-1 negatively regulates nucleolar protein pool and mitochondrial activity: a cell protective mechanism. *Genes and Environ* 46, 18.

POSTER PRESENTATION

1. "Development of Glioma Patient-derived Cellular Models that Capture Tumorigenic Features & Chemo-response" presented in 'NH Research Day' on 18-19 July 2025 at MSMC, Bengaluru
2. "Analysis of clinically relevant deubiquitinases and their functional role in Glioblastoma" presented in "ProUPS-2025- Proteostasis & Ubiquitin Proteasome System- 1st International

Conference on Cellular Symphony: Decoding Protein Homeostasis in Human Health” on 3-5 Feb 2025 at SRMIST, Tamil Nadu

PATENTS / DELIVERABLES

- CNS cancer repository (Total- 593 samples; Glioma: 248 samples)
- Panel of mesenchymal biomarkers for post-treatment surveillance of GBM
- Panel of GBM prognostic markers based on immunosuppression feature
- Panel of 9 Glioma cell lines with different grades (LGG, HGG, GBM)

THE TEAM

CORE TEAM:

Dr. Ravi Sirdeshmukh (Principal Investigator), Dr. Atanu Ghorai (Senior Research Scientist)

Dr. Vijina (Research Associate), Suniti Ahuja (Project Staff), Gnana Ajay (Project Staff), Rakshitha S (Project Staff), Aksa Ann Mathew (Intern)

Raksha Ganesh (PhD Student) (Completed)

CLINICAL COLLABORATORS:

DEPARTMENT OF NEUROSURGERY

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Dr. Dheeraj (DNB),

Department of Pathology

Dr. Akhila L.,

Department of Pathology

Dr. Saurabha Kumar, Department of Radiation Oncology

MSMF COLLABORATORS:

Dr. Sujan Dhar

Dr. Smitha PK

STEM CELL PROGRAM

NEUROSCIENCE RESEARCH PROGRAM

Under the umbrella of Mazumdar Shaw Medical Foundation (MSMF) and Narayana Institute of Neurosciences (NIN), MSMC, Narayana Health, the Neuroscience Research Program has been initiated. One of the main areas of interest is stroke. Stroke is emerging as significant contributor to disability burden in our country. Neurological recovery after middle cerebral artery strokes remains variable and treatment of impairments are challenging with residual deficits being refractory to existing treatments. Standard of care include thrombolysis, mechanical thrombectomy, decompressive craniectomy if indicated, early rehabilitation. To address residual impairments arising from stroke despite best practices, new treatments in focus include stem cell therapy, neuromodulation, brain machine interface, robotic rehabilitation and multi-modal treatments. The program has been initiated with multiple studies

1) STEM CELL-BASED STROKE MANAGEMENT PROGRAM: Stroke stands as a prominent contributor to both disability and mortality on a global scale, presenting a significant concern for public health. The journey of neurological recuperation post-cerebral stroke varies greatly among individuals, with complexities in impairments, some of which persist despite conventional treatments. Timely intervention, whether through clot-dissolving medications or surgical procedures, plays a crucial role in mitigating stroke-induced damage and enhancing recovery prospects. The established standard of care encompasses interventions such as thrombolysis, mechanical thrombectomy, decompressive craniectomy when necessary, and early rehabilitation. Advancing treatment modalities include stem cell therapy, neuromodulation, brain-machine interface technology, robotic rehabilitation, and comprehensive multi-modal approaches. The objectives of this stroke program are to minimize primary ischemic injury, mitigate secondary inflammatory damage, and expedite regeneration and neuroplasticity.

2) HEART ATTACK AND STROKE PREDICTABILITY TOOL: This program initiated by the SKAN team is aiming to integrate Allopathic principles and assessments, Ayurvedic algorithms and principles with a study of the Gut health status over 10 years or longer. This Triangulation naturally increases the predictive value and specificity of statistical conclusions arrived at. MSMF and NH are a part of the consortium carrying out this study. This research is aimed at developing 3 different products for risk predictability of Stroke and Heart attacks - specific to the Indian population across different streams of medicine; Ayurveda and Allopathy. The work is initiated in these studies.

GRANTS

- Stem Cell-based Stroke Management Program (SKAN Research Grant)
- Heart Attack and Stroke Predictability Tool (SKAN Research Grant)

TEAM

Dr Paul Salins, Managing Director, **Dr Amritha Suresh**, Head, Operations

Dr Debprasad Dutta, Research Scientist, Ms Aiswarya RK (JRF), Ms Moupali Saha (JRF)

Collaborators

Narayana Institute of Neurosciences

Dr Thimappa Hegde, Director, Senior Consultant Neurosurgeon,

Dr Komal Prasad, Clinical Lead, Neurosurgery, Senior Consultant Neurosurgeon.

Dr Srikant Venkatakrishnan, Consultant, Department of Physical Medicine and Rehabilitation

Narayana Institute of Cardiac Sciences

Dr Srikant KV, Senior Consultant Cardiologist

CONFERENCES

1st International Online Conference on Clinical Case Reports (IOCCR) on Mar 19-20, 2025

5. Hyperbaric Oxygen Therapy to Enhance Functional Recovery in Bell's Palsy: a Case Series (Dr. Debprasad Dutta)

ICGEB-SLIBTEC NGS symposium in Colombo, Sri Lanka, on May 10, 2024

6. Differential mRNA expression pattern and regulated pathopathways in ischemic stroke: meta-analytic inferences?" (Dr. Debprasad Dutta).

Indian Society of Human Genetics (ISHG) annual conference in Bangalore, India, on January 20-22, 2025

7. Functional annotations of transcriptomic heterogeneity in ischemic stroke: Evidence from bioinformatic analyses" (Dr. Debprasad Dutta)

OVARIAN CANCER PROGRAM

The program is trying to understand the relationship between chemotherapy, cancer stem cell mediated relapse and development of chemoresistance in high grade serous ovarian carcinoma. High grade serous ovarian cancers (HGSOC) are the most lethal gynecological malignancy worldwide despite being only the fifth common gynecological malignancy. Due to absence of effective screening tests, more than 80% of HGSOC present in advanced stage with extensive peritoneal dissemination. As a result, surgical clearance of all cancer affected tissues is impossible even today, and chemotherapy plays an important role in management of advanced cancers. Despite several therapeutic advances, the overall five year survival in advanced disease is dismal and has largely remained unchanged in last few decades. Cancer stem cells have been shown to be responsible for relapse and chemoresistance in many malignancies, including HGSOC. Our research is trying to understand how chemotherapy influences cancer stem cell mediated relapse in advanced HGSOC. We are also interested in understanding the interaction between ovarian cancer stem cells (CSCs) with peritoneal tissue and how the interaction shapes the behaviour of both the tissues. The major study ongoing in this program is Relapse and Chemoresistance in Advanced High Grade Ovarian Carcinoma Post Chemotherapy. We are in the process of trying to establish a biorepository of samples that can help in future projects.

GRANTS

8. Role of cancer stem cell markers in predicting chemoresistant phenotype in advanced high grade serous ovarian carcinoma (AMPOK grant).

CONFERENCES

9. 5th MVR CANCON Indian Society of Oncology (ISO) and MVR Cancer Centre Kozhikode Kozhikode 2024 Aug29-Sep1 Updates in the management of carcinoma cervix (Dr Durga, Invited speaker)

10. NATCON IASO 2024 Annual National Conference of Indian Association of Surgical Oncology Bangalore 2024 Sep26 – 29 Panel - Challenging scenarios in management of Advanced ovarian cancer (Dr Durga, Invited speaker)

11. POACON 2025 Pondicherry State Orthopedic Association JIPMER Pondichery 2025 Jan3-5 How clinicians can perform high impact research ((Dr Durga, Invited speaker)

12. IACR 2025 Indian Association for Cancer research Kolkata 2025 Jan16-18 Understanding chemoresistant relapse in advanced high-grade serous ovarian carcinoma-a gene expression meta-analysis based approach (Delegate-Poster presentation; Dr Durga Prasan)

TEAM

Dr Amritha Suresh (PI)

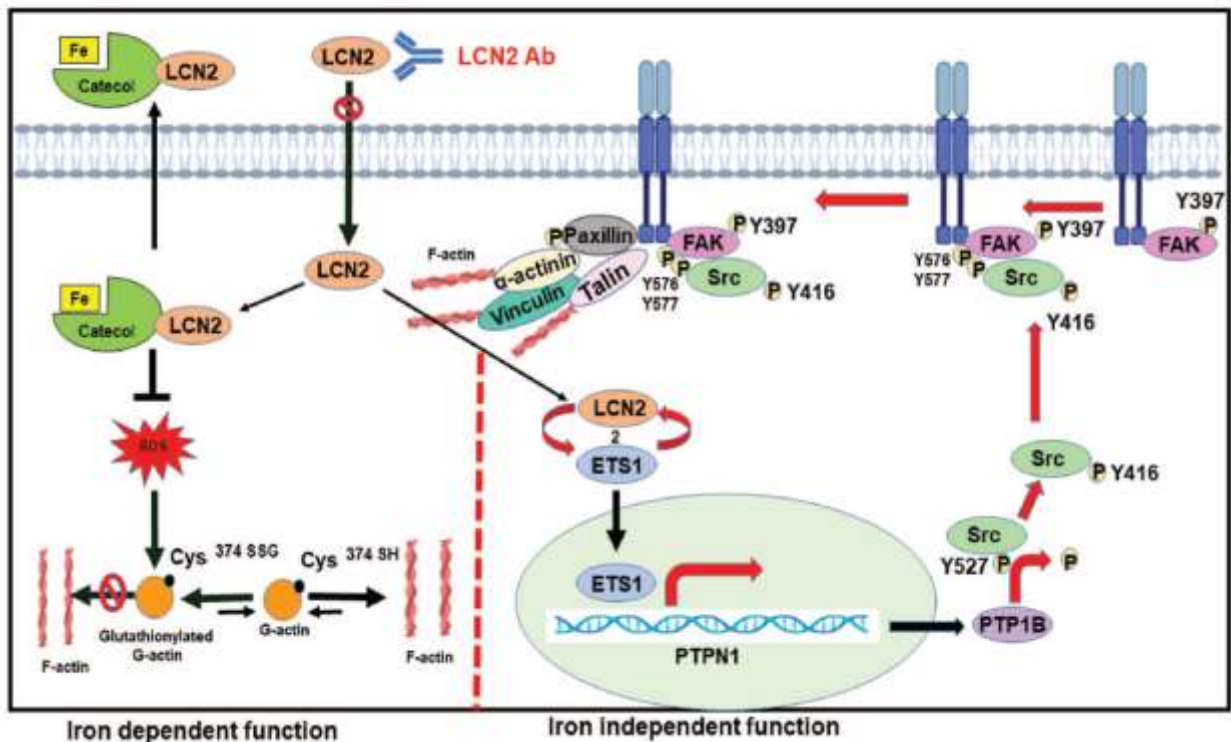
Dr Durga Prasan, Research Scientist. (PM fellow)

MOLECULAR IMMUNOLOGY

In addition to tumor cells neoplasia is known now to contain an abundant and heterogeneous non-transformed component like stromal, endothelial and immune cells. Cancer associated Fibroblasts (CAF) play a major role not only in modulating the tumor cells, but often leading the way as in metastatic migration. The Molecular Immunology group at MSMF concentrates on developing anti-cancer therapy by looking for therapeutic targets beyond the cancer cells.

THERAPEUTIC TARGET PROMOTING TUMOUR CELL INVASION AND MIGRATION

The molecular immunology group has been long working on Lipocalin 2 (LCN2), a neutrophil-associated protein that promotes tumour cell invasion and migration. In a recent study along with Dr Sorab Dalal, the following model has been proposed:



LCN2 promotes invasion in two ways: the first is by stimulating actin polymerization by preventing the glutathionylation of G-actin, which requires the ability of LCN2 to bind iron and inhibit ROS generation. LCN2 stimulates the expression of ETS-1 leading to c-Src activation and focal adhesion formation in a manner that does not require the ability of LCN2 to bind iron. This is the first report of an LCN2 function that is not dependent on the ability of LCN2 to bind iron. Both functions of LCN2 are required to promote invasion and LCN2 expression is associated with increased tumor stage in colorectal cancer and LCN2 is expressed in 60-70% of colorectal cancers. Thus, combining therapeutics targeting LCN2 and c-Src in invasive tumors might result in better patient outcomes and improved responses to chemotherapy in colorectal cancer.

