TATA MEMORIAL CENTRE
ADVANCED CENTRE FOR TREATMENT, RESEARCH AND EDUCATION IN CANCER
Kharghar, Navi Mumbai- 410 210
www.actrec.gov.in
Phone No : 91-22-27405000

No. ACTREC/ADVT/05/2026 **28th January, 2026**

ADVERTISEMENT FOR THE MIZUHO POST DOCTORAL FELLOWSHIP AT CRI ACTREC

Applications are invited from highly motivated and eligible candidates for the **Mizuho postdoctoral fellowship** at the Cancer Research Institute, ACTREC. The applicant must have obtained a PhD degree from a recognized University. Those who have submitted their thesis and are awaiting the award of the degree are also eligible to apply. However, such candidates, if selected, will be offered a fellowship equivalent of a Senior Research Fellow until they obtain their degree. **The position is for seven months, extendable for another year. The selected candidates will be encouraged to apply for extramural grants under the mentorship of the PIs**.

The upper age limit for the fellowship is 35 years at the time of application submission. Age will be calculated by taking the last date of application. **Age relaxation of 5 years will be given to candidates belonging to SC/ST/OBC/Physically Challenged & Women. For other exceptional candidates, the age limit may be relaxed at the discretion of the competent authority.** Since this fellowship is meant to bring in the best of candidates outside of ACTREC so that the faculty and the fellow are mutually benefited from new expertise and a fresh perspective, the following conditions apply for the internal candidates:

At the time of application, candidates who have graduated from ACTREC should not have completed more than six months after the award of the degree. In either case, the fellowship will be awarded for 7 months, with the option to extend for 1 year.

Essential Qualifications and Experience:

- PhD degree from a government-recognised University or research institution.
- At least one research article publication in a well-reputed international journal.
- Expertise in any one or more of these areas: Molecular Biology, Cell Biology, Structural Biology, Computational Biology, Proteomics and Genomics.
- Candidates must be capable of conducting independent research under the mentorship of the PI, developing their own ideas and designing experiments. They should be capable of working in a collaborative environment.

Application details:
Send an email with a full CV and Statement of Purpose following the guidelines [Appendix-1]. SOP is graded and will be an important criterion for shortlisting applicants. Arrange for two letters of recommendation to be sent to the email ID given in the advertisement. This is an important aspect of the recruitment process. An incomplete application will be rejected.

Consolidated Salary: Rs. 1,00,000 per month. The candidate's work progress will be monitored, and an extension will depend on satisfactory progress.

Candidates with provisional certificates and candidates who have cleared the viva voce can apply. The latter has to provide an official statement from their Institute confirming the same

Candidates fulfilling these requirements should pre-register by sending their application in the prescribed format with

1. Recent CV (Refer to format: Appendix-1)
2. Statement of purpose (Refer to format: Appendix-2)
3. List of key publications
4. Letters of recommendation – Two
5. Contact details of referees - Two

by e-mail to projects.advt@gmail.com at latest by 2:00 pm on or before 17th February, 2026

The Interview will be scheduled on 23rd February, 2026.

The interview slot & venue will be informed by email to the shortlisted candidates only.

No T.A. / D.A. is admissible for attending the interview in person. If needed, candidates must make their own arrangements for accommodation/stay in Navi Mumbai. Interviews will also be conducted online.

For offline interviews, candidates should bring **original certificates** with photocopies (attested), CV and a recent passport-size photograph.

All correspondence should be strictly made only to projects.advt@gmail.com as indicated.

