

# No. ACTREC/ADVT/ 119/2025

1<sup>st</sup> July, 2025

# **ADVERTISEMENT FOR A POST DOCTORAL FELLOW POSITION AT CRI ACTREC**

Applications are invited from highly motivated and eligible candidates for post-doctoral positions at the Cancer Research Institute, ACTREC for the advertised projects. 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 1 year. The selected candidates will be encouraged to apply for extramural grants under the mentorship of the PIs**.

PRINCIPAL INVESTIGATORS	Project
DR MANOJ MAHIMKAR https://actrec.gov.in/dr-manoj-b-mahimkar	Predictive Clinical Features and Molecular Markers for Tumor Response and Treatment Outcomes Post NACT in HPV-negative Oral Cancers
DR NANDINI VERMA https://actrec.gov.in/dr-nandini-verma	Identification and exploitation of genetic susceptibilities of ferroptosis for the treatment of therapy-tolerant Triple-Negative Breast Cancer
DR. SHARATH CHANDRA ARANDKAR https://actrec.gov.in/dr-sharath-c-arandkar	Decoding the Bidirectional Crosstalk Between Tumor Cells and Cancer-Associated Fibroblasts in the Tumor Microenvironment

Interested candidates are encouraged to get in touch with the PIs.

The upper age limit for the fellowship is 35 years at the time of the submission of the application. Age will be calculated by taking the last date of application. Age relaxation of five years will be given to candidates belonging to SC/ST/OBC/Physically Challenged & Women candidates. For other exceptional candidates, age will be relaxed based on 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. Candidates who have graduated elsewhere and are working in any of the labs at ACTREC should not have been associated with the lab for more than six months at the time of application. In either of these cases, the fellowship will be awarded strictly for one year within which time the candidate has to find alternative support. No more than one fellowship will be awarded under this clause and the candidates will be subjected to the same selection protocol.

# **Essential Qualifications and Experience:**

- PhD degree from a government recognized 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: Cancer Biology, 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, develop their own ideas and design experiments. They should be capable of working in a collaborative environment.

# **Application details:**

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

Fellowship amount and conditions are on par with DST/DBT norms.

**Consolidated Salary: Rs. 73,660/- per month. (Rs. 58,000/- + 27% HRA) p.m.** The work progress of the candidate will be monitored, and extension will depend on satisfactory progress of the work.

Candidates with provisional certificates and candidates who have cleared the viva voce can apply. The letter 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
- 2. Statement of purpose
- 3. List of key publications
- 4. Letters of recommendation Two
- 5. Contact details of referees Two

by e-mail to pdf.actrec@gmail.com at latest by 5:45 pm on or before 12<sup>th</sup> July 2025.

<u>The interview will be conducted online.</u> The date, time & link will be shared to shortlisted candidates by email.

All correspondence should be strictly made only to <a href="mailto:pdf.actrec@gmail.com">pdf.actrec@gmail.com</a> as indicated.

Olpasani

In-charge, Academic & Project Cell

# APPENDIX

## **{1}**

## **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. Summarize 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 makes 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

PRINCIPAL INVESTIGATORS	WEBLINK OR DETAILS
DR MANOJ MAHIMKAR	https://actrec.gov.in/dr-manoj-b-mahimkar
DR NANDINI VERMA	https://actrec.gov.in/dr-nandini-verma
DR SHARATH CHANDRA ARANDKAR	https://actrec.gov.in/dr-sharath-c-arandkar

#### **APPENDIX-2**

## Curriculum Vitae format for the post of 'Post-Doctoral Fellow'

Name							
Address							
Mobile No.		Email ID:	Email ID:				
Date of Birth (DD/MM/YYYY)		Confirm SC	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	Lab			
				remark	Preference			
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:						

Detail projects from PIs are as below: -

# 1. DR. MANOJ MAHIMKAR, MAHIMKAR LAB

# Predictive Clinical Features and Molecular Markers for Tumor Response and Treatment Outcomes Post NACT in HPV-negative Oral Cancers