ROLE OF CANCER-ASSOCIATED FIBROBLASTS IN CANCER

Cancer-associated fibroblasts (CAFs) actively remodel the tumour microenvironment (TME), modulating tumour progression, immune evasion, and metastatic potential. Their functional impact, however, varies based on tumour-CAF interactions. MhCT08 and MhCT12 epithelial-CAF autologous pairs were established from OTSCC patients. Epithelial cells alone or co-injected with matched CAFs were administered subcutaneously into CD1 nude mice. MhCT08 epithelial cells generated high-burden tumours *in vivo*, with tumour growth significantly enhanced upon co-injection with autologous CAFs. In contrast, MhCT12 cells exhibited limited tumorigenicity, forming smaller or no tumours despite prior evidence suggesting higher immunogenic potential. These observations were corroborated by tumour volume and endpoint weights. H&E staining revealed densely packed malignant epithelial structures in MhCT08 xenografts, while MhCT12-injected sites showed poorly organized or absent tumour tissue. RNA sequencing revealed distinct transcriptional landscapes across the models. MhCT08 tumours—especially in the CAF co-injection group—exhibited pronounced upregulation of epithelial markers and mesenchymal-to-epithelial transition (MET)-associated genes. These findings indicate a CAF-mediated enhancement of tumour growth and epithelial plasticity.

PUBLICATIONS

1. Choudhary BS, Chaudhary N, Khan BK, Vijan A, Mandal D, Pilankar L, Gawand S, Uttankar P, Sharma M, Shivashankar A, Doloi R, Joshi N, Das M, Dalal SN. LCN2 promotes focal adhesion formation and invasion by stimulating c-Src activation. *J Cell Sci.* 2025; 138(11):jcs263663. doi: 10.1242/jcs.263663.
2. Apala Pal, PritamKumar Ghosh, Sahana Ghosh, SachinKumar Tripathi, Sohini Guha, Pragnya Coca, Subrata Patra, K.M. Prathima, Debjit Khan, Manjula Das, Arindam Maitra, Saumitra Das; p53 translational-isoform $\Delta 40p53$ regulates cell cycle by modulating the miR-4671-5p/SGSH axis bioRxiv 2024.04.04.535506; doi: <https://doi.org/10.1101/2024.04.04.535506>
3. Nehanjali Dwivedi, Tahmina Mazumder, Shivani Tihara, Gayathri Veeraraghavan, Ramanujam Siva, Smitha P K, Rohit Ranade, Anil K M, Sujan K Dhar, Manjula Das. In vitro and In Vivo Evidences Propound Potential of Lipocalin 2 as a Therapeutic Target in Cervical Carcinoma. *Journal of Cancer Science and Clinical Therapeutics.* 7 (2024): 233-248. DOI: [10.26502/jcsct.5079216](https://doi.org/10.26502/jcsct.5079216)

GRANTS

1. Repurposing of anti-lcn2 Mab for treatment of lung fibrosis: BT/CS0114/06/22: BIRAC: 49L; 15 Jan 2024 - 14Jan 2025

CONFERENCE/PRESENTATIONS

- Chief Guest, National Science Day meet , NIPER Hajipur, 28 Feb, 2024 Making an Industry-ready Novel Therapeutic Mab, Dr Manjula Das
- Dr Manjula Das (Poster evaluator), Cardiovascular Research Convergence 2024, NIPER Guwahati, 26-27 October 2024
- Invited Speaker Data for Public Good, Bangalore, 20-21 Sep, 2024 Data designs diagnostics and drugs, Dr Manjula Das
- Invited Speaker Transcription and Disease, Bangalore, 18 Oct, 2024 The King and I, Dr Manjula
- Invited Speaker South Zone ACBI Conference, JIPMER, Pondicherry, 24-25 Jan 2025 Translating the micro-RNA, Dr Manjula Das
- Invited Speaker 5th Annual Summit of Biologics Conferences and Workshop on Biopharmaceutical Product Development Goa 30-31 Jan 2025, Dr Manjula Das

44th Annual Meeting of the Indian Association of Cancer Research Kolkata, 16-18 Jan 2025

- Dr Manjula Das (Poster evaluator),
- Sohini Guha LCN2 IS THE LANGUAGE THAT TUMOR CELLS SPEAK TO THE MICROENVIRONMENT
- Shashikumar NOVEL METHOD TO DETECT PAN IDH-R132 MUTATIONS IN CANCER
- Sagar Ballikai, STUDYING THE ASSOCIATION OF FIBROSIS AND CANCER IN PATIENT DERIVED LUNG TISSUES 6AND IN VIVO MOUSE MODEL
- Rohit Indurkar STUDY OF HER2-NEU AND PD-L1 CO-EXPRESSION IN CANCER OF THE GASTRO-INTESTINAL TRACT
- Shraddha Vijay, LCN2/MMP9 COMPLEX, RATHER THAN THE INDIVIDUAL PROTEIN IS THE BIOMARKER FOR METASTASIS IN CANCER
- Mrudula Gosavi, Study of Tumorigenicity of Cancer Associated Fibroblasts
- Bhaskarjyaa Chatterjee ROLE OF IMMUNE MICROENVIRONMENT IN PRE AND POST CANCER FIBROSIS
- Ushnaa Kuri RECOMMENDATION FOR THERAPEUTIC COMBINATIONS BASED ON ANAPLASTIC THYROID CARCINOMA'S ANATOMICAL BASIS

MOLECULAR IMMUNOLOGY TEAM

Principal Investigator: Dr Manjula Das

Team Members: Sohini Guha, Shashikumar T, Sagar Balikai, Mrudula Gosavi, Rohit Indulkar, Shraddha Vijay, Jesna Salim, Anushka Vijaysimha and Dr Syeda Lubna

Collaborators: Dr Sujan K Dhar (MSMF), Dr Sorab Dalal (ACTREC), Dr Pragnya Coca (Kaveri Hospitals), Dr Annapoorni Rangarajan (IISc) and Dr Prathima K (BMJH)

COMPUTATIONAL BIOLOGY

Computational Biology group at MSMF aims to employ emerging computational and AI-based techniques beyond conventional bioinformatics to develop solutions that can aid patient care and aid in our understanding of disease.

For the past few years, we have been working on AI-based analysis of hematoxylin and eosin (H&E) stained histopathology slide images that are used for routine pathology of tumors. Using neural network-based AI models we have been able to identify molecular features in brain tumor slides that cannot be detected through visual inspection by pathologists. We aim to take this research forward to solve similar diagnostic challenges in other solid tumors.

As part of the clinician PhD program, we have undertaken research to understand the platinum resistance mechanism in high-grade serous ovarian carcinoma. An extensive analysis of publicly available gene expression data indicates that neoadjuvant chemotherapy alters the transcriptomic profile of ovarian tumors towards a more resistant phenotype, a finding that is likely to have major implication in clinical practice. We have also initiated research in the area of pulmonary fibrosis, a major health burden in India with very limited treatment options. Using publicly available gene expression data, we are aiming to arrive at a set of blood biomarkers that can predict the progression to advanced stage of fibrosis.

Antibodies are important biological molecules used as probes in research and diagnosis as well as a therapeutic agent to inhibit a target. Over the years the antibody sequence database has grown multifold setting the platform for computational engineering and development of antibodies using machine learning algorithm. We are currently working on methods to derive antibody designs from transcriptomic profile of patients or immunized animals.

The Computational Biology group also works with multiple research groups at MSMF to build disease prognosis models through biomarkers generated from Next Gen Sequencing data generated in-house or acquired from public datasets. We use a blend of conventional functional genomics tools and advanced algorithms to create a functional landscape of the underlying biology captured in the sequence data snapshot.

DETECTION OF IDH1 MUTATION FROM H&E-STAINED HISTOPATHOLOGY IMAGES OF BRAIN TUMORS

In tumors formed in glial cells around neurons, mutations observed in the isocitrate dehydrogenase (IDH) family of genes are linked with an improved prognosis. Detection of this mutation, primarily by immunohistochemistry (IHC) using mutation-specific antibodies is common clinical practice to decide the therapeutic course. However, IHC is often limited to detect only the most commonly observed mutation whereas the non-canonical mutations are missed out. In this study, in collaboration with pathologists from NH, Bangalore and NIMS, Hyderabad we are developing an AI-based computational model that can categorize the histopathology images into IDH-mutant and IDH-wildtype molecular subtypes. This study is funded by ICMR through an extramural grant.

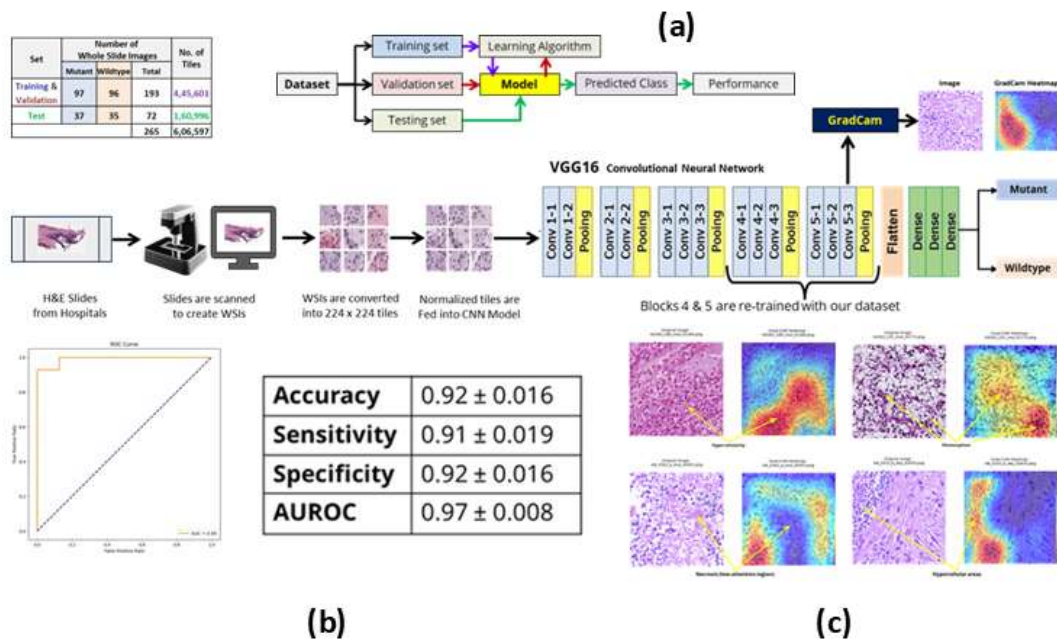


Figure 1: Detection of IDH1 mutation from H&E slide image: (a) Number of samples, workflow and neural network model, (b) ROC curve and performance figures and (c) Attention maps depicting regions that contribute most to classification.

For this task we standardized a VGG16-based transfer learning model with retraining of blocks 4 and 5 with our dataset of $n = 197$ slides to yield the best classification accuracy (Fig 1a). On a test set of 72 slides, the model obtained an overall accuracy of 0.92 in classifying the slides as wildtype or mutant with both sensitivity and specificity exceeding 0.9 (Fig 1b). Further, we also established explainability of the AI model using a GRAD-CAM layer that highlights the regions in each image contributing the most in classification (Fig 1c). From the highlighted regions we find that hypercellularity, pleomorphism and necrotic regions are the features that contribute most between IDH1 wildtype and IDH1 mutant classification. This study was first of this kind taken up by Computational Biology group of MSMF and its success will prompt us to explore similar studies in other solid tumors.

PLATINUM RESISTANCE MECHANISMS IN HIGH-GRADE SEROUS OVARIAN CARCINOMA

Chemoresistance is the key determinant of long-term survival in advanced high-grade serous ovarian cancer (HGSOC). The molecular mechanisms underlying chemoresistance in clinical populations is not clearly known. The study aimed to analyze the molecular mechanisms promoting chemoresistance, as well as neoadjuvant chemotherapy (NACT)-induced sensitive-to-resistant transformation in advanced-HGSOC patients. We acquired RNA-sequencing data from Gene Expression Omnibus datasets GSE162714, GSE173420 and GSE227100 database and categorized the patients in pre-chemotherapy (resistant vs sensitive) and chemo-sensitive (post-chemotherapy vs pre-chemotherapy) subgroups. For each subgroup, differential-gene-expression meta-analysis and downstream analysis for pathway enrichment, protein-protein network and cancer stem cell expression were performed.