Alpasani

In-charge, Academic & Project Cell

APPENDIX

{1}

Curriculum Vitae format for the post of 'Mizuho postdoctoral fellowship'

Name					
Address					
Mobile No.		Email ID:			
Date of Birth (DD/MM/YYYY)		Confirm SC/ ST/ OBC / Physically Challenged / Female			
Educational Qualification					
Exam Passed	Board / University	Subjects	Year	Marks (%)	Thesis Title
PhD					
MSc					
BSc					
Relevant Work Experience with current position at the TOP					
From - To	Institute / Organisation	Position	Experience	Any specific remark	
Research Publications					
Total Number of research publications		First author publications			
Name & Contact details of 2 referees:					
Name, Designation, Institutional affiliations & address, Contact no., Email addresses					
Referee 1:					
Referee 2:					
Any other information					
Date:		**Signature:**			

APPENDIX

{2}

Expected Statement of Purpose (SOP):

The Introduction

- Indicate the specific position you are applying for with the advertisement number and date.
- Follow it up with a short description of yourself – 'I have submitted my PhD/ I have a PhD in (field) at (name of university); My dissertation is titled (title) and is supervised by Professor (name)'.

Candidature: Why are you the right candidate for this postdoc?

1. Describe your dissertation or current research project. This should cover the broad aim, your key findings, and why they matter to the field. **100 words**.
2. Summaries in your own words what you understand about the project aim and the long-term goal of the lab you wish to join as a post-doc. **100 words**.
3. Highlight your qualifications, research experience and knowledge that make you the best candidate for the post. **150 words**.
4. Propose any ideas you may have that can help or direct the project. **50 words**
5. If you are applying for more than one lab, you can add the specific information for each lab (2-4) in the same letter.

A list of PIs who wish to take postdocs is as follows:-

PRINCIPAL INVESTIGATORS	EMAIL ID
DR SORAB DALAL	sdalal@actrec.gov.in
DR KAKOLI BOSE	kbose@actrec.gov.in
DR ASHOK VARMA	avarma@actrec.gov.in
DR VIKRAM GOTA	vikramgota@gmail.com
DR SANJEEV WAGHMARE	swaghmare@actrec.gov.in
DR SEJAL PATWARDHAN	spatwardhan@actrec.gov.in
DR SHARATH CHANDRA ARANDKAR	sarandkar@actrec.gov.in
DR ROHAN KHADILKAR	rkhadilkar@actrec.gov.in
DR SUNIL SHETTY	sunil.shetty@actrec.gov.in
DR MALAY KUMAR SANNIGRAHI	malay.sannigrahi@actrec.gov.in

Detailed projects from PIs are as below:-

1. DR SORAB DALAL, SORAB LABAdvertisement

Title: Regulation of 14-3-3γ function by glutathionylation.

Name and e-mail address of the Guide: Sorab N Dalal sdalal@actrec.gov.in

Introduction. The 14-3-3 protein family in mammals is a conserved set of small acidic proteins that regulate several cellular pathways (reviewed in (1, 2)) by forming a complex with ligands containing a phosphorylated serine residue in one of two consensus motifs (3, 4). Previous work from the laboratory has demonstrated that 14-3-3γ is required to regulate the S-phase and G2-DNA damage checkpoints by inhibiting cdc25C function (5, 6), and that a loss of 14-3-3γ leads to decreased desmosome formation (7-9) and centrosome amplification (10, 11). Our recent results demonstrated that changes in reactive iron species and increased ROS levels lead to the glutathionylation of actin (12). We have attempted to identify additional glutathionylated proteins, and our preliminary results indicate that 14-3-3γ is glutathionylated in mammalian cells. The goal of this project is to assess the role of glutathionylation in regulating 14-3-3γ function.

Objectives

1. Identify the glutathionylation site in 14-3-3γ.
2. Determine the role of 14-3-3γ glutathionylation in the regulation of checkpoint control and centrosome duplication.
3. Determine how glutathionylation of 14-3-3γ regulates desmosome formation.

Experimental design.

1. Glutathionylation is the addition of glutathione to a Cysteine residue in proteins. To identify the site of glutathionylation in 14-3-3γ, we will alter the Cysteine residues in 14-3-3γ to Serine, an amino acid with a similar structure that cannot be glutathionylated as described (13). HA-epitope-tagged versions of these proteins will be expressed in HCT116 cells. An HA-tagged WT 14-3-3γ will serve as a positive control, and the vector control as a negative control. The ability of these mutants to be glutathionylated will be tested as previously described (12, 13). In addition to testing these in untreated cells, we will determine whether activation of the S-phase and G2-DNA damage checkpoints leads to additional glutathionylation of 14-3-3γ and whether checkpoint activation results in glutathionylation of different Cysteine residues.