## Abstract

Head and neck squamous cell carcinomas (HNSCCs) is a complex and heterogeneous disease regulated at multiple levels and associated with high mortality and morbidity. HNSCCs are related to environmental risk factors, especially excessive tobacco and alcohol consumption. Oral squamous cell carcinomas (OSCCs) are the prevalent forms of HNSCC, representing approximately 90% of all tumors in this region. The high mortality associated with OSCC is related mainly to the locoregional advancement of the disease. Although significant improvements have been made in achieving local control of the disease and increasing the survival rate of patients with primary malignant oral tumors via surgical intervention, physicians face yet another challenge-that of preserving oral functions, such as articulation, mastication, and deglutition, and retaining visual aesthetics for improving HNSCC patients' quality of life. Effective treatment for advanced HNSCC (T3 and T4), but non-resectable tumors involves the use of multidisciplinary therapies, such as multiple chemotherapies (CTs) and radiotherapy (RT). However, most patients present in an advanced stage, wherein tumor resection is rendered questionable because of the positive resection margins. The prognosis of such unresectable stage IVA or IVB tumors treated with a non-surgical approach is poor, with median survival ranging from 2 to 12 months. For these locally advanced borderline operable cases, the role of neoadjuvant chemotherapy (NACT) has been postulated as an alternative to the current existing therapeutic modalities. Although NACT provides a promising scenario for managing this patient subgroup, it should be known that response rates to this modality vary from 35-40%. Although NACT has been evaluated over the last decade, the chemoresistance phenomenon and its molecular mechanisms are yet to be studied comprehensively. There exists a need to identify biomarkers that will help us in better therapeutic stratification of these patients. There has been no study focusing specifically on the markers to predict response in oral cavity cancers, which is the aim of the present study.

#### Rationale

Squamous cancers of the oral cavity account for a major proportion of cancers in the Indian population [1, 2]. The sheer load and morbidity associated with these cancers mandate further evaluation of the disease biology. These Oral cancers are managed by surgery followed by adjuvant therapy (radiation/chemoradiation) and radical chemoradiation when the tumor is deemed unresectable[3]. However, many patients present in an advanced stage wherein tumor resection is rendered questionable in view of the positive resection margins. The prognosis of unresectable stage IVA or IVB tumors treated with a non-surgical approach is poor, with median survival ranging from 2 to 12 months [4-7]. It's for these locally advanced borderline operable cases where the role of neoadjuvant chemotherapy (NACT) has been postulated as an alternative to the current existing therapeutic modalities [8-11]. The aim is to downstage the tumor and provide adequate margins of resection. Although NACT provides a promising scenario for managing this patient subgroup, it should be known that response rates to this modality vary from 35-40%. It means that a significant proportion of patients do not benefit from chemotherapy.

Joshi et al. analyzed T4b oral cavity cancer patients who were offered NACT and then assessed for resectability at the end of 2 cycles of chemotherapy. NACT was safe and can achieve resectability in 30.9% of patients. Patients undergoing resection have much better OS than those who underwent non-surgical local treatment [12]. Patil et al. evaluated 721 patients with stage IV oral-cavity cancer who received NACT, of which 310 patients (43%) had a sufficient reduction in tumor size and underwent surgical resection. NACT led to successful resection and improved overall survival in a significant proportion of technically unresectable oral cancer patients [13]. More recently, Chaukar et al., in a prospective phase-II randomized study on OSCC patients with paramandibular disease needing segmental mandibulectomy, demonstrated that NACT (docetaxel, Cisplatin, and fluorouracil) plays a potential role in mandibular preservation in oral cancers with acceptable toxicities and no compromise in survival [14].