Prechemotherapy inherent-resistant samples showed elevation of inflammation, epithelial-mesenchymal-transition processes, higher stromal proportion in tumors with upregulation of cancer-associated-fibroblasts (CAF) and some of the cancer stem cell markers over the sensitive phenotype. On the other hand, exposure to NACT in chemo-sensitive patients led to similar increase in inflammation, immune evasion, CSC-led proliferation and drug-efflux-pump overexpression, with increased immune and CAF cells in stroma mirroring an inherent-resistance phenotype, implying a sensitive to resistant transformation (Fig 2). This study indicates inflammatory cytokines CCL2/CCL5 could potentially be used as serum biomarkers for prospective identification of chemo-resistant patients, thus paving the way for personalized therapy.

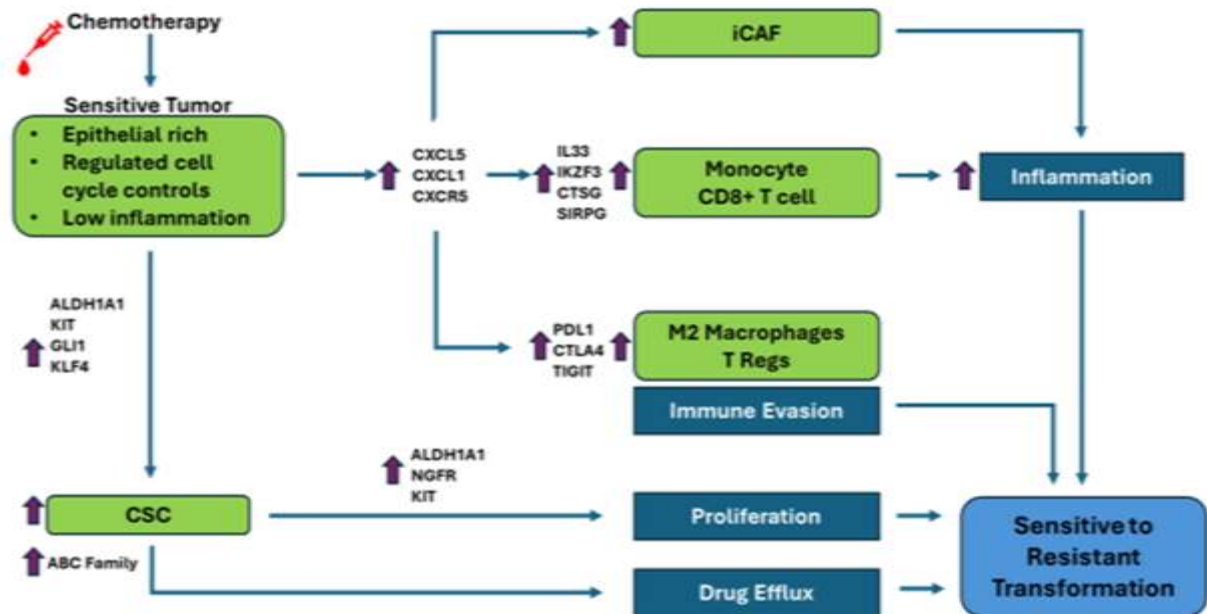


Figure 2: Possible mechanism for neoadjuvant chemotherapy induced sensitive-to-resistant transformation in high grade serous ovarian carcinoma

PROGNOSTIC BIOMARKERS FOR IDIOPATHIC PULMONARY FIBROSIS

Interstitial lung diseases (ILDs) encompasses a group of disorders characterized by varying degree of inflammation, fibrosis, or both in the interstitium of lungs. Among them Idiopathic pulmonary fibrosis (IPF) is one of the forms of ILD with an unknown etiology. It is an irreversible, severe form of fibrotic ILD IPF which causes scarring of the interstitium and formation of fibroblasts leading to respiratory failure. IPF is histologically defined by the presence of usual interstitial pneumonia and has a poor long-term prognosis with progressive fibrosis. IPF is traditionally staged with terms such as mild or early and severe or advanced based on pulmonary function tests and imaging. Despite advances in diagnostic imaging and pulmonary function testing, IPF remains a major diagnostic challenge, especially in its early stages.

In this study, we address the critical gap in prognosis of IPF through a wide transcriptomic analysis of publicly available gene expression datasets of lung tissue samples from early and advanced stage IPF patients. Using techniques such as differential gene expression, co-expression clustering, pathway enrichment and machine learning models we arrive at a panel of six genes that could be used to classify early and advanced stage with an overall accuracy of 0.97. These genes include collagen markers, matrix metalloproteases and inflammation markers and all of them code for secretory proteins. Going forward, we will aim to develop a blood-based diagnostic using these markers that could predict onset of progressive IPF at an early stage of disease.

DEVELOPMENT OF MONOCLONAL ANTIBODY THROUGH REPERTOIRE SEQUENCING

Since the Nobel prize-winning hybridoma technique that was developed more than forty years ago, monoclonal antibody development have evolved towards more data-oriented approaches to derive antibody variable fragment sequences that could be expressed as recombinant antibody clones. One such method is the immune repertoire sequencing in which transcriptome sequencing data of infected individuals or immunized animals are analyzed to assemble the antibody transcripts. Further these antibody sequences are modelled in silico and computational techniques such as docking, molecular dynamics or deep learning models such as AlphaFold are used to predict their interaction with the target antigen.

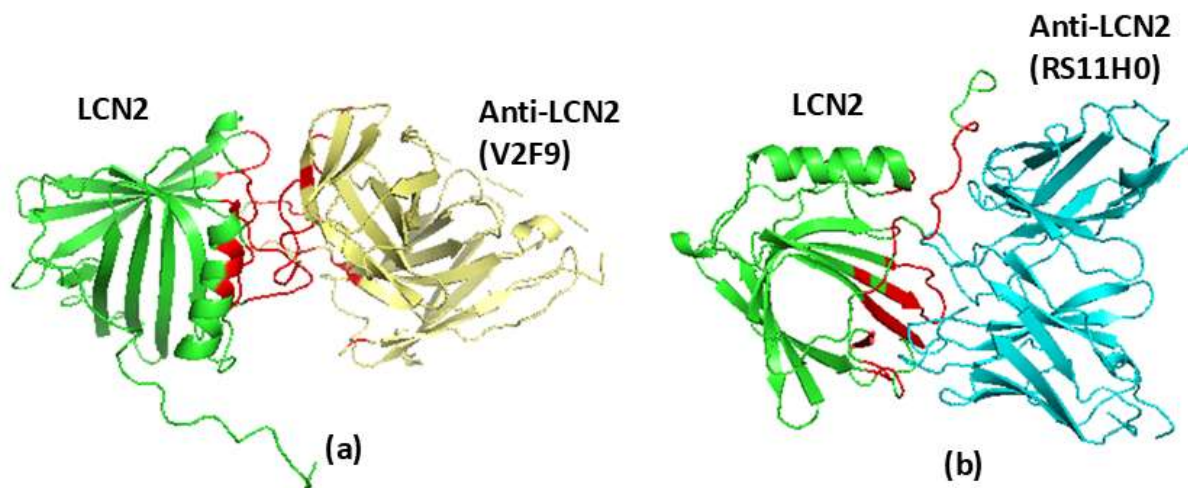


Figure 3: Flexible docking of anti-LCN2 antibodies with LCN2 (a) Hybridoma-derived clone V2F9 and (b) Rabbit immunoglobulin-derived and framework humanized clone RS11H0

In collaboration with Molecular Immunology group, we have identified multiple antibody sequences by sequencing RNA from splenocytes of rabbit immunized with Lipocalin 2 (LCN2) protein. The sequences were modelled and their binding with LCN2 protein were assessed in comparison with binding of an antibody clone developed from the hybridoma (Fig 3). Antibody clones with best binding affinity were shortlisted and humanized by grafting the CDRs into a human IgG framework. The clones are currently being synthesized and will soon be expressed in mammalian systems to check their binding affinity. Once validated, this will become a more efficient and time-saving method for development of monoclonal antibodies.

PROJECTS PLANNED FOR NEXT YEAR

We have planned following projects in the next year:

1. Development of an AI-based model for prediction of HER2 IHC score from H&E-stained histopathology slides: currently proof-of-concept model development is being carried out using funds from existing ICMR project, will apply for funds from ICMR in 2026.
2. Development of a prognostic test to predict progressive IPF: This will be a follow-up study from the gene expression analysis work, and we have applied for fund for this in the current ICMR grant call of 2025.
3. Assessment of auto-antibodies in atherosclerosis patients through immune repertoire analysis of publicly available gene expression data: Initial bioinformatics analysis will be carried out using MSMF funds and subsequently grant application will be made for clinical studies and data generation.

PUBLICATIONS

Khan B, Singhvi A, Dhar SK, Shetty V, Punnen J, Rahguraman B, Mohan BM, Raj V, Tousheed SJ, Patangi S, Gupta T. *Long-Term Outcome of Patients with Chronic Thromboembolic Pulmonary Hypertension Following Pulmonary Thromboendarterectomy Surgery-Results from a Referral Centre in India*. The Journal of Heart and Lung Transplantation. 2024 Apr 1;43(4):S311-2.

James BL, Zaidi SN, Aiswarya RK, Shetty V, Vidya Bhushan R, Dokhe Y, Naveen BS, Pillai V, Dhar SK, Kuriakose MA, Suresh A. *Modeling the lymph node stromal cells in oral squamous cell carcinoma: insights into the stromal cues in nodal metastasis*. Human Cell. 2025 Jan 6;38(2):41.

D Prasan, Unnati Raut, Madhumathi HK, G Siddappa, Bonney LJ, A Suresh, SK Dhar, *Does neoadjuvant chemotherapy bias the transcriptomic profile of platinum-sensitive advanced high grade serous ovarian cancer patients towards a resistant phenotype? Findings from a gene expression meta-analysis* (manuscript under preparation)

Raut U and Dhar SK, *Prognostic Biomarkers for Idiopathic Pulmonary Fibrosis* (manuscript under preparation 2025)

GRANTS

2. Development of an AI-enabled computation model for IDH1 mutation detection from H&E-stained glioma histopathology images, in collaboration with NIMS Hyderabad (funded by ICMR), 2023-26
3. In silico modelling and target binding assessment of generated antibody fragments (funded by Invitrogen Bioservices India), Aug-Dec 2024

CONFERENCES TALKS/PRESENTATION

CONFERENCE TALKS

1. Part of panel discussion in Cardiovascular Research Convergence 2024, NIPER Guwahati, 26-27 October 2024
2. Invited talk on "Orthogonal methods for IDH mutation detection in CNS tumors: from ddPCR to AI", South Zone ACBI Conference, JIPMER, Pondicherry, 24-25 Jan 2025
3. Invited talk on "Application of AI in Translational Research: Case studies with IDH1 mutation detection in CNS tumor", Research Symposium on AI in Biophysics, IISc, Bengaluru, 28-29 April 2025

PRESENTATIONS BY TEAM MEMBERS

44th Annual Meeting of the Indian Association of Cancer Research, Kolkata, 16- 18 Jan 2025

- Unnati Raut, Poster presentation in Kolkata, 16- 18 Jan 2025
- Durga Prasan, Poster presentation

Research Symposium AI in Biophysics, IISc, Bengaluru, 28-29 April 2025

- Unnati Raut, Poster presentation in Research Symposium on April 2025
- Abhijna Chandra, Poster presentation

TEAM

Principal Investigator: Dr Sujan K Dhar

Research Scientist: Dr Durga Prasan (jointly with Dr Amritha Suresh)

Project Associates: Unnati Raut, Abhijna Chandra

Consultant: Sreejith Puthenveetil

PRODUCT RESEARCH GROUP

FOCUS OF PRODUCT RESEARCH GROUP: The focus of this group is to translate potential diagnostic and therapeutic molecules generated as research outcomes from the discovery groups (Head and Neck Oncology/ Molecular Immunology/Neuro-oncology) at MSMF or a product initiated from the product research group.

Group structure: Head of the product research group with two Junior Research Fellows and project interns

COMPLETED/ ON ONGOING PROJECTS

DEVELOPMENT OF FUNCTIONAL PRECISION ONCOLOGY PLATFORM USING PATIENT-DERIVED 3-DIMENSIONAL OVARIAN ORGANOIDS:

Funding: MSMF PRG group Fund and Invitrogen Fund (**IBSC approval:** MSMF/N/022/2024-25; **IEC approval:** NHH/AEC-CL2024-1334)

AIM:

1. To develop, Characterize and biobank long-term expandable ovarian cancer PDOs for high-throughput personalized drug screening
2. To integrate tumor genomic and transcriptomic profiles with PDO-based drug sensitivity data to identify biomarkers of resistance.
3. To model tumor-stromal interaction using co-culture systems.