2. Once the sites of glutathionylation are identified, we will test their ability to regulate checkpoint function and centrosome duplication. HCT116 cells will be transfected with either the vector control, WT 14-3-3γ or the glutathionylation mutants generated above. Post-transfection, the S-phase or G2 DNA damage checkpoints will be activated by treatment with hydroxyurea and adriamycin, respectively, as described (6, 14). PCC and cell cycle assays will be performed as described to determine whether these mutants can prevent cell cycle progression upon checkpoint activation. These experiments will be performed in cells with endogenous levels of 14-3-3γ and in cells with 14-3-3γ knockdown. Finally, we will test the ability of these mutants to form complexes with cdc25C and other checkpoint proteins to identify the mechanism by which glutathionylation regulates 14-3-3γ function in checkpoint control.

Our previous results have indicated that 14-3-3γ inhibits centriole duplication by forming a complex with NPM1 (10). To determine if glutathionylation of 14-3-3γ inhibits centriole duplication, m-Orange-tagged WT or mutant versions of 14-3-3γ will be transfected into HC116 cells. The m-Orange vector control will serve as a negative control. The transfected cells will be arrested in mitosis with nocodazole or in G2 with

a cdk1 inhibitor, and centrosome and centriole numbers will be measured as described previously (10). The ability of these mutants to form a complex with NPM1 will also be determined.

3. Previous work from the laboratory has demonstrated that 14-3-3γ promotes the transport of plakoglobin (PG) to the cell border in multiple cell types, thus promoting desmosome formation (7-9). We previously generated HCT116 and HaCaT cell lines lacking 14-3-3γ. These cells will be transfected with WT or mutant versions of 14-3-3γ, and desmosome formation will be measured by staining for desmosome proteins as described. In addition, dispase and hanging drop assays will be performed to measure the strength of already formed adhesion structures or the formation of new adhesion structures, respectively (15). The ability of the glutathionylation mutants to bind to PG and the motor protein required for transport of PG, KIF5B, will be determined as described (7). These experiments will determine whether glutathionylation of 14-3-3γ is required for the regulation of multiple cellular pathways or a subset of cellular pathways.

References

1. Aitken, A. (2006) 14-3-3 proteins: a historic overview *Semin Cancer Biol* **16**, 162–172
2. Yaffe, M. B. (2002) How do 14-3-3 proteins work? - Gatekeeper phosphorylation and the molecular anvil hypothesis. *FEBS Letters* **513**, 53–57
3. Muslin, A. J., Tanner, J. W., Allen, P. M., and Shaw, A. S. (1996) Interaction of 14-3-3 with signaling proteins is mediated by recognition of phosphoserine. *Cell* **84**, 889–897
4. Yaffe, M. B., Rittinger, K., Volinia, S., Caron, P. R., Aitken, A., Leffers, H. *et al.* (1997) The structural basis for 14-3-3 phosphopeptide binding specificity. *Cell* **91**, 961–971
5. Dalal, S. N., Yaffe, M. B., and DeCaprio, J. A. (2004) 14-3-3 family members act coordinately to regulate mitotic progression. *Cell Cycle* **3**, 672–677
6. Hosing, A. S., Kundu, S. T., and Dalal, S. N. (2008) 14-3-3 Gamma is required to enforce both the incomplete S phase and G2 DNA damage checkpoints *Cell Cycle* **7**, 3171–3179
7. Sehgal, L., Mukhopadhyay, A., Rajan, A., Khapare, N., Sawant, M., Vishal, S. S. *et al.* (2014) 14-3-3γ-Mediated transport of plakoglobin to the cell border is required for the initiation of desmosome assembly in vitro and in vivo *Journal of cell science* **127**, 2174–2188
8. Tilwani, S., Gandhi, K., Narayan, S., Ainavarapu, S. R. K., and Dalal, S. N. (2021) Disruption of desmosome function leads to increased centrosome clustering in 14-3-3gamma-knockout cells with supernumerary centrosomes *FEBS Lett* **595**, 2675–2690
9. Vishal, S. S., Tilwani, S., and Dalal, S. N. (2018) Plakoglobin localization to the cell border restores desmosome function in cells lacking 14-3-3gamma *Biochem Biophys Res Commun* **495**, 1998–2003
10. Bose, A., Modi, K., Dey, S., Dalvi, S., Nadkarni, P., Sudarshan, M. *et al.* (2021) 14-3-3gamma prevents centrosome duplication by inhibiting NPM1 function *Genes to cells : devoted to molecular & cellular mechanisms* **26**, 426–446
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12. Choudhary, B. S., Chaudhary, N., Shah, M., Dwivedi, N., P, K. S., Das, M. *et al.* (2023) Lipocalin 2 inhibits actin glutathionylation to promote invasion and migration *FEBS Lett* **597**, 1086–1097
13. Choudhary, B. S., Chaudhary, N., Khan, B. K., Vijan, A., Mandal, D., Pilankar, L. *et al.* (2025) LCN2 promotes focal adhesion formation and invasion by stimulating c-Src activation *J Cell Sci* **138**,
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15. Gurjar, M., Raychaudhuri, K., Mahadik, S., Reddy, D., Atak, A., Shetty, T. *et al.* (2018) Plakophilin3 increases desmosome assembly, size and stability by increasing expression of desmocollin2 *Biochem Biophys Res Commun* **495**, 768–774

