Saleembhasha Asanigari

Postdoc Fellow (Visiting Fellow)
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Objective

Distinguished computational biologist and postdoctoral fellow with extensive expertise in high-throughput sequencing technologies, genomic and epigenomic data analysis, and machine learning model development. Seeking to contribute to groundbreaking research in translational cancer biology and cancer data science. Dedicated to leveraging advanced deep learning and machine learning models to analyze large-scale datasets, advance precision oncology through multimodal data integration, and drive innovative therapeutic strategies to enhance patient outcomes

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Research Experience

Postdoc Fellow (Visiting Fellow)
National Institutes of Health, CCR/NCI, Bethesda, Maryland, USA
March 2020 – March 2025
Principal Investigator: Kenneth Aldape, M.D.

A Multi-Omics and Artificial Intelligence Framework Reveals Prognostic Malignant Cell Diversity and Immune Interactions in Group 3/4 Medulloblastoma Tumor Microenvironment

Our study focused on unraveling the tumor microenvironment of Group 3 and Group 4 medulloblastomas using a combination of single-cell, spatial, bulk RNA-seq, and DNA methylation data. By analyzing gene expression profiles of malignant and myeloid cells alongside spatial transcriptome data, we gained deep insights into the transcriptional diversity and prognostic implications of these tumors. We identified four transcriptionally heterogeneous malignant cell clusters: Neuronal, Neural-Crest, Photoreceptor, and Proliferative, each with distinct associations with survival outcomes and early embryonic cell lineage markers. Notably, the Proliferative cluster exhibited poor survival outcomes, while the Neural-Crest cluster showed improved survival. Furthermore, our myeloid cell gene expression analysis revealed three polarized macrophage clusters (Macrophage M0, M1, and M2), with M2 macrophages associated with poor prognosis and enriched in the aggressive Proliferative malignant cluster. The interaction between malignant and immune cell clusters highlighted the critical role of tumor immune cells in prognosis. We validated the neoplastic and immune cell states using the matched and unmatched methylation profiles.

Spatial transcriptome analysis expanded this understanding of malignant cell states, varying distributions across tissue and distinct correlations with macrophage cell states in Group 3 and Group 4 samples. These findings shed light on the intricate interactions within the tumor microenvironment. Additionally, we developed a Graph Neural Network (GNN) deep learning model to predict Medulloblastoma

subgroups and malignant cell states at spatial resolution. This model utilizes features extracted from H&E diagnostic whole slide images. The model provides a valuable tool for researchers to explore the Medulloblastoma tumor microenvironment's underlying mechanisms and develop new therapeutic strategies for therapeutic application.

Immune cell gene expression signatures in diffuse glioma are associated with IDH mutation status, patient outcome, and malignant cell state and highlight the importance of specific cell subsets in glioma biology

The tumor microenvironment (TME) plays an important role in various cancers, including gliomas. We estimated immune cell type-specific gene expression profiles in 3 large clinically annotated glioma datasets using CIBERSORTx and LM22/LM10 blood-based immune signatures. We found that specific immune cells' proportions and estimated gene expression patterns significantly varied according to IDH mutation status. When IDH-WT and IDH-MUT tumors were considered separately, cluster-of-cluster immune cell gene expression analyses identified groups with distinct survival outcomes. We confirmed and extended these findings by applying a signature matrix derived from single-cell RNA-sequencing data from 19 glioma tumor samples to the bulk profiling data, validating findings from the LM22/LM10 results. To link immune cell signatures with outcomes in checkpoint therapy, we then showed a significant association of monocytic lineage cell gene expression clusters with patient survival and mesenchymal gene expression scores. Integrating immune cell-based gene expression with previously described malignant cell states in glioma demonstrated that macrophage M0 abundance significantly correlated with mesenchymal state in IDH-WT gliomas, with evidence of a previously implicated role of the Oncostatin-M receptor and macrophages in the mesenchymal state. Among IDH-WT tumors enriched for the mesenchymal cell state, the estimated M0 macrophage expression signature also trended to a mesenchymal signature coordinately. We also examined IDH-MUT tumors stratified by 1p/19q status, showing that a mesenchymal gene expression signature of the M0 macrophage fraction was enriched in IDH-MUT, non-codeleted tumors. Overall, these results highlight the biological and clinical significance of the immune cell environment related to IDH mutation status, patient prognosis, and the mesenchymal state in diffuse gliomas.