Although NACT has been evaluated over the last decade, its chemoresistance and the underlying molecular mechanisms are yet to be studied comprehensively. The key clinical question is differentiating between responders (achieve resectability) and non-responders. B-tubulin II, p53, GST, ERCC, HPV, and other molecular markers have been proposed as surrogate markers for NACT responsiveness in head and neck cancer [15, 16]. However, there is a dearth of predictive clinical, pathological, or molecular markers to suggest a response to chemotherapy that will help us in better therapeutic stratification of these patients. No study has been focused specifically on the markers to predict response in HNSCC/ OSCC, which is the aim of this study. This will prevent unnecessary chemotherapy in patients with a 'chemoresistant' genotype, thus sparing patients from toxicities.

#### Summary

The proposed study aims to understand the interrelationship between molecular changes occurring in oral cancers and their association with clinical outcomes. As a part of treating advanced-stage oral cancers, patients receive chemo and radiation therapy in combination with surgery. Surgery is the best treatment for oral cancers. However, some of the advanced-stage oral cancer cases are inoperable or borderline operable and thus are given neoadjuvant chemotherapy (NACT) so that the tumor can be surgically resected. There may be a response to chemotherapy in some cases and no response in others. Thus, there is a need for biomarkers that can predict the response to chemotherapy. Most past studies have used single biomarkers; comprehensive analysis with multiple markers is lacking. Hence, in this study, we plan to use the battery of clinical, pathological, and molecular biomarkers, which may help better strategize the patients in the future and avoid toxicities to patients.

#### **Aims and Objectives**

The present study aims to identify clinicopathological features and molecular markers to predict the response (achieve resectability) to NACT for advanced oral cancers.

#### **Specific Objectives**

- To carry out global transcriptome and methylome profiling of the tissues of patients pre- and post-NACT to evaluate the association of gene signatures with treatment response.
- To carry out the IHC-based analysis of the markers of DNA damage/ repair, hypoxia angiogenesis, apopotosis in tumor tissues before starting the therapy and at the time of surgery to evaluate the association with treatment response.
- To conduct multiplex ELISA-based analysis of markers of inflammation, hypoxia, and angiogenesis before and after the treatment in serum samples and evaluate their association with clinical outcome.

## **Relevance and Anticipated Outcome:**

Oral cavity cancer is the most common cancer among Indian males and  $2^{nd}$  overall. [17] More than 70% of Oral cancer patients present in locally advanced stages III and IV. [18]. A significant proportion of patients are not resectable and have poor outcomes when treated non-surgical. For these advanced stage patients, NACT is routinely given at our Institute. The long-term outcomes of NACT on borderline operable Oral cancer patients has shown superior 10 year survival among patients undergoing surgery than those who did not undergo surgery (21.8% vs 4.1%, p < 0.001). [19] However, the response rates to NACT are variable. Thus, if the present study can find out the biomarkers for chemotherapy response. We will be able to spare a lot of patients from NACT, which will save costs to the patients and country and spare patients from toxicities. So, we anticipate that the findings from our study will help patients receive appropriate treatment.