2. DR KAKOLI BOSE, BOSE LAB

Project Title: Deciphering Mutations of Procaspase-8 in Chemoresistant Tumour Cells to Uncover Apoptosis Regulation in Cancer

Name and E-mail address of the Guide: Dr. Kakoli Bose kbose@actrec.gov.in

Collabs: Dr Pratik Chandrani, Dr Rajesh Dixit and group (Department of Molecular Epidemiology and Population Genomics)

Abstract:

Apoptosis is a program of cell death, which is deregulated in tumors, leading to resistance to cancer therapy. Caspase-8, a cysteinyl protease, is the key initiator of the extrinsic, *aka* death receptor-mediated pathway of apoptosis. Activation of the initiator protease from its zymogen (procaspase-8) is a tightly-regulated multi-step process that involves homotypic protein-protein interactions involving death effector domains (DED), leading to an effective death-inducing signalling complex (DISC) formation, which is a prerequisite for apoptotic induction. Previous studies have established a correlation between deregulation of caspase-8 functions and several cancers, in particular the ones that are characterized by chemoresistance, such as HNSCC (head and neck squamous cell carcinoma) and breast cancer, though underlying molecular mechanisms are still largely unknown. It is well established that in tumors, biochemical changes in the apoptotic pathway lead to resistance to chemotherapeutic agents that are potent apoptotic inducers. This persistent issue is therefore a major bottleneck in the efficient cancer treatment regime and hence demands dire attention. Keeping this in mind, and also given the reciprocity between caspase-8 deregulation and several chemoresistant cancers, this proposal attempts to fill in the lacuna by investigating procaspase-8 mutations derived from chemoresistant cancer patients in breast and HNSCC. This will be performed using leading-edge next-generation sequencing (NGS) and bioinformatics analysis. This will also provide a detailed map of the deregulation of genes of the apoptotic pathway due to the mutations. The identification of mutations in procaspase-8 will be followed by deciphering their role in apoptosis in cancer cells using advanced structural and functional approaches supported by biochemical and cell biology investigations. This will allow a broad-scale analysis of the functions of procaspase-8 mutants in cancer cell death networks *via* three-dimensional structure determination, along with *in silico* and experimental validation of their functions in cancer cell lines. Furthermore, this work would provide a basis for the development of rationally designed drugs and pave the way towards new anti-cancer therapies.