ABSTRACT: High-grade serous ovarian carcinoma (HGSOC) is the most prevalent and lethal subtype of ovarian cancer, accounting for a significant proportion of gynecologic cancer deaths. Its poor prognosis stems from challenges in early detection, widespread peritoneal dissemination at diagnosis, and the near-inevitable development of resistance to first-line platinum-based chemotherapy. While next-generation sequencing has improved our understanding of the genomic alterations in HGSOC (e.g., BRCA1/2, TP53, HR pathway defects), these insights alone have not sufficed for reliable treatment personalization. This underscores the need for **functional precision oncology platforms** that can bridge the gap between genomic data and therapeutic outcomes. We propose to develop a **patient-derived organoid (PDO) platform** integrated with **genomic and transcriptomic profiling** and **drug screening**, to model individual tumor behavior and guide therapy selection in real-time. We hypothesize that **patient-derived ovarian tumor organoids (PDOs)** can serve as functional avatars to faithfully mimic individual tumor response to chemotherapy *ex vivo*. By integrating **organoid-based drug response assays** with **multi-omic tumor profiling**—including genomic and transcriptomic data—we can generate a high-dimensional dataset that, when analyzed using **AI/machine learning (ML)**, will enable accurate prediction of **chemotherapy sensitivity and resistance** in ovarian cancer patients.

Anticipated Significance and Impact:

- **Real-time precision medicine tool:** Enable oncologists to select the best-suited drug regimen tailored to the patient's tumor biology.
- **Improved clinical outcomes:** Reduce ineffective treatment cycles and prevent toxicity from non-responding agents.
- **New resistance mechanisms:** Discovery and validation of novel genes and signalling networks contributing to chemoresistance.
- **Translational potential:** The data generated can inform future biomarker-driven clinical trials or companion diagnostics.

RESULTS:

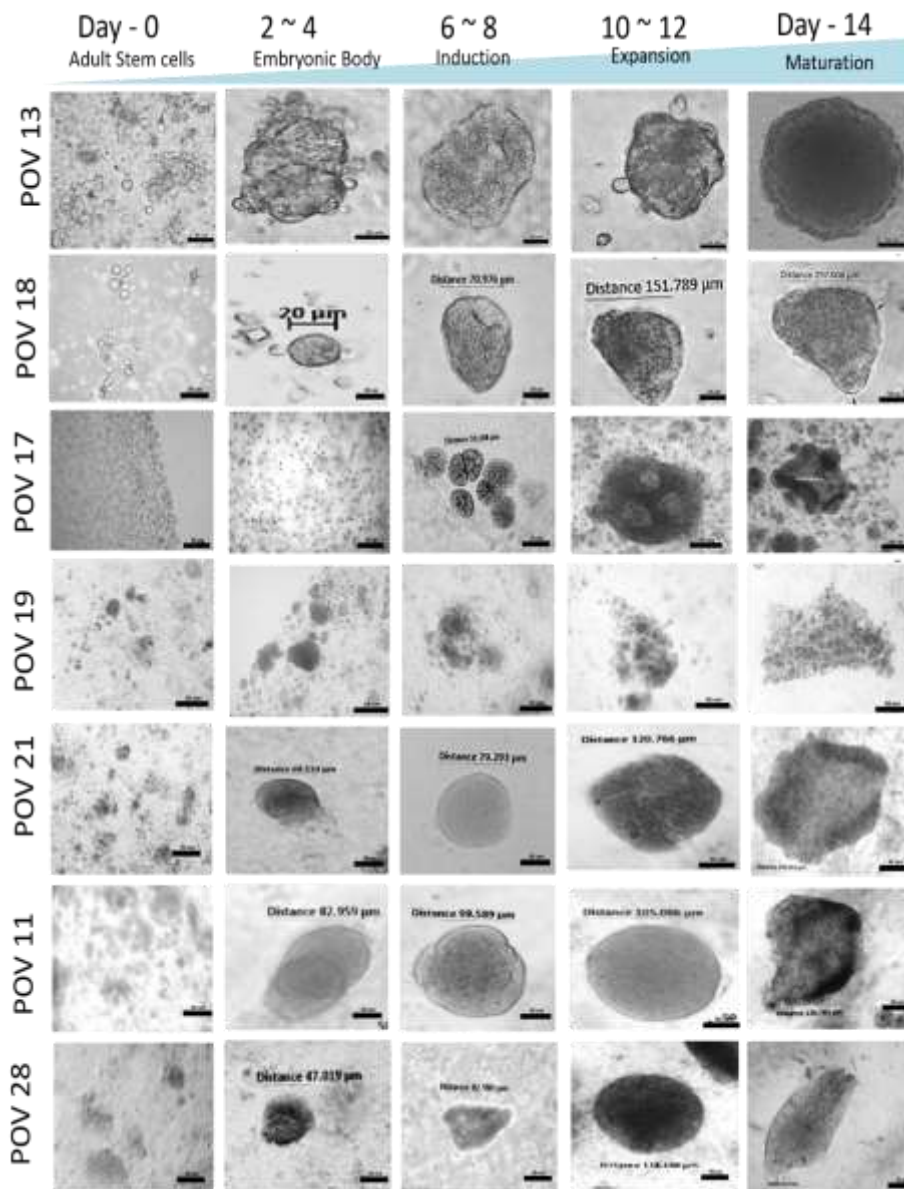


Fig 1. Progression of Organoid Morphogenesis from Adult Stem Cells over a 14-Day Culture Period. Brightfield microscopy images illustrating the sequential morphological stages of organoid development derived from adult stem cells. The progression encompasses the initial stem cell state (Day 0), embryonic body formation (Days 2–4), lineage induction (Days 6–8), organoid expansion (Days 10–12), and terminal maturation (Day 14). Multiple samples are presented to represent variability in organoid size and structural complexity at each stage. Scale bars indicate spatial dimensions for quantitative reference.

Identification no. of PDOs	Indications	No. of Passages
POV - 11	Endometroid carcinoma	6
POV - 13	HGSOC	15
POV - 16	HGSOC	4
POV - 17	HGSOC	9
POV - 18	HGSOC	12
POV - 19	HGSOC	5
POV - 21	HGSOC	8
POV - 22	Borderline serous carcinoma	4
POV - 23	HGSOC	4
POV - 24	HGSOC	4
POV - 27	HGSOC	6
POV - 28	Low-grade serous carcinoma	7
POV - 30	HGSOC	3
POV - 31	HGSOC	3
POV - 32	HGSOC	1

Table 1. Summary table of patient-derived organoids (PDOs) used in the study, showing identification numbers (POV codes), tumor indications, and the number of culture passages achieved. The PDOs represent various ovarian cancer subtypes, predominantly high-grade serous ovarian carcinoma (HGSOC), with passages ranging from 1 to 15, indicating successful expansion and maintenance of tumor models in vitro.

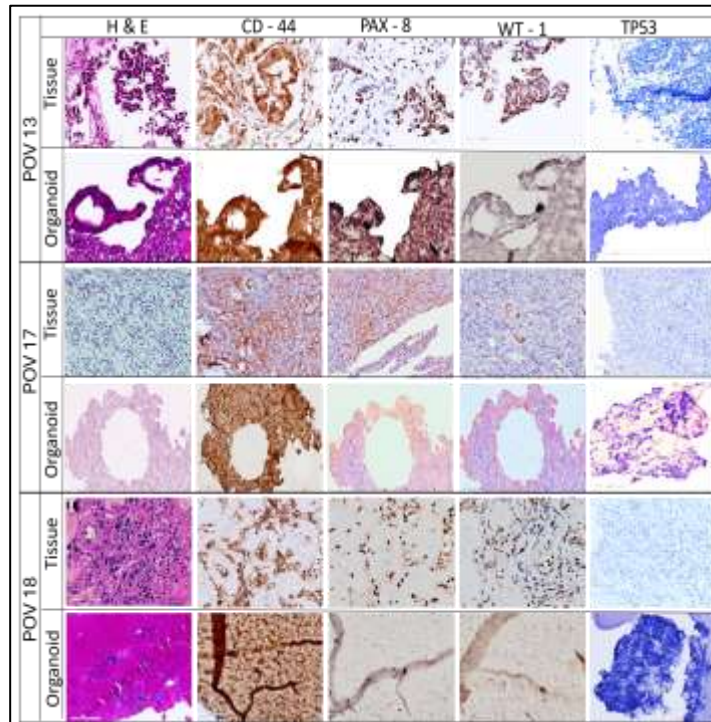


Fig. 2. Histological and immunohistochemical analysis of patient tumor tissues and matched organoids (POV13, POV17, POV18), stained for H&E, CD44, PAX8, WT1, and TP53. Organoids preserve the key marker expression and architecture of the original tumors. Scale bars: 100 μ m.

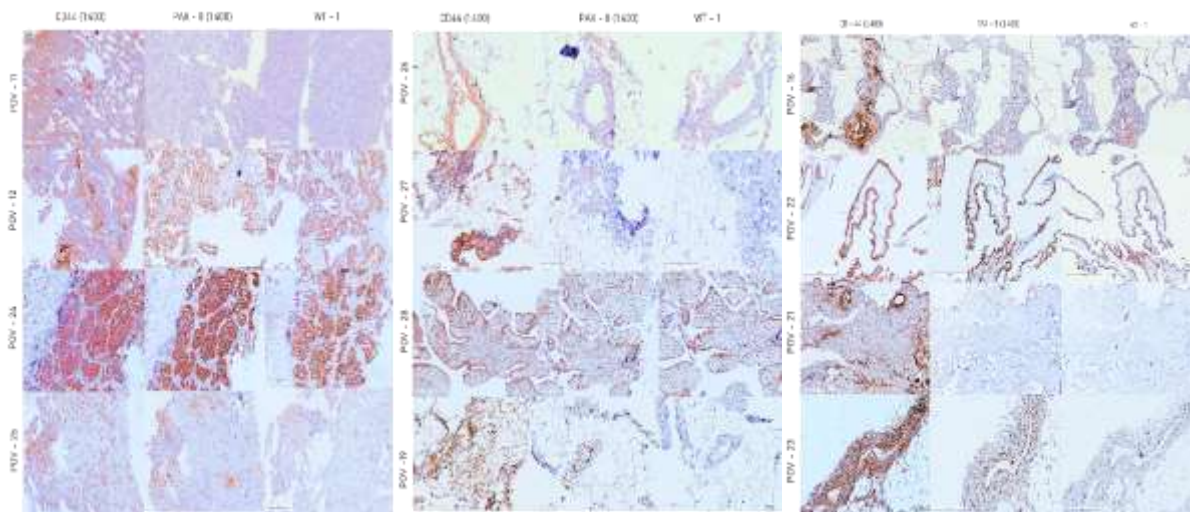


Fig. 3. Representative histological and immunohistochemical staining of patient tumor tissues. Panels show H&E and immunostaining for CD44, PAX8, and WT1 across multiple patient samples (e.g., POV-11, -12, -24, -25, -26, -27, -28, -19, -16, -22, -21, -23). Rows compare original tumor tissues, while columns represent different markers. Positive staining (brown) indicates preserved marker expression and tumor architecture, demonstrating organoids faithfully recapitulate key histopathological and immunophenotypic features of their parental tumors. Scale bars: 100 μ m.