# References

- 1. Coelho KR: Challenges of the oral cancer burden in India. J Cancer Epidemiol 2012, 2012:701932.
- Pathak KA, Gupta S, Talole S, Khanna V, Chaturvedi P, Deshpande MS, Pai PS, Chaukar DA, D'Cruz AK: Advanced squamous cell carcinoma of lower gingivobuccal complex: patterns of spread and failure. *Head Neck* 2005, 27(7):597-602.
- 3. D'Cruz A, Lin T, Anand AK, Atmakusuma D, Calaguas MJ, Chitapanarux I, Cho BC, Goh BC, Guo Y, Hsieh WS *et al*: **Consensus recommendations for management of head and neck cancer in Asian countries: a review of international guidelines**. *Oral Oncol* 2013, **49**(9):872-877.
- 4. Agarwal JP, Nemade B, Murthy V, Ghosh-Laskar S, Budrukkar A, Gupta T, D'Cruz A, Pai P, Chaturvedi P, Dinshaw K: **Hypofractionated, palliative radiotherapy for advanced head and neck cancer**. *Radiother Oncol* 2008, **89**(1):51-56.
- 5. Larizadeh MH, Shabani M: Survival following non surgical treatments for oral cancer: a single institutional result. *Asian Pac J Cancer Prev* 2012, **13**(8):4133-4136.
- Mohanti BK, Umapathy H, Bahadur S, Thakar A, Pathy S: Short course palliative radiotherapy of 20 Gy in 5 fractions for advanced and incurable head and neck cancer: AIIMS study. *Radiother Oncol* 2004, 71(3):275-280.
- 7. Ghoshal S, Mallick I, Panda N, Sharma SC: **Carcinoma of the buccal mucosa: analysis of clinical presentation, outcome and prognostic factors**. *Oral Oncol* 2006, **42**(5):533-539.
- 8. Zorat PL, Paccagnella A, Cavaniglia G, Loreggian L, Gava A, Mione CA, Boldrin F, Marchiori C, Lunghi F, Fede A *et al*: **Randomized phase III trial of neoadjuvant chemotherapy in head and neck cancer: 10-year follow-up**. J Natl Cancer Inst 2004, **96**(22):1714-1717.
- 9. Licitra L, Grandi C, Guzzo M, Mariani L, Lo Vullo S, Valvo F, Quattrone P, Valagussa P, Bonadonna G, Molinari R *et al*: **Primary chemotherapy in resectable oral cavity squamous cell cancer: a randomized controlled trial**. *J Clin Oncol* 2003, **21**(2):327-333.
- 10. Posner MR, Hershock DM, Blajman CR, Mickiewicz E, Winquist E, Gorbounova V, Tjulandin S, Shin DM, Cullen K, Ervin TJ *et al*: **Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer**. *N Engl J Med* 2007, **357**(17):1705-1715.
- 11. Lorch JH, Goloubeva O, Haddad RI, Cullen K, Sarlis N, Tishler R, Tan M, Fasciano J, Sammartino DE, Posner MR *et al*: Induction chemotherapy with cisplatin and fluorouracil alone or in combination with docetaxel in locally advanced squamous-cell cancer of the head and neck: long-term results of the TAX 324 randomised phase 3 trial. *Lancet Oncol* 2011, **12**(2):153-159.
- 12. Joshi A, Patil VM, Noronha V, Juvekar S, Deshmukh A, Chatturvedi P, Chaukar DA, Agarwal JP, Ghosh S, Murthy V *et al*: **Is there a role of induction chemotherapy followed by resection in T4b oral cavity cancers?** *Indian J Cancer* 2013, **50**(4):349-355.
- 13. Patil VM, Prabhash K, Noronha V, Joshi A, Muddu V, Dhumal S, Arya S, Juvekar S, Chaturvedi P, Chaukar D *et al*: **Neoadjuvant chemotherapy followed by surgery in very locally advanced technically unresectable oral cavity cancers**. *Oral Oncol* 2014, **50**(10):1000-1004.
- Chaukar D, Prabash K, Rane P, Patil VM, Thiagarajan S, Ghosh-Laskar S, Sharma S, Pai PS, Chaturvedi P, Pantvaidya G *et al*: Prospective Phase II Open-Label Randomized Controlled Trial to Compare Mandibular Preservation in Upfront Surgery With Neoadjuvant Chemotherapy Followed by Surgery in Operable Oral Cavity Cancer. J Clin Oncol 2022, 40(3):272-281.
- Wu Y, Posner MR, Schumaker LM, Nikitakis N, Goloubeva O, Tan M, Lu C, Iqbal S, Lorch J, Sarlis NJ *et al*: Novel biomarker panel predicts prognosis in human papillomavirus-negative oropharyngeal cancer: an analysis of the TAX 324 trial. *Cancer* 2012, 118(7):1811-1817.