Objectives:

1. Identification of mutations in procaspase-8 and associated signalling networks in therapy-sensitive and therapy-resistant HNSCC & Breast cancer patients by NGS *or* Sanger sequencing

2. Deciphering the molecular mechanisms of the procaspase-8 mutations in apoptotic and anti-apoptotic cancer networks using biochemical and cell biology approaches

Key references:

1. Parui AL, Bose K, Caspases: Regulatory Mechanisms and Their Implications in Pathogenesis and Therapeutics." Pathophysiological Aspects of Proteases, Springer International Publishing, 423-488
2. Singh N, Hassan A, Bose K. (2016) Molecular basis of death effector domain chain assembly and its role in caspase-8 activation. FASEB J. 30:186-200
3. König C, Ivanisenko NV,.... Bose K, Lavrik IN. Targeting type I DED interactions at the DED filament serves as a sensitive switch for cell fate decisions. Cell Chemical Biology. 2024. https://doi.org/10.1016/j.chembiol.2024.06.014

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3. DR ASHOK VARMA, VARMA LAB

Title: Indian Cancer Database for Translational Research –ACTREC **(ICDTRA)**

Name and Email address of the Guide: Ashok K Varma; avarma@actrec.gov.in

An operational cancer database server that supports the nationwide cancer research community. Researchers and clinicians are looking for a comprehensive platform—"A complete cancer database under one umbrella," which should encompass information on:

(1) Research:

- **Cancer Genomics:** Identify changes in the genomes of tumors that drive cancer progression.
- **Cancer Proteomics:** Looking at the growing populations of oral cancer, the proteomics-based approach will be applied to study a set of predictive and prognostic protein biomarkers
- Cancer Research based on regions and community-epidemiology

(2) **Data Releases:** Compilation of information from

- All the cancer research publication from India
- International Cancer Genome Consortium

(3) Diagnostic: Information regarding the New Biomarkers for Diagnosis

- Available Diagnostics tools
- Tissue bank information

(4) **Treatment:** Information regarding available cancer hospitals in India etc

- Drug available in the market

(5) Clinical trials

- Information regarding the patient Selection
- Drug Response Prediction
- Knowledge of the biochemical pathways in which potential target molecules operate – important for drug mechanism
- Drug under discovery

(6) **Education:**

- Training and Teaching component in cancer biology will be included for the faculty and students
- Information related to high-throughput cancer data is available in our country.
- The information for the cancer awareness program.

This consolidated information will be gathered from cancer databases across India and globally. It will act as a comprehensive platform connecting clinicians, basic scientists, and also providing information to cancer patients.

4. DR VIKRAM GOTA, DEPT OF CLINICAL PHARMACOLOGY

Title: Bridging Traditional Medicine and Modern Oncology for Evidence-Based Anticancer Drug Discovery

Name and E-mail address of the Guide: Dr. Vikram Gota, vikramgota@gmail.com

The proposed position is required to support ongoing research activities under the AYUSH-CoE framework aimed at the discovery and development of anticancer agents derived from traditional medicinal knowledge. The research program focuses on scientifically validating phytochemicals from Indian traditional medicine using modern computational and experimental approaches, with relevance to clinically important cancer targets.

The work involves systematic in silico screening of phytochemicals curated in Indian databases such as IMPPAT against well-established cancer driver mutations. Computational tools such as molecular docking, molecular dynamics simulations, and drug-likeness and ADME analysis are used to prioritize promising leads. This approach allows efficient selection of bioactive candidates from large traditional medicine-based chemical libraries and reduces unnecessary experimental screening.

Selected leads are then evaluated in appropriate cancer cell line models relevant to the target mutation. The position supports coordination and analysis of in vitro studies, followed by basic mechanistic investigations to understand pathway modulation and target engagement. Compounds showing consistent biological activity are further advanced to in vivo efficacy studies and pharmacokinetic-pharmacodynamic (PK/PD) evaluation to assess exposure, safety, and therapeutic relevance.

This position is essential for maintaining continuity between computational prediction, experimental validation, and translational assessment. It directly contributes to the generation of high-quality scientific data required for AYUSH-supported projects, publications, and future grant applications. The role also strengthens the integration of traditional medicine knowledge with modern oncology research, aligning with national priorities to promote evidence-based development of AYUSH-derived therapeutics.