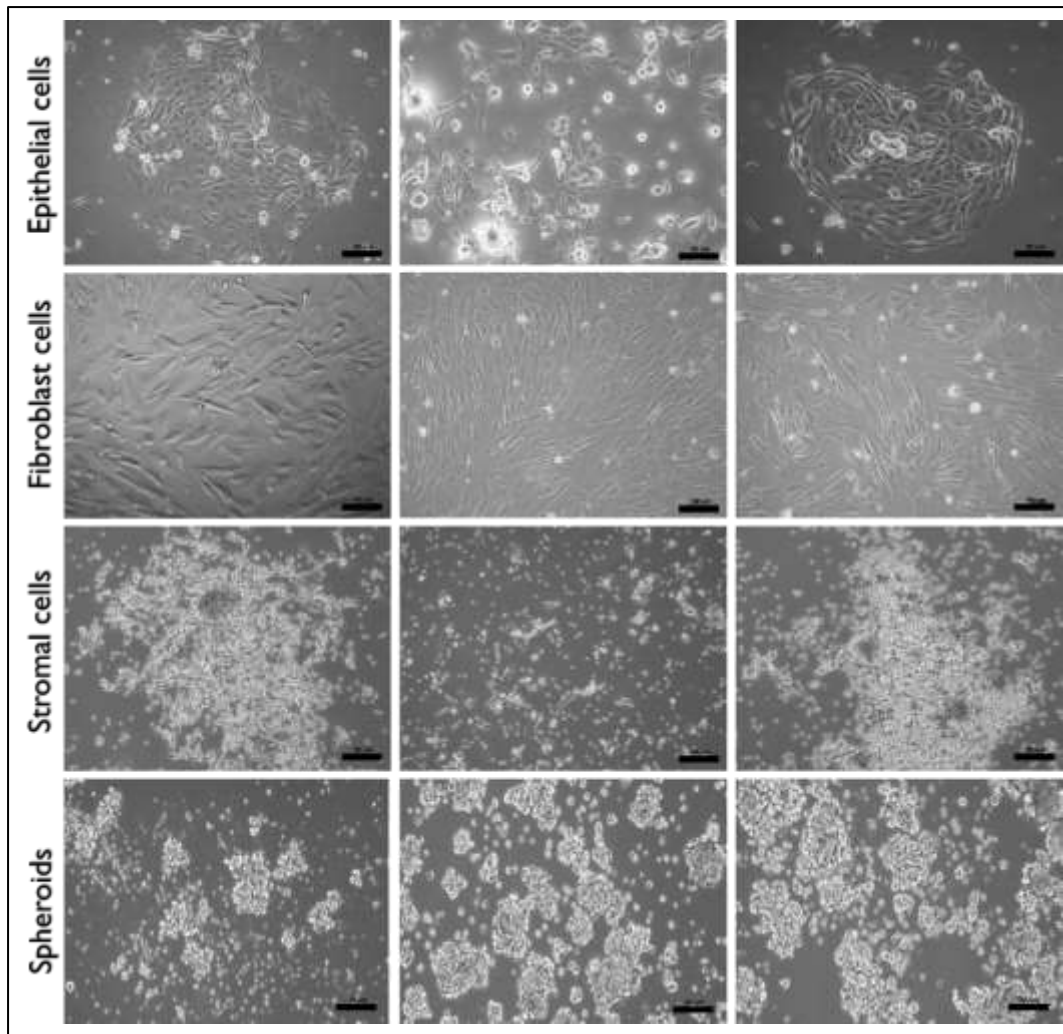


Fig.4. Phase-contrast microscopy images showing heterogeneous cell populations in culture. Spindle-shaped adherent cells forming monolayers and cancer-associated fibroblast cell lines, as well as clusters of round, loosely attached stromal cells forming spheroid-like aggregates, derived from resected ovarian tumor tissue and ascitic fluid, respectively.

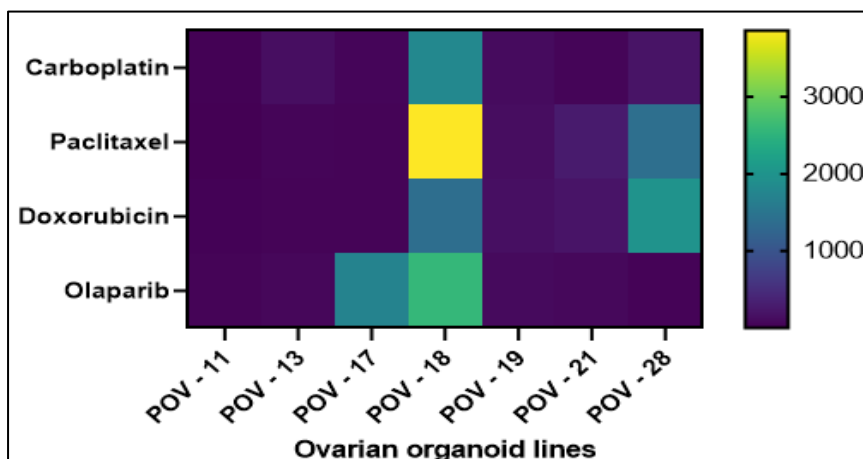


Fig.5. Heatmap showing drug response profiles of ovarian cancer organoid lines (POV-11 to POV-28) to carboplatin, paclitaxel, doxorubicin, and olaparib. Variability in sensitivity highlights inter-patient heterogeneity captured by organoid models.

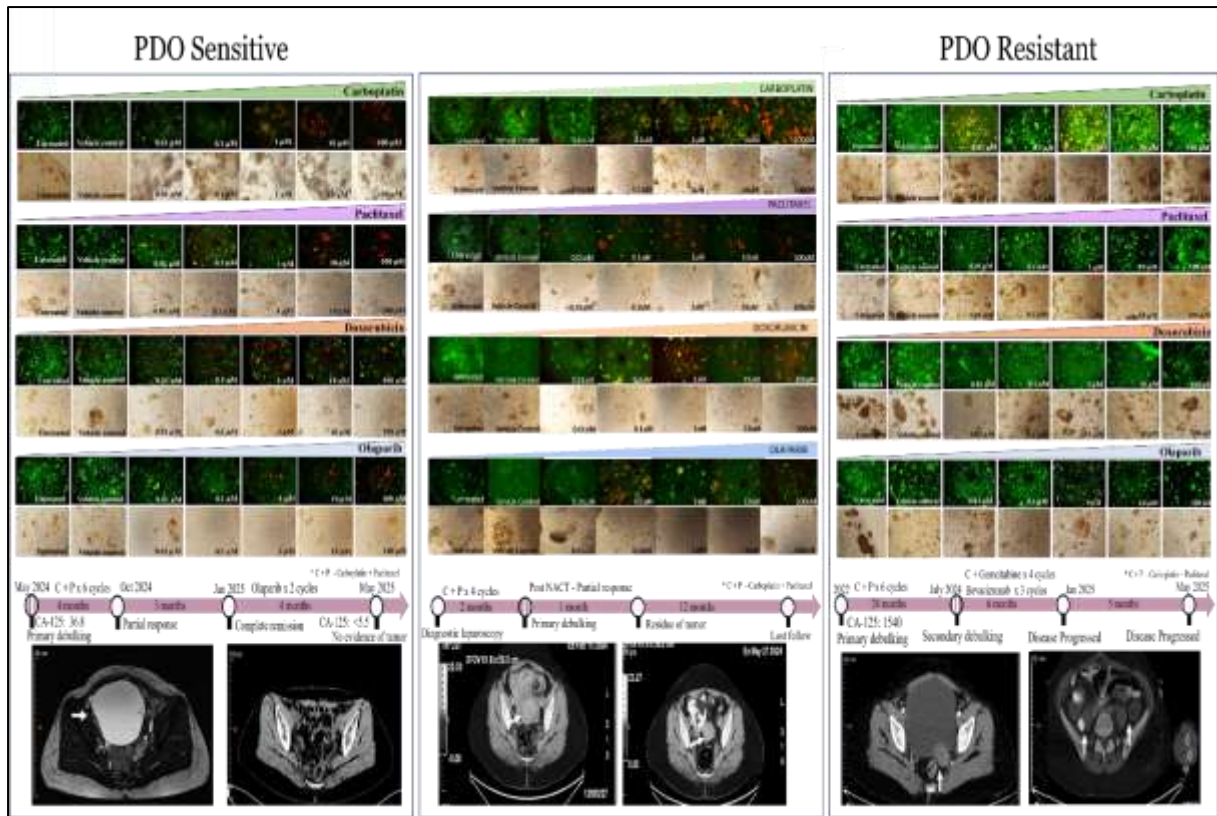


Fig.6. Drug sensitivity of patient-derived ovarian cancer organoids(POV - 13, 17, & 18) to carboplatin, paclitaxel, doxorubicin, and olaparib. Live/dead staining (green/red) and brightfield images show dose-dependent cytotoxicity, demonstrating the utility of organoids for personalized drug screening.

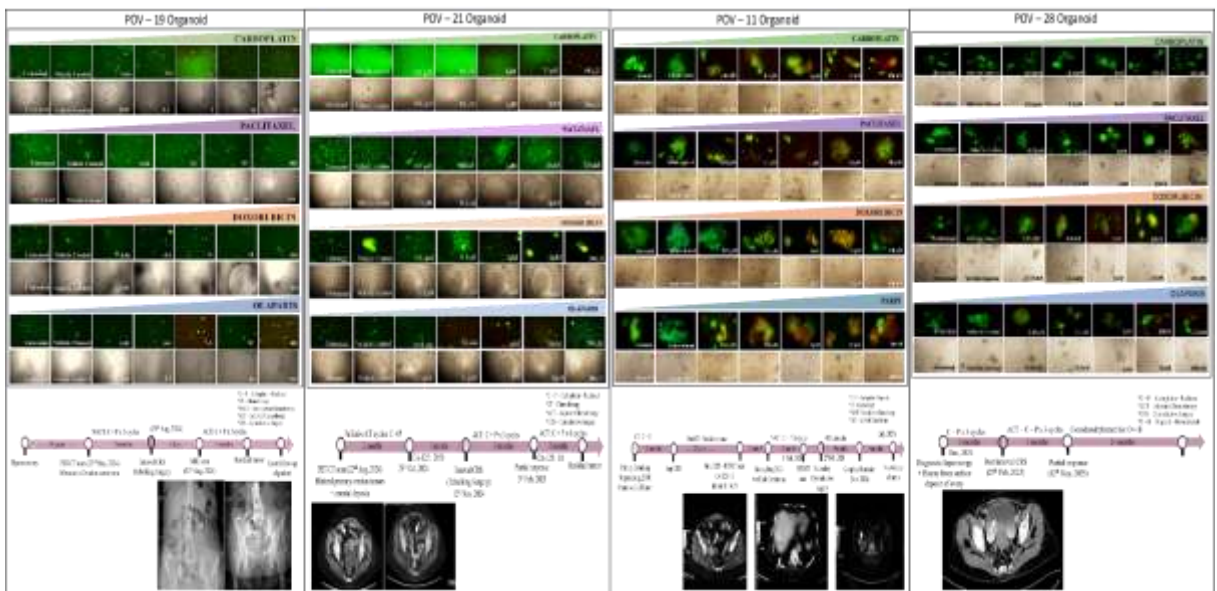


Fig 7. PDO-based drug screening mirrors clinical response in ovarian cancer patients (POV -19, 21, 11, and 28). Fluorescence and brightfield images show the effect of Carboplatin, Paclitaxel, Doxorubicin, and Olaparib on patient-derived organoids (PDOs) over time. Viability and morphological changes reflect differential drug sensitivity. Corresponding patient MRI and CT scans over follow-up periods demonstrate clinical response, aligning with PDO assay results. This highlights the utility of PDOs in predicting personalized treatment outcomes.