Doctor of Philosophy (Ph.D.)
University of Hyderabad, Department of Biochemistry, Hyderabad, India
July 2015 – August 2019
Principal Investigator: Dr. Seema Mishra.

Coding (mRNA) and long non-coding (lncRNA) genes in pan-cancer regulation: a systems biology approach

From the previous studies, hallmark capabilities enable incipient cancer cells to acquire the traits that allow them to become tumorigenic and ultimately malignant. Based on this information, we hypothesized that commonly differentially expressed genes must be responsible for hallmark capabilities. To rationalize this, we analyzed RNA-seq data for protein-coding genes and lncRNA genes from eight cancer types taken from the TCGA database. We identified significantly differentially expressed mRNA and lncRNA genes, and we annotated the biological functions of these identified gene lists, which are involved in gene expression, transcription regulation, DNA replication and repair, and

the mitotic cell cycle. We compared the transcript expression levels of these genes with protein expression levels to find a correlation in their expression levels, considering that the ultimate functional effector molecules are proteins in the case of protein-coding genes. Then, we analyzed the Gene regulatory network (Transcription factor-target gene interaction) of commonly significantly differentially expressed coding and non-coding genes to identify master gene regulators; with this, we identified a common regulatory path, E2F1/FOXM1/PVT1 axis. We also predicted lncRNA-mRNA interaction to identify a regulatory molecule, which may be involved in the respective mRNA splicing, stability, and degradation. This study identified common cancer-causing factors that could use oligonucleotide therapy in modulating cancer targets to improve cancer diagnosis and treatment.

Education

Ph.D. in Computational and Systems Biology
University of Hyderabad, Department of Biochemistry, India
July 2015 - August 2019

- Thesis title: “Coding (mRNA) and long non-coding (lncRNA) genes in pan-cancer regulation: a systems biology approach.”
- Advisor: Dr. Seema Mishra

Master of Science in Biochemistry
Yogi Vemana University, Department of Biochemistry, India
2010 - April 2012

Bachelor of Science in Biotechnology
Sri Krishnadevaraya University, India
2006 - April 2009

Publications

1. **Saleembhasha A**, Bharati M, Chung H-J, Karen D, Di W, Omkar S, David D, Sidharth M, Kenneth A**.** A Multi-Omics and Artificial Intelligent Framework Reveals Prognostic Malignant Cell Diversity and Immune Interactions in Group 3/4 Medulloblastoma Tumor Microenvironment. (Manuscript under communication).
2. Mehani B*, **Saleembhasha A***, Chung H-J, et al. "Immune cell gene expression signatures in diffuse glioma are associated with IDH mutation status, patient outcome and malignant cell state, and highlight the importance of specific cell subsets in glioma biology." Acta Neuropathologica Communications, 2022; 10: https://doi.org/10.1186/s40478-022-01323-w.
3. **Saleembhasha A**, Mishra S. "Long non-coding RNAs as pan-cancer master gene regulators of associated protein-coding genes: a systems biology approach." PeerJ, 2019; 7: e6388, https://doi.org/10.7717/peerj.6388.

4. **Saleembhasha A**, Mishra S. "Novel molecules lncRNAs, tRFs, and circRNAs deciphered from next-generation sequencing/RNA sequencing: computational databases and tools." Brief Funct Genomics, 2017; pp. 1–11, https://doi.org/10.1093/bfgp/elx013.