Given the multidisciplinary nature of the work and the scale of ongoing and proposed studies, hiring for this position is necessary to ensure timely execution, scientific rigor, and successful translation of AYUSH-based research outputs.

5. DR SANJEEV WAGHMARE, WAGHMARE LAB

Title: Investigating the epigenetic landscape, cell signaling and metabolic regulation during the differentiation of induced pluripotent stem cells into various lineages

Name and email address of the Guide: Dr. Sanjeev Waghmare, swaghmare@actrec.gov.in

Background: Induced pluripotent stem cells (iPSCs) cells are derived from adult somatic cells that have been genetically reprogrammed to an embryonic stem (ES) cell-like state by ectopic expression of ES cell genes. Takahashi and Yamanaka showed that adult cells were reprogrammed into iPSCs by adding four specific transcriptional factors: Oct3/4, Sox2, Klf4, and c-Myc. In more recent studies, it has been observed that DNA methylation plays a role in suppressing genes related to cell differentiation and aiding in the

modification of chromatin structure. iPSC generation from the somatic cells by using the Yamanaka factors revealed that DNA methylation, histone modifications, histone variants, and ATP-dependent chromatin remodeling affect transcription factors' ability to bind their recognition elements. Recently, studies from Gupta Lab have shown the differential incorporation of histone isoforms in different tissue types and during cancer development. However, the dynamics of histone isoform alterations in lineage differentiation at various stages of reprogramming are still unknown. Cell signaling pathway such as Wnt/ β-Catenin interacts and regulates the expression of Oct4, Sox2, and Klf4, which is involved in efficient generation of mesodermal progenitors; however, molecular mechanism is obscure. Further, metabolic regulation is crucial during the differentiation of IPS cells in to multiple lineages. However, the metabolic control involved in the regulation is yet to be unraveled.

Hypothesis: The intriguing plasticity of iPSC during reprogramming is potentially due to the differential incorporation of histone proteins, altering the site-specific post-translational modification, leading to differential chromatin organization and gene expression. Therefore, uncovering the epigenetic landscape, metabolic and cell signaling during different cell lineages during iPSC reprogramming will provide insights into the mechanisms for various cell fate decisions.

Objectives:

1. Characterization of induced pluripotent stem cells and reprogramming into different lineages
2. Identifying epigenetic landscape during differentiation into different lineages, ectoderm, mesoderm, and endoderm.
3. Investigating the differentialial cellular signaling pathways during the process of IPSC differentiation into multiple lineages

Brief Methodology:

- iPSC reprogramming will be achieved in the human adult fibroblast cells (procured from the Hi-media) using the CytoTune™-iPS 2.0 Sendai Reprogramming Kit to generate iPSCs cultured feeder-free on vitronectin-coated culture dishes. *In vivo* and *in vitro* characterization of iPSCs will be performed through embryoid body formation and teratoma formation assays.
- Differentiation of iPSCs into lineages: iPSCs will be differentiated into hematopoietic, neural, and muscle lineages. Further, histone modification and histone isoforms will be assessed during the early, mid, and late stages of differentiation of iPSCs to different lineages. Moreover, RNA sequencing will be carried out to define gene expression profiles.

6. DR SEJAL PATWARDHAN, PATWARDHAN LAB

Title: Decoding the role of ECM mechanics in cancer prognosis and therapy outcome

Name and email address of the Guide: Dr Sejal Patwardhan, spathwardhan@actrec.gov.in

The extracellular matrix (ECM) is a fundamental component of multicellular organisms, providing essential physicochemical cues that regulate cellular behavior and tissue organization. Dysregulation of the ECM—through excessive deposition, degradation, or alterations in composition and architecture—is closely associated with numerous pathological conditions, including cancer. Gaining a deeper understanding of ECM composition, remodeling, and mechanotransduction-mediated signaling may therefore reveal novel prognostic and diagnostic biomarkers, as well as therapeutic targets. In this study, we aim to characterize alterations in ECM composition in breast tumors through proteomic analysis of ECM-derived proteins. In parallel, we will examine ECM fiber curvature, bundling, and architectural patterns in tumor tissue sections using specialized staining techniques, and correlate these features with

tumor histological subtypes, stage, and grade and therapy response. Given that the physicochemical properties of the ECM are dynamic and cancer-specific, and that they profoundly influence tumor microenvironment–driven processes such as cell adhesion, proliferation, migration, motility, stemness, angiogenesis, and immune modulation, we further seek to evaluate the expression of key mechanosensors and mechanotransducers in primary cultures established from fresh tumor tissues. Additionally, by employing stiffness-tunable in vitro and in vivo models, we will investigate how ECM remodeling contributes to cancer progression and metastasis, along with the underlying molecular mechanisms driving these processes.