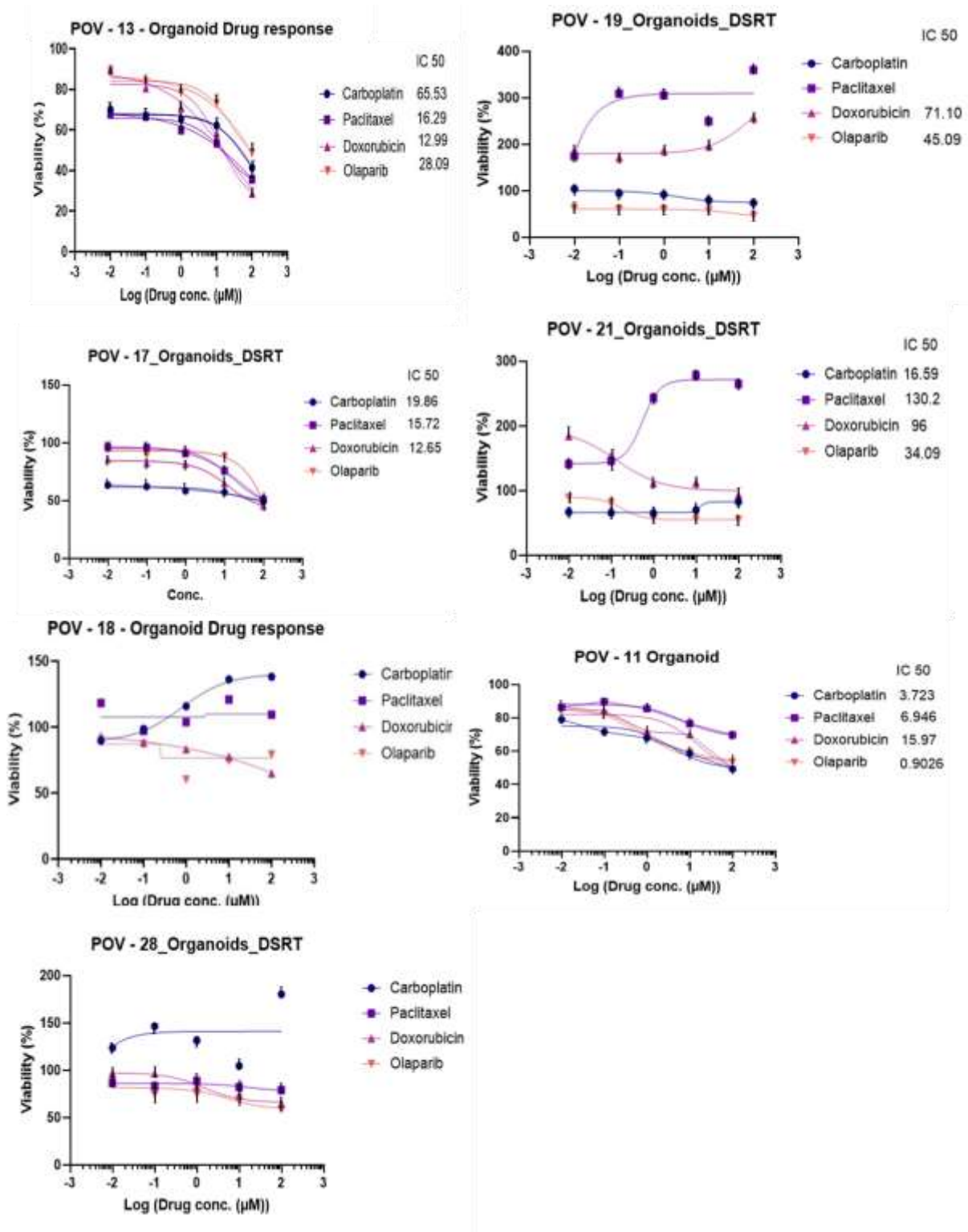


Fig8. Invitro Drug sensitivity profiling of patient-derived ovarian cancer organoids, Dose-response curves showing the viability of organoids derived from multiple patients (POV-11, 13, 17, 18, 19, 21, and 28) upon treatment with increasing concentrations of chemotherapeutic agents: Carboplatin, Paclitaxel, Doxorubicin, and Olaparib. Each curve represents the percentage of viable cells plotted against the log-transformed drug concentrations (μM). IC₅₀ values are indicated where available, reflecting the drug concentration required to reduce viability by 50%. Variability in response across different organoid lines

illustrates the heterogeneous drug sensitivity among patients, highlighting potential for personalized therapy guidance

PATIENT VALIDATION OF SALIVARY S100A7 AND S100P AS NON-INVASIVE BIOMARKERS FOR EARLY DETECTION AND RISK STRATIFICATION OF ORAL POTENTIALLY MALIGNANT AND MALIGNANT DISORDERS (IN COLLABORATION WITH DR. AMRITHA SURESH, HEAD AND NECK ONCOLOGY)

Funding: ICMR (Oral Potentially Malignant Lesion Atlas project: validating the efficacy of Novel Point-of-Care diagnostics and developing an integrated multidimensional prognostic nomogram). **IBSC approval:** MSMF/R/016/2023-24 **IEC approval:** NHMEC; A41/2022/EA-2/A-1

ABSTRACT: Oral squamous cell carcinoma (OSCC) is among the most prevalent cancers globally, with especially high incidence rates in South Asia. Nearly 80% of OSCC cases arise from oral potentially malignant disorders (OPMDs), which display variable and often unpredictable malignant transformation potential. Early detection and risk stratification are essential, yet current diagnostic methods remain invasive and nonspecific. In this study, we assessed the clinical utility of two salivary biomarkers, S100A7 and S100P, for non-invasive detection of OSCC and high-risk OPMDs. A sensitive in-house enzyme-linked immunosorbent assay (ELISA) was developed to quantify these proteins in saliva samples collected from 355 participants, including 116 OSCC patients, 116 with OPMDs, and 123 with benign oral conditions. Both biomarkers showed significantly elevated levels in OSCC and OPMD groups compared to benign lesions. The combined panel achieved 87% sensitivity and 92% specificity in distinguishing OSCC/OPMDs from benign cases, and 96% sensitivity and 92% specificity when discriminating OPMDs alone. Furthermore, the assay differentiated high-grade dysplasia and OSCC from low-grade dysplasia with 90% sensitivity and 75% specificity. **Importantly, the study also evaluated the biomarkers' ability to distinguish OPMDs and oral cancer from inflammatory lesions—addressing a key limitation in current biomarker-based diagnostic validation.** This distinction is critical, as inflammatory conditions often mimic early neoplastic changes, leading to diagnostic ambiguity. Overall, the findings support the clinical potential of salivary S100A7 and S100P as a non-invasive, cost-effective screening tool for early detection and monitoring of oral cancer progression, particularly in resource-constrained healthcare settings.

RESULTS

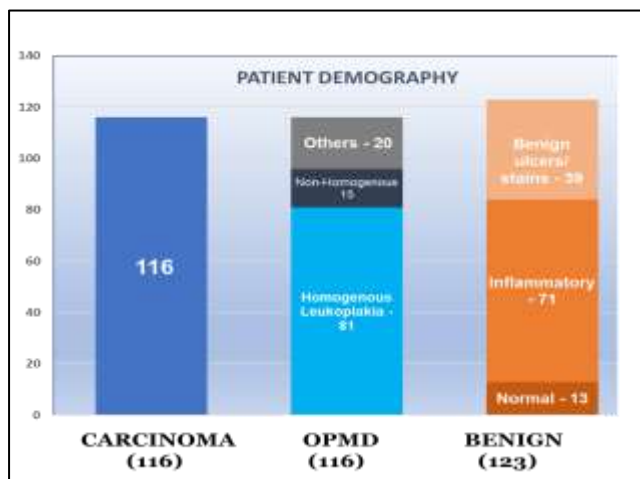


Fig9: Patient Demographic details

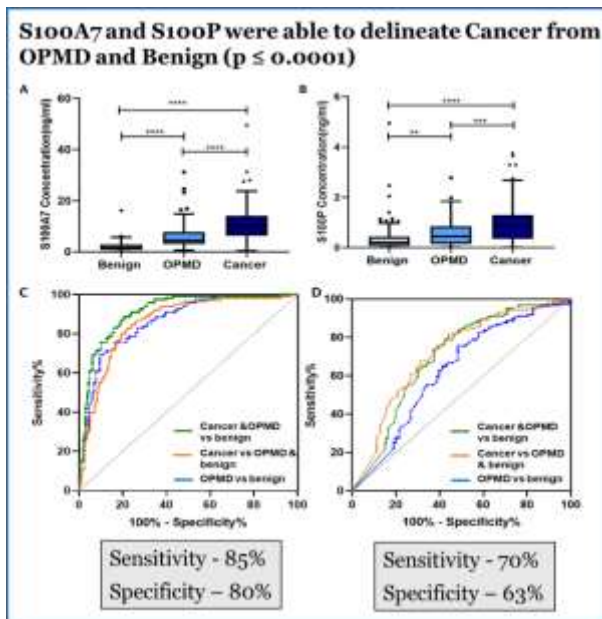


Fig10: Expression of S100A7 and S100P in saliva from cancer (n = 116), OPMD (n = 116), and benign (n = 123) groups. (A) Salivary S100A7 levels across groups. (B) Salivary S100P levels across groups. (C) ROC curve demonstrating diagnostic performance of S100A7 (D) ROC curve demonstrating diagnostic performance of S100P. Differential expression significance assessed using Kruskal-Wallis test (****)

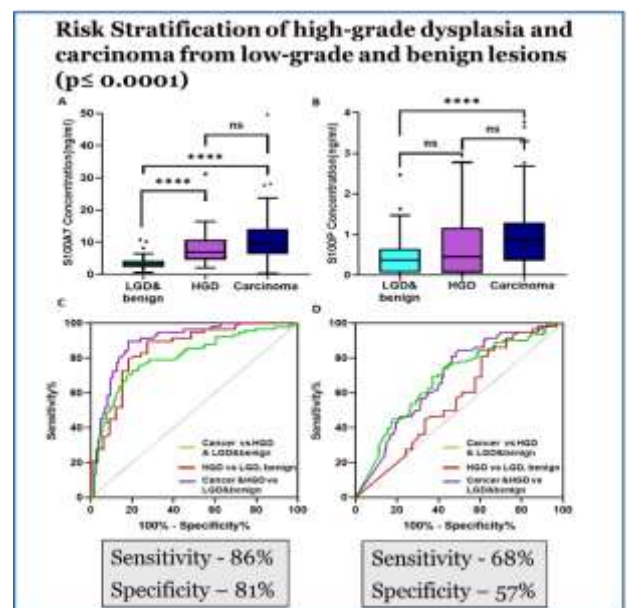


Fig11: Salivary expression of (A) S100A7 and (B) S100P across benign/LGD (n = 58), HGD (n = 33), and carcinoma (n = 116). (C–D) ROC curves for classification based on S100A7 and S100P. Kruskal–Wallis test used for statistical comparison (**** $P \leq 0.0001$; ns, not significant)

STUDY OUTCOME AND FUTURE PROSPECTS

- Salivary S100A7 levels progressively increase from benign lesions to low-grade dysplasia (LGD), high-grade dysplasia (HGD), and ultimately OSCC.
- The study underscores the clinical relevance of salivary S100 biomarkers in monitoring and managing oral precancerous and cancerous lesions.
- Future work will focus on retrospective validation in larger and independent cohorts and the development of a rapid PoC diagnostic kit.

ELISA ASSAY DEVELOPMENT AND VALIDATION FOR THE DETECTION OF SALIVARY CD44 PROTEIN

(In collaboration with Dr. Amritha Suresh, Head and Neck Oncology)

Funding: ICMR (Oral Potentially Malignant Lesion Atlas project: validating the efficacy of Novel Point-of-Care diagnostics and developing an integrated multidimensional prognostic nomogram). **IBSC approval:** MSMF/R/016/2023-24 **IEC approval:** NHMEC; A41/2022/EA-2/A-1

AIM:

1. To make recombinant CD44 protein in *E. coli* expression system
2. Purification of anti-CD44 polyclonal antibodies and conjugation to HRP enzyme.
3. ELISA Assay development and validation for the detection of CD44 from Saliva Samples

Production of recombinant protein

Synthetic gene corresponding to the 21 to 649 amino acids (extracellular domain) of CD44 was synthesized from Genscript, USA in pET 28A+ vector. The vector was transformed into BL21 Rosetta cells

and cultured for the production of the CD44 recombinant protein. The recombinant protein was purified on Ni-NTA resin. The proteins produced was validated with commercial anti-CD44 polyclonal antibody

Polyclonal Antibody development

The in-house generated protein was immunized into New Zealand white rabbits and mice to develop polyclonal and monoclonal antibodies respectively. The rabbits were administered up to five booster doses until sufficient titer was obtained, post which the animals were bled and the antisera separated. The antibodies were purified using protein A-based affinity chromatography

ELISA Method development and validation

Purified polyclonal CD44 antibodies were used for ELISA-based assay method development and validation of the same in the Saliva matrix. The polyclonal antibodies were used both as capture and detection antibody. For preparing the detection antibody, the purified polyclonal antibody was conjugated to HRP. Enzyme. The detection range of these proteins was determined using a saliva matrix.