* Denotes (co-) first authorship; All publications are listed in Google Scholar

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Research Technique Skills

- **High-Throughput Sequencing Analysis:** Whole-genome/exome sequencing, RNA-seq, ATAC-seq, ChIP-seq/CUT&RUN, DNA methylation, single-cell/nucleus RNA-seq, spatial transcriptomics, and quantitative proteomics. I also have experience in other omics data, including somatic mutation and copy number variation analysis.
- **Computational Biology:** Expertise in multi-omics data analysis using R and Python, focusing on applications in transcriptomics and proteomics relevant to cancer, especially adult and pediatric brain cancer research.
- **Data Integration and Visualization**: Expertise in analyzing, interpreting, and visualizing human genomics datasets, including short-read (Illumina) and long-read (PacBio, Oxford Nanopore) sequencing platforms.
- **Machine Learning**: Development of unsupervised machine learning models for predicting cancer subgroups and cell states.
- **Deep Learning**: Development of Vision Transformer (ViT), Convolution Neural Networks (CNN), Graph Neural Networks (GNN), and Multi-Layer Perception (MLP) deep learning models, particularly well-suited for image and spatial data analysis.
- **Programming Languages**: Experience with **Python, R**, SQL, Git, GitHub, and ML libraries such as **PyTorch, pytorch-geometric, TensorFlow**, **scikit-learn,** or other AI tools.
- **High-Performance Computing (HPC) Environment**: Proficiency in computational analyses and troubleshooting in Unix and Linux environments.

Training and Certifications

- Proficient in statistical analysis and programming (R and Python, SQL).
- APIs and Web Scraping with Python Path - Dataquest.io certificate id: 52NXYABD3SU40Y1JNDYG
- Machine Learning A-Z™: Hands-on Python and R in Data Science (Udemy, October 2019).
- Deep Learning with PyTorch- Zero to GANs (Udemy, October 2019).

Seminars and Workshops

- Presented poster "**Biologic and clinical significance of neoplastic and immune cell states in group 3 and group 4 medulloblastomas**" at the 27th Annual Meeting and Education Day of the **Society for Neuro-Oncology**, Tampa, Florida, November 2022.

- Presented poster "**Identification of regulatory lncRNAs for Protein-coding genes in pan-cancer regulation by systems biology approach**" at the 17th **International Conference on Bioinformatics** (InCoB 2018) at JNU, New Delhi, 2018.
- Presented a poster in 'GENOME BIOLOGY 2018: Mechanisms in Health and Disease'. Organizing by the Department of Biochemistry at the **Indian Institute of Science** (IISC), Bangalore, 2018.
- Attended "**workshop on Tumor Microenvironment in Cancer Research**" in UK-India Education and Research Initiative (UKIERI) organized by the School of Medical Science, University of Hyderabad, India, 2018.
- Seema Mishra, A. Saleembhasha, Akash Ghosh '**Immunoinformatic and Molecular Modeling exploration of T-cell Epitope-based Cancer Immunotherapy**': Poster presented at Systems Biology of Adaptive Immunity Conference (SystIms2017) organized by ETH Zurich, Switzerland, 2017. *A lab head, correspondence and presentation author, email address: smsl@uohyd.ernet.in, seema_uoh@yahoo.com.*
- Presented poster in **Academia Sinica, Taiwan- UoH Joint Workshop on Frontiers in Life Sciences** at University of Hyderabad, 2016.

Awards and Accomplishments

- **Best Poster Award** at 17th International Conference on Bioinformatics, JNU, New Delhi (2018)
- **UGC-**Senior Research Fellowship (2017-2019).
- **CSIR-UGC** Junior Research Fellowship (2014, 2015).
- **GATE- Graduate Aptitude Test for Engineers** with a 78-percentile score ().

Professional Service

- **Technology in cancer research & treatment**
- **Editorial Review Board member** (January 2020 – Present)
  Regularly review submissions on cancer detection, diagnosis, prognosis, and treatment. Recognized for thorough and timely reviews.
- **PloS one**- (Peer Reviewer)
- **Science Progress**-- (Peer Reviewer)

References

1. Dr. Kenneth Aldape, M.D.
   Chief of the laboratory of pathology
   National Institutes of Health
   Current Supervisor
   Phone: 301-480-7403
   Email: kenneth.aldape@nih.gov
   Address: Building 10, Room 2S235, Bethesda, Maryland-20892, USA

2. Dr. Sridhar Hannenhalli
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   Address: Building 15G1, Bethesda, Maryland-20814, USA

3. Dr. Seema Mishra
   Associate Professor
   Department of Biochemistry
   University of Hyderabad
   Ph.D. Advisor
   Phone: +918332-045217
   Email: smsl@uohyd.ac.in
   Address: CRR Rao Road, University of Hyderabad, Hyderabad, India

4. Dr. Omkar Singh
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   National Cancer Institute
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