7. DR SHARATH CHANDRA ARANDKAR, SHARATH LAB

Title: Unravelling the mechanisms of Cancer-Associated Fibroblasts heterogeneity in Tumour microenvironment

Name and email address of the Guide: Dr. Sharath Chandra Arandkar, **sarandkar@actrec.gov.in**

The continuous cross-talk between tumour cells and their surrounding microenvironment will define tumour growth and metastasis outcome. The tumour microenvironment (TME) consists of fibroblasts, immune cells, endothelial cells and extracellular matrix and often plays a crucial role in many solid cancers. Stromal cells constitute a large part of the overall tumour mass in multiple cancers, among which cancer-associated fibroblasts (CAFs) are the most abundant stromal cell population. CAFs are a heterogeneous population of cells known to modulate cancer cell behaviour by secreting various growth factors, cytokines, and miRNA, such as TGFβ, IL-1α/β, PDGF, FGF, etc. CAF-derived secretory factors, through direct or indirect communications with other components of the TME, exert their functions in the TME. These CAFs can influence other stromal cells such as immunosuppression of cytotoxic immune cells and recruitment of tumour-promoting cells, thereby creating a hospitable micro-environmental niche favouring tumour promotion, angiogenesis, ECM remodelling leading to fibrosis and desmoplasia, promoting invasion and metastasis. In the current project, we will decipher the molecular mechanisms underlying the cancer-associated fibroblast generation and their constant interaction with tumour cells. We will employ various *in vitro* and *in vivo* approaches to uncover the molecular drivers of CAFs heterogeneity.

References:

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2. Cheng, P.S.W., Zaccaria, M. & Biffi, G. Functional heterogeneity of fibroblasts in primary tumors and metastases. *Trends Cancer* **11**, 135–153 (2025).

8. DR ROHAN KHADILKAR, KHADILKAR LAB

Title: Understanding the crosstalk between tumor and innate immune cells in cancer induced cachexia using Drosophila and mice models.

Name and Email address of the Guide: Dr. Rohan Khadilkar (Stem Cell and Tissue Homeostasis lab, ACTREC), rkhadilkar@actrec.gov.in

Background: Cancer induced cachexia is a multifactorial syndrome that involves complex interactions between the tumor and host organs. It is characterized by systemic inflammation, inefficient energy expenditure, wasting of peripheral organs and metabolic dysfunction like muscle protein degradation, lipolysis in adipose tissues that worsens the condition in advanced stage cancer patients. Cachexia is observed in all solid tumors and presents a major challenge in the clinic as very little is known about the molecular characterization of cachexia onset and progression. Our lab is actively engaged in understanding how inter-organ communication and systemic signalling gets altered in the context of cachexia. We utilize the Drosophila and mammalian models to address how the bi-directional crosstalk between tumor and host tissues is regulated in this disease context. Previous reports suggest that there is active remodelling of hematopoiesis that occurs in solid tumors like pancreatic cancer. Our studies in the Drosophila model corroborates these findings suggesting an active remodelling of the stem cell – niche microenvironment during cachexia.

Hypothesis: Our hypothesis is that innate immune cells could undergo reprogramming at multiple levels during cancer cachexia progression. This reprogramming could tune the innate immune cells to be either pro or anti-tumorigenic in function. However, whether these cells actively regulate cachexia onset and progression remains to be determined.

Approach: We plan to investigate this question using Drosophila gut tumor and mammalian models. Elucidating how the innate immune cells are rewired in terms of gene expression profile and metabolic profile will help in understanding the underlying mechanisms of systemic inflammation and multi-organ wasting.