RESULTS

CD44 Recombinant protein production

Western blot confirmation

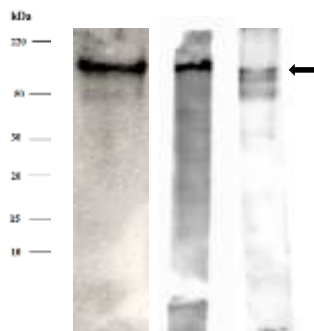


Figure 11: Western blot developed for blot 1- CD44 recombinant protein incubated with anti CD44 polyclonal rabbit antibody, blot 2- monoclonal CD44 developed against in-house generated protein, blot 3- monoclonal CD44 developed against commercially available CD44 antigen

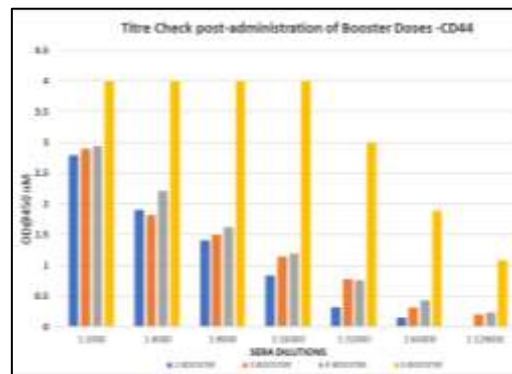


Figure 12: Polyclonal anti-CD44 antibody Titer check results

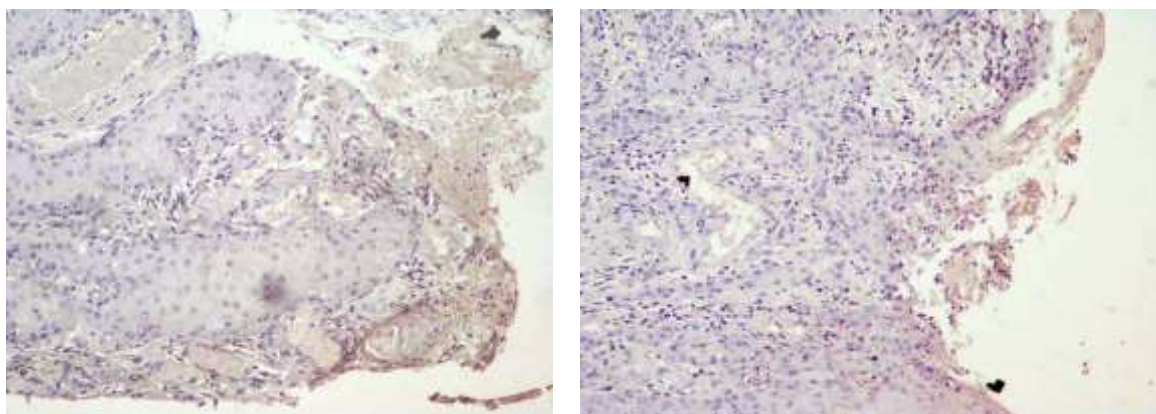


Figure 13: Polyclonal anti-CD44 Antibody Validation by Immunohistochemistry

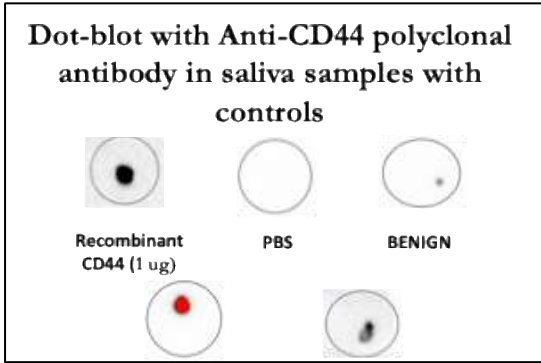
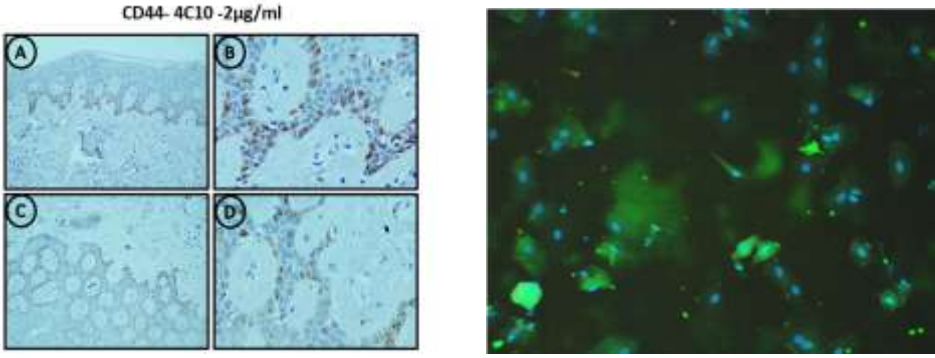


Figure14: Dot blot

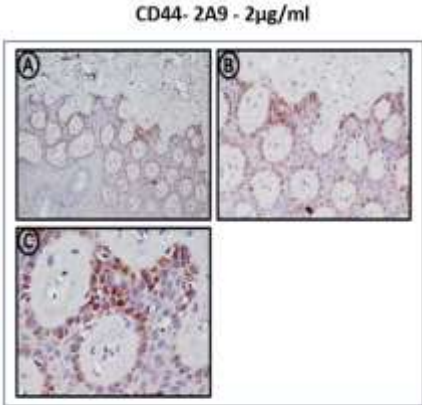
Characterization of Anti-CD44 monoclonal Antibodies (4C10, 2A9, 5F6)

Validation by Immunohistochemistry and Immunocytochemistry

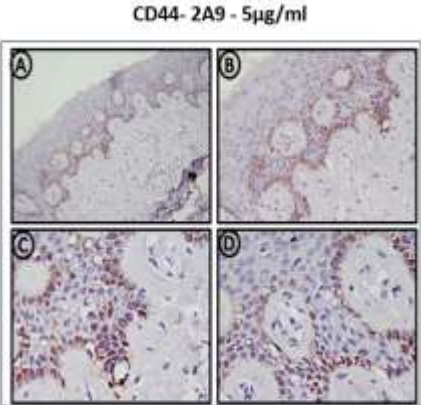


CD44- 4C10 - 5µg/ml
 A- 10X at 2ug/ml, B- 40X at 2ug/ml
 C- 10X at 5ug/ml, D- 40X at 5ug/ml

Anti-CD44 mAb (4C10) FITC on OSCC tongue cell



A- 10X 2A9 - 2µg/ml, B- 20X 2A9 - 2µg/ml
 C- 40X 2A9 - 2µg/ml



A- 10X 2A9 - 5µg/ml, B- 20X 2A9 - 5µg/ml
 C- 40X 2A9 - 5µg/ml, D- 40X 2A9 - 5µg/ml

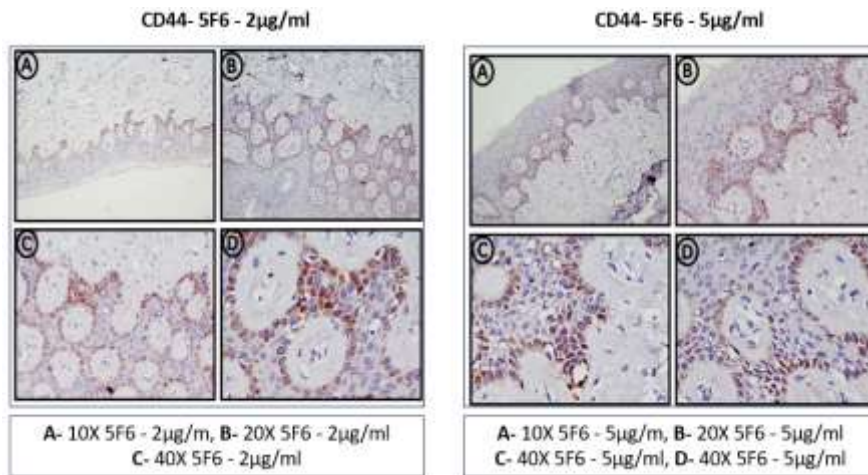


Figure 15. CD44 showed differential staining in the nuclear and cytoplasmic regions mainly in keratotic nodules which can be observed at 5ug/ml dilution of 4C10, **15.2** CD44 showed differential staining in the nuclear and cytoplasmic regions mainly in keratotic nodules which can be observed at 5ug/ml dilution of 2A9, **15.3** CD44 showed differential staining in the nuclear and cytoplasmic regions mainly in keratotic nodules which can be observed at 2ug/ml dilution of 5F6

ELISA assay CD44:

Assay development:

- Purification of polyclonal antibody: to be used as capture and detection: completed
- HRP-Conjugation of an anti-CD44 polyclonal antibody to be used as a detection antibody for assay development: completed

ELISA Assay method development

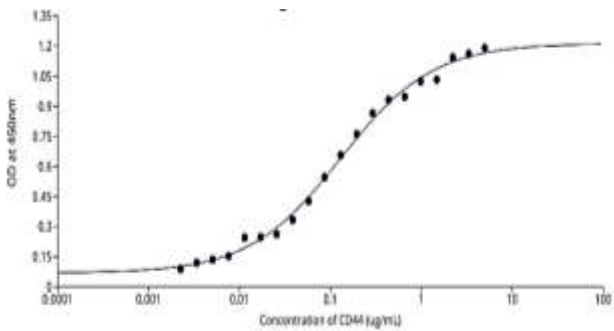


Figure 16: 4-PL curve depicting the assay range for the detection of CD44 from Saliva matrix

Table2: Assay development parameter

PARAMETERS	CD44
Sensitivity	0.007 µg/mL
Linearity	2.2- 0.007 µg/mL
Range	5 - 0.002 µg/mL
Specificity	detects native and recombinant CD44 protein
LOD	0.002 µg/mL
Assay matrix	Saliva

Future work

- **Patient recruitment:** A large recruitment of different cohorts of patients is planned in order to validate the assay through ELISA.
- **PCB Chip-based detection:** Multiplexed PCB chip is being developed and standardization is being carried out for S100A7, S100P proteins (this work is in collaboration with IISc Bangalore).

POSTER PRESENTED

1. Poster Presented: “Reducing Animal Testing In Preclinical Studies: Organoids as a Promising Game Changer?” at MSMF TRANSCON 2025
2. Poster Presented: “Predicting Chemotherapy Outcomes in High-Grade Serous Ovarian Carcinoma: A Multi-Omics Framework for Personalized Therapy” at University of Liverpool (2025).
3. EPISKIN challenge 2025: “Organoid-Based Preclinical Testing: A Human-Relevant Alternative for Drug Testing in the Era of FDA-Endorsed NAMs”
4. NH Research Day: “Organoid-Based Preclinical Testing: A Human-Relevant Alternative for Drug Testing in the Era of FDA-Endorsed NAMs”

MANUSCRIPT IN PREPARATION

- Salivary S100A7 and S100P as Non-Invasive Biomarkers for Early Detection and Risk Stratification of Oral Potentially Malignant and Malignant Disorders
- Precision Oncology Pipeline for Ovarian Carcinoma: A case study from Indian Cohort.

PATENT DOCUMENT (TO BE FILED)

- A method for long term culturing, biobanking and drug screening using Ovarian cancer Organoids

TEAM

Smitha PK (Senior Research Scientist)

Ms Shruti Ragotham (JRF-PRG)
Leah Achsa John (Intern student-VIT),
Muskan Iqbal Kazi (Intern Student-Garden City University),
Ambika K (Intern Student-Garden City University),
Raghuveer Reddy (Intern Student-Garden City University)
Keerthi J (With Head and Neck)

ADVANCED DIAGNOSTIC RESEARCH CENTRE



Advanced Diagnostic Research Center (ADRC), is in the process of developing a robust ecosystem to meet the demands of today and anticipate tomorrow's challenges of diagnostic research and development solutions. In the past one year, ADRC has bloomed to providing analytical support to biotech, nutraceuticals and pharma industries for R&D and clinical trials in addition to providing niche diagnostic solutions to patients.

ADRC has expanded the diagnostic service offering to NGS based molecular diagnostic through an agreement with Histotech, an established diagnostic company in Bangalore. In collaboration with CPDTRI (Center for Precision Diagnostic and Therapeutic Research, India), ADRC has gained access to the Industry to act as a central laboratory for the efficacy analysis for clinical trial as well as content estimation for nutraceuticals and pharmaceuticals. ADRC has also gained expertise for diagnostic assay development

TESTS OFFERED

Test	Sponsor
HLA- high resolution-6 Loci (A, B, C, DPB1, DQB1, DRB1)	Hospitals
IDH mutations by ddPCR	Hospitals
Metagenomic Content	Hospitals
T cell Activation Assay	Vaccine Developers
In vitro efficacy study for inflammatory skin condition	Nutraceutical Industry
Metagenomic content analysis of Clinical trial samples by NGS	Nutraceutical Industry
Undenatured Collagen content estimation of	Nutraceutical Industry

RESEARCH AND DEVELOPMENT AT ADRC

With appropriate consent from the patients, ADRC performs research with the excess sample and the data obtained from the test. The research improves the tests themselves, brings out possibilities of new tests and helps in knowledge creation of the disease. Major driver of the research is to establish tests that are reliable to clinicians and affordable to patients.