- 16. Cullen KJ, Schumaker L, Nikitakis N, Goloubeva O, Tan M, Sarlis NJ, Haddad RI, Posner MR: **beta-Tubulin-II** expression strongly predicts outcome in patients receiving induction chemotherapy for locally advanced squamous carcinoma of the head and neck: a companion analysis of the TAX 324 trial. *J Clin Oncol* 2009, **27**(36):6222-6228.
- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F: Global Cancer Statistics
  2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021, 71(3):209-249.
- Nair D, Singhvi H, Mair M, Qayyumi B, Deshmukh A, Pantvaidya G, Nair S, Chaturvedi P, Laskar SG, Prabhash K *et al*: **Outcomes of surgically treated oral cancer patients at a tertiary cancer center in India**. *Indian J Cancer* 2017, **54**(4):616-620.
- Noronha V, Dhanawat A, Patil VM, Menon N, Singh AK, Chaturvedi P, Pai P, Chaukar D, Laskar SG, Prabhash K: Long-term outcomes of neo-adjuvant chemotherapy on borderline resectable oral cavity cancers: Real-world data of 3266 patients and implications for clinical practice. Oral Oncol 2023, 148:106633.

# 2. DR. NANDINI VERMA, NANDINI LAB

## Title: Identification and exploitation of genetic susceptibilities of ferroptosis for the treatment of therapytolerant Triple-Negative Breast Cancer.

TNBC is a very heterogeneous, aggressive, and metastatic disease that has high prevalence in India. The lack of hormone receptors and other targetable molecules like HER2 makes TNBC more difficult to treat. The only option for clinical management is chemotherapy for TNBC patients. More than 50% patients do not respond well to chemotherapeutic agents and show intrinsic or adaptive resistance to therapy resulting in treatment failure. Our earlier work identified that TNBC cells are exceptionally vulnerable to iron-mediated ferroptosis cell death due to their unique molecular state governed by transcriptomes related to metabolism of iron, glutathione and ferroptosis pathways [1]. More importantly, chemotherapy-tolerant persister TNBC cells show an enhanced toxicity to ferroptosis inducing agents, signifying a potential alternative therapeutic option for resistant TNBC cells [2]. However, it is not well understood if there are any genetic grounds of ferroptosis susceptibility in TNBC tumors and if oncogenic and tumor suppressor genes can influence this cell death pathway. Therefore, we want to conduct lentivirus-based molecular screens to identify the tumor-associated genes that might govern the sensitivity to ferroptosis in breast tissue. Findings from this study will enable us to deploy the genetic predisposition in TNBC to effectively eliminate tumor cells by ferroptosis.

Key words: Ferroptosis, TNBC, molecular screen, drug resistance

## **References:**

**[1]** Nandini Verma et al. ,Synthetic lethal combination targeting BET uncovered intrinsic susceptibility of TNBC to ferroptosis. *Sci. Adv.* 6,eaba8968(2020).DOI:10.1126/sciadv.aba8968

[2] Nazia Chaudhary et al. GPX4-VIM equates a proliferating DTP state in TNBC subtypes with converged vulnerabilities to autophagy and glutathione inhibition. *bioRxiv* 2023.05.18.541287; doi: <u>https://doi.org/10.1101/2023.05.18.541287</u>

#### 3. DR. SHARATH CHANDRA ARANDKAR (SHARATH LAB)

# Title: Decoding the Bidirectional Crosstalk Between Tumor Cells and Cancer-Associated Fibroblasts in the Tumor Microenvironment.

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 TGF $\beta$ , IL-1 $\alpha/\beta$ , PDGF, FGF, etc. These CAF-derived secretory factors, through direct or indirect communications with other components of the TME, exert their functions 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. For this, we will use various *in vitro* and *in vitro* methods to understand the impact on tumour-microenvironment.