References:

1. Liu, M., Ren, Y., Zhou, Z., Yang, J., Shi, X., Cai, Y., ... & Li, M. (2024). The crosstalk between macrophages and cancer cells potentiates pancreatic cancer cachexia. *Cancer Cell*, *42*(5), 885-903.
2. Yu, J., Choi, S., Park, A., Do, J., Nam, D., Kim, Y., ... & Park, K. S. (2021). Bone marrow homeostasis is impaired via JAK/STAT and glucocorticoid signaling in cancer cachexia model. *Cancers*, *13*(5), 1059.
3. Chowdhury, U., Panzade, G., Karnik, P. N., Birwadkar, P., Tashu, T., & Khadilkar, R. J. (2025). Drosophila midgut tumor-induced insulin resistance systemically remodels lymph gland hematopoiesis during cancer cachexia. *bioRxiv*, 2025-11.

9. DR SUNIL SHETTY, SHETTY LAB

Title: Investigating alternative translation initiation mechanisms in hepatocellular carcinoma animal models

Name and email address of the Guide: Sunil Shetty, sunil.shetty@actrec.gov.in

Deregulation of ribosome biogenesis and translation is an early hallmark of malignancy. Numerous therapeutic strategies have been developed to target and kill cancer cells by inhibiting protein translation. However, cancer cells can utilize alternative routes such as initiation with internal ribosome entry sites or upstream open reading frames to compensate for translation inhibition. Several mechanisms, such as IRES-mediated initiation, uORF-mediated initiation, and non-AUG initiation, can provide bypass routes. As normal cells do not rely on such alternative translation mechanisms, targeting them can be a potential therapeutic strategy against cancer. Hence, in this project, we will investigate such alternative translation

mechanisms in liver cancer animal models. Hepatocellular carcinoma (HCC) is the major form of liver cancer. We will utilize multiple HCC mouse models to investigate this question. We will generate alternative translation initiation reporters in an adeno-associated viral background and analyze the reporter activity in the tumor versus normal tissue. Furthermore, global elicitation of translation reprogramming will be monitored by ribosome profiling and proteomic approaches. Overall, the proposal will help to understand the various compensatory mechanisms of protein synthesis in HCC.

10. DR MALAY SANNIGRAHI, CRI-1 LAB

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Abstract:
Human Papillomavirus (HPV) types 16 and 18 account for approximately 90% of cervical cancer and 20% of head and neck cancer cases. Despite the efficacy of prophylactic vaccines, the management of established infections remains a critical challenge, particularly regarding recurrence and metastasis. These resistant phenotypes are driven by tumor metabolic plasticity, where cancer cells in nutrient-deprived environments adapt via heightened mitochondrial bioenergetics. While mitochondrial hyperactivity typically activates innate immune signaling via Reactive Oxygen Species and mitochondrial DNA-mediated innate immune pathways, current immunotherapy trials have shown limited success, underscoring a gap in understanding innate immune activation mechanisms.

Our preliminary data in HPV+ head and neck cancers identifies a paradox: tumors prone to recurrence exhibit increased mitochondrial mass and oxidative metabolism yet display an immune-desert phenotype with minimal T-cell infiltration. We hypothesize that heterogeneity in the expression of HPV oncogenes (E6, E7, and E5) rewires tumor mitochondrial bioenergetics to suppress innate immune activation, thereby limiting therapeutic efficacy.

We aim to: (1) Elucidate the mechanistic role of HPV oncogenes in modulating mitochondrial biogenesis, innate immune signaling, and immune cell recruitment using *in vitro* syngeneic cell lines and orthotopic murine models; and (2) Evaluate a novel combinatorial therapeutic strategy by screening mitochondrial inhibitors *in vitro* and assess their *in vivo* efficacy in combination with E6/E7 peptide vaccination. The ultimate goal is to validate a strategy that reprograms the metabolic state of "cold" HPV+ tumors to restore innate immune recognition, converting them into "hot" vaccine-responsive lesions.

References:

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