Topic	Sponsor
Development of Mutation-specific Antibody	DBT
Development of Assays for Inflammatory Markers	CPDTRI
Detection of IDH mutations by Liquid Biopsy	Intramural

GRANTS

4. Construction of immune phage display library for developing diagnostic platform for screening point mutations in cancer patients; DBT; 102L; Jul 2024-Jul 2026
5. Characterization of IHC-panels for stratification of various cancers : Invitrogen: 8L: Jul 2025- Jul 2026

ADRC TEAM

Laboratory Director: Dr Manjula Das

Scientists: Dr Syeda Lubna, Rohit Indurkar, Jesna Salim and Shashikumar T

Collaborators: NH: Dr. Komal Prasad, Dr Basha J Khan, Dr Aditi Singhvi, Dr R Bagirath, Dr Shobha, Dr Vidya and Dr Sharat Damodar

BMJH: Dr Prathima

Kaveri Hospitals: Dr Pragnya Coca

TECHNOLOGY BUSINESS INCUBATOR



As the first hospital-based incubator, we've proudly nurtured over 50 groundbreaking ideas with the guidance of 100+ mentors. With Invest India's backing, as part of the Startup India Seed Fund Scheme Program, we are fueling early-stage innovations. We're also facilitating the soft landing of startups in India, helping them penetrate the market by partnering with various embassies. Additionally, we're active in accelerator forums and host numerous ecosystem interaction events.

Top News

Catalyst Compass 1.0: A Success!
Scroll to page [02] to read about Catalyst Compass 1.0, featuring **40 speakers, 20 stalls, and 200+ attendees**

Showcasing at GBI 2024!
Scroll to page [03] to read about our proud participation at GBI 2024, held at Pragathi Maidan, New Delhi.

Global Interactions and Partnerships
Scroll to page [04] to read about the vibrant global ecosystem interactions and partnership developments that lit up Q3 2024.

MSMF-TBI: Committed to Health, Festivities, and Engagement
Scroll to page [05] to read more





20 stalls

25 partners

40 Speakers

200+ audience





MSMF-TBI is proud to have partnered with VaidyaRx for the successful OTCCON 2024, bringing together leaders and innovators in healthcare. The event saw over **70 premium organizations, 150 delegates in person, and 300+ virtual participants.** This collaboration fostered valuable insights and connections for all the participants

IMPACT WITNESSED



We were honored to host Dr. Sanjay Tyagi, Jurisdictional Director of STPI - Software Technology Parks of India, and his team at MSMF-TBI and Narayana Health. Dr. Tyagi engaged in insightful discussions with our founders, Dr. Devi Shetty and Dr. Paul C. Salins, exploring potential collaborations.



YKG Academy for Continuing Education in Health and Pharmaceutical Sciences

vaidyaRx

YKG Academy in association with VaidyaRx Presents:

Webinar cum Panel Discussion:
Preparing for Interviews for Clinical Trial Related Jobs

Panelists:

 Prof. Y.R. Gupta Professor, IISM's Institute Former Dean, AIIMS Delhi	 A. R. Pradhan Former Joint Dean Coordinator, C-DECS, MSMIFW	 Dr. Renu Swarup Former Senior Lecturer, DRI, Ministry of Science & Technology	 Prof. R.M. Pandey Senior Chair, IISM DRI, Ministry of Science & Technology, IISM's Institute	
 Prof. Bikash Mehta Professor, PDI, Chandigarh	 Dr. Shubhadeep Sinha Senior Vice President, Harrow-King's Limited, London	 Dr. Shobha Mukharjee Clinical Research, London	 Varun Gupta Value and Service Director, International, Novartis	 Tarun Gupta Founder, A.C.T.O., VaidyaRx

29-03-2025

YKG Academy in collaboration with MSMF-TBI and VaidyaRx conducted a high-impact webinar on Clinical Trial Career and pharma career aspirants

YKG Academy for Continuing Education in Health and Pharmaceutical Sciences

vaidyaRx

YKG Academy in association with VaidyaRx Presents:

Upskilling Events for Pharma & Healthcare Professionals
First Webinar cum Panel Discussion:
Preparing for Pharma Industry Expectations - Orientation Session for Aspiring Pharma Graduates

Panelists:

 Prof. Y.R. Gupta Professor, AIIMS Institute Former Dean, AIIMS Delhi	 A. R. Pradhan Former Joint Dean Coordinator, C-DECS, MSMIFW	 Dr. Kamala Bai Vice President, St. Lukes Hospital, Bangalore	 Varun Gupta Value and Service Director, International, Novartis	 Tarun Gupta Founder, A.C.T.O., VaidyaRx
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24-02-2025



MSMF-TBI is proud to witness Thermaissance achieve this incredible milestone as the official supplier of tracksuits for the Tri-Services Sports Team at the National Games 2025.



Listen to founder Mr. Arijit Majumdar as he shares insights on their groundbreaking technology. We are delighted to welcome them under the support of the Startup India Seed Fund Scheme.

MSMF-TBI'S ECOSYSTEM INTERACTION



REPRESENTATIVES FROM THE JAPANESE GOVERNMENT AGENCIES METI, DIGITAL AGENCY, AND IPA, ALONG WITH HEALTHCARE GIANTS HEALIOS AND FUJI FILM.



DYNAMIC DELEGATION FROM DENMARK'S BIOINNOVATION INSTITUTE AND LEADING MEDTECH AND BIOTECH COMPANIES



DR RAHUL AMRITRAJ, HEAD OF THE CENTRE FOR MEDICAL INNOVATION, GIMS STARTUP CENTRE FOR MEDICAL INNOVATION A PUBLIC HOSPITAL BASED INCUBATOR (GOVT. OF UP) VISITED MSMF WITH ABRAR AHMED



SHUN SAGARA, SEED INVESTOR AT GENESIA VENTURES



SWISS STARTUPS PART OF SWISSNEX INDIA'S AIT PROGRAM



ECOSURE TEAM FROM ZIMBABWE



START2 GROUP - GERMAN ACCELERATOR TEAM



JETRO STARTUP ECOSYSTEM INVITATION PROGRAM



DR. VIKNISH KRISHNAN, CEO OF CELLIVATE TECHNOLOGIES, AT MSMF-TBI TO EXPLORE AVENUES FOR EXPANDING CELLIVATE'S CUTTING-EDGE CELL-BASED INNOVATIONS IN INDIA. IN COLLABORATION WITH WE FOUNDER CIRCLE, MSMF-TBI AIMS TO PROVIDE THE NECESSARY SUPPORT FOR CELLIVATE'S ENTRY AND GROWTH IN THE INDIAN HEALTHCARE AND MEDTECH SECTORS.

03/05

MAZUMDAR SHAW CANCER OUTREACH PROGRAM

The philanthropic wing of the Mazumdar Shaw Medical Foundation is devoted to supporting underprivileged patients by providing financial aid, nutritional assistance, and psycho-social support, thereby helping them lead healthier and more fulfilling lives. Although advancements in medical science have significantly improved cancer care, access to such care remains limited for many individuals. MSCOP seeks to address this disparity by assisting families in successfully completing their treatment. This is achieved through a comprehensive approach that encompasses both medical treatment and financial support for those in need.

ACTIVITIES OF MSCOP

- Providing financial assistance to underprivileged families for treatment.
- Organizing activities for children in pediatric oncology wing.
- Daily nutritional supplement support program.
- Drug discounts for needy patients.
- Liaise with various organizations for the benefit of patients
- Providing emotional support to patients and their families
- Counselling patients and caregivers

SUPPORT PROVIDED TO NUMBER OF PATIENTS IN 2024-25

CATEGORY	NEW PATIENTS	PATIENTS AVAILED DRUG DISCOUNT	PATIENTS SUPPORTED
Adult	16	8	21
Pediatric	35	9	48

FINANCIAL ASSISTANCE TO UNDERPRIVILEGED FAMILIES

Patients undergoing treatment at the Mazumdar Shaw Cancer Centre (MSCC) come from a wide range of socio-economic backgrounds. Treatment costs can vary significantly—from ₹1,00,000 to ₹50,00,000 or more depending on the diagnosis and associated risk factors. The Mazumdar Shaw Centre for Oncology Philanthropy (MSCOP) works closely with doctors and social workers at the hospital to identify patients in need. The Mazumdar Shaw Medical Foundation (MSMF) team evaluates the financial condition of each patient's family and allocates funds accordingly, ensuring the continuity of treatment without delay. MSCOP also offers oncology medication discounts to patients who are unable to afford high-cost drugs, supporting them throughout their treatment and follow-up care. Additional discounts are made available through the MOU signed between MSMF and the hospital, further assisting patients in successfully completing their treatment journey.

DAILY NUTRITIONAL SUPPLEMENT SUPPORT PROGRAM

During treatment, patients receive high doses of medication, and adequate nutrition is essential to support their recovery. Many families supported by MSCOP come from economically disadvantaged backgrounds and struggle to afford the cost of treatment, making it even harder to provide the necessary nutritional care for their loved ones. To address this, MSCOP has launched a daily nutrition support program that

offers supplements like almonds, cookies, and fruits to patients attending the 'Day Care' center for chemotherapy and related treatments. This initiative has benefited around 400 patients per month, who are undergoing treatment at the center.

EMOTIONAL SUPPORT AND COUNSELLING TO PATIENTS AND THEIR FAMILIES

In addition to the financial strain, both patients and their caregivers experience significant emotional stress during diagnosis and treatment. Alongside financial assistance, MSMF staff offer essential psychosocial support to help them cope. This support also creates a safe space for caregivers to express their feelings and share the challenges of being constantly present with the patients and witnessing their suffering.

ORGANIZING ACTIVITIES FOR CHILDREN IN PEDIATRIC ONCOLOGY WING

Our team organizes activities in the pediatric oncology ward to boost the spirits of hospitalized children and keep them engaged. We try to celebrate different festivals and distribute small gifts to the children with the help of volunteers and bring them joy. These activities sometimes include games that encourage new friendships and offer a brief escape from their difficult treatments

DISTRIBUTING CHRISTMAS GIFTS TO PATIENTS IN PEDIATRIC WING



TESTIMONIALS

1. Bhuvaneshwari Subramani

"My name is Bhuvaneshwari and I am a cancer patient. I have been undergoing treatment for the past two years and now I am on medication. My doctors have supported me so much and I have received a huge help from the MSMF foundation. The foundation has supported me for both my treatment and now for my medications. I would like to convey my heartfelt gratitude to the foundation and its staff for their help and support", say's Bhuvaneshwari.

Bhuvaneshwari is a 43 year old diagnosed with Carcinoma of breast. She was diagnosed at another hospital and was brought to NH for further management. She underwent chemo followed by surgery and radiation and is now on medications, which cost around one lakh per month. She has been provided support for radiation and supportive care and discounts for medications under MSMF.

2. Simrin Sultana

"My name is Tuhina Khatun and my child's name is Simrin Sultana. We are from West Bengal. After coming here, MSMF has been supporting my child's treatment", say's Simrin's mother.

Simrin Sultana is a 5yr old diagnosed with Calla Positive B Cell Acute Lymphoblastic Leukemia. Her family is from West Bengal and her father is a farmer. Simrin first consulted in local hospitals due to increasing weakness. She was later referred to Bangalore and was diagnosed at NH. The family belong to BPL category and MSMF is supporting the patient for chemo and supportive care needs.

3. Basawaraj

“My name is Anil and my son’s name is Basawaraj. We are from Gulbarga. My son is undergoing treatment at Narayana hospital and MSMF is helping with my son’s treatment”, say’s Basawaraj’s father.

Basawaraj is a 6yr old diagnosed with T Cell Acute Lymphoblastic Leukemia. His family is from Karnataka and his father is a driver. Basawaraj first consulted in local hospitals due to fever and was later referred to NH and was diagnosed here. MSMF is supporting the patient for chemo, supportive care and BMT.

IN DOCTOR’S WORDS

“As a treating oncologist, I have witnessed the critical role that MSMF plays in supporting oncology patients from economically challenged backgrounds. Their timely financial assistance has enabled many of our patients, particularly those with curative treatment intent, to complete their prescribed treatment plans without delay. This support removes a major barrier to care and allows the clinical teams to offer the appropriate and standard treatment without having to compromise due to cost constraints. The impact is profound in raising medical adherence, where many are able to complete their cancer treatment successfully and return to leading normal and healthy lives.”

*Dr. Rohit Raghunath Ranade, Senior Consultant and Clinical Lead , Gynaecologic Oncology
Mazumdar Shaw Medical Centre, Narayana Health City*

“I would like to express my whole hearted gratitude to Mazumdar Shaw Medical Foundation for the timely financial assistance provided to children undergoing chemotherapy for various cancers. The assistance provided has ensured appropriate treatment was initiated. These children suffered from Osteosarcoma and Leukemia. Kindly continue your valuable support.”

Dr. Shobha B, Consultant, Pediatric Hemato - Oncologist
Mazumdar Shaw Medical Centre, Narayana Health City

TEAM

Ms Archana Ann J, Manager MSCOP

Ms Jismy , Executive, Philanthropy, MSCOP