BIOGRAPHICAL SKETCH

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NAME: Ansu O. Perekatt

eRA COMMONS USER NAME (credential, e.g., agency login): APEREKATT

POSITION TITLE: Assistant Professor
Stevens Institute of Technology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Marathwada Agricultural University, India	B.Sc.	07/1995	Agricultural Sciences
Kerala Agricultural University, Kerala, India	M.Sc.	05/1999	Plant Pathology
California State University, Hayward	MS	11/2009	Biological Sciences
University of Illinois, Chicago	Ph.D.	08/2011	Biochemistry and Molecular Genetics
Rutgers, The State University of New Jersey	Postdoc	09/2011 to 07/2018	Transcriptional regulation in the intestinal epithelium
Stevens Institute of Technology	Assistant Professor	08/2018 to present	Transcriptional regulation of oncogenic plasticity

A. Personal Statement

I established my independent research lab in September 2018 with a career transition award (K22) from NCI. My project builds on my postdoctoral work in Dr. Michael Verzi's lab, which was published in 2018.

The overarching goal of my research is to determine how cancer stemness is initiated and maintained in colon cancer. My lab is currently investigating the molecular basis of fate reversal from mature to oncogenic stem cell fate in the intestinal epithelium using a mouse model of tumorigenesis in the intestine. By performing single-cell RNA seq analysis, my lab has confirmed that in our mouse model, oncogenic stemness arises by cell-fate reversal. Stemness in tumors sustains tumorigenesis. Hence, it's imperative to determine the mechanism underlying fate reversal that enables oncogenic stemness. The goal of my lab is to investigate the cell-intrinsic causes and extracellular cues triggering the fate transition to stemness.

My research career has been focused on cancer and intestinal biology with an emphasis on signal transduction and transcriptional regulation. My pre-doctoral work familiarized me with the complexities of signal transduction, while my postdoctoral training focused on transcriptional regulation in the intestinal epithelium as it relates to stem cell biology and cancer.

In my second postdoctoral research at the Cancer Institute of New Jersey, I investigated the immunosuppressive milieu that develops during Pancreatic cancer metastases to the liver. This experience is helping me better understand immune changes observed during colon tumorigenesis and is informing my ongoing research on inflammatory bowel diseases. I am confident that my diverse research experience will help me answer my research questions more effectively.

a) Christina Li, Jeel Shah, Kylee Wrath, Dahlia Matouba, Connor Mills, Kishore Punnath, and **Ansu Perekatt.** 3D Culturing of organoids from intestinal epithelium undergoing dedifferentiation. ***JoVE***. 2021 Apr 1;(170). doi: 10.3791/61809. (2021 Apr 1;(170) ed.). PMID:33871463

b) **Perekatt AO,** Valdez MJ, Davila M, Hoffman A, Bonder EM, Gao N, Verzi MP. YY1 is indispensable for Lgr5+ intestinal stem cell renewal. **Proc. Natl. Acad. Sci.** U S A. 2014;111(21):7695-700.

c) **Perekatt AO,** Shah PP, Cheung S, Jariwala N, Wu A, Gandhi V, Kumar N, Feng Q, Patel N, Chen L, Joshi S, Zhou A, Taketo MM, Xing J, White E, Gao N, Gatza ML, Verzi MP. SMAD4 Suppresses WNT-Driven Dedifferentiation and Oncogenesis in the Differentiated Gut Epithelium. **Cancer Research.** 2018;78(17):4878-90.

d) Chen L, Toke NH, Luo S, Vasoya RP, Fullem RL, Parthasarathy A, **Perekatt AO,** Verzi MP. A reinforcing HNF4-SMAD4 feed-forward module stabilizes enterocyte identity. **Nature Genetics** 2019;51(5):777-85.

B. Positions and Honors

- Postdoctoral Fellow, Rutgers. 09/2011 to 07/2018
- Assistant Professor, Stevens Institute of Technology 08/2018 present
- New Jersey Commission on Cancer Research Fellowship 05/2013- 04/2015
- Gallow Award for Outstanding Cancer Research 05/2014
- Gallow Award for Outstanding Cancer Research 05/2016
- Gallow Award for Outstanding Cancer Research 05/2018
- NCI Career Transition Award (K22) 09/2018 - 02/2023

C. Contributions to Science

Cancer Biology

a) Loss of Smad4, the transcriptional effector of TGF signaling is associated with aggressive colon cancer. I found that Smad4 prevents cell fate reversal under conditions of high Wnt signaling. The study showed that combinations of two of the most deregulated pathways in colon cancer can result in dedifferentiation to oncogenic stemness. I was the primary person responsible for planning and executing the experiments and interpreting the results.

Perekatt AO, Shah PP, Cheung S, Jariwala N, Wu A, Gandhi V, Kumar N, Feng Q, Patel N, Chen L, Joshi S, Zhou A, Taketo MM, Xing J, White E, Gao N, Gatza ML, Verzi MP. SMAD4 Suppresses WNT-Driven Dedifferentiation and Oncogenesis in the Differentiated Gut Epithelium. **Cancer Research** 2018;78(17):4878-90.

b) Mechanism of B-raf driven colon tumors is not entirely understood. I contributed to the understanding that less differentiated tissues are susceptible to B-Raf-driven tumors that involved transcriptional profiling.

Tong K, Pellon-Cardenas O, Sirihorachai VR, Warder BN, Kothari OA, **Perekatt AO**, Fokas EE, Fullem RL, Zhou A, Thackray JK, Tran H, Zhang L, Xing J, Verzi MP. Degree of Tissue Differentiation Dictates Susceptibility to BRAF-Driven Colorectal Cancer. **Cell Reports** 2017;21(13):3833-45

c) Epigenomic status is altered in tumors. I contributed to elucidating the epigenomic landscape of $Apc^{min/+}$ tumors and found changes in DNA methylation patterns to influence Wnt signaling and epithelial mesenchymal transition.

Guo Y, Lee JH, Shu L, Huang Y, Li W, Zhang C, Yang AY, Boyanapalli SS, **Perekatt A,** Hart RP, Verzi M, Kong AN. Association of aberrant DNA methylation in Apc(min/+) mice with the epithelial-mesenchymal transition and Wnt/beta-catenin pathways: genome-wide analysis using MeDIP-seq. **Cell Biosci**. 2015;5:24.

Intestinal Tissue Homeostasis

a) How does intestinal tissue respond to DNA damage through apoptotic signaling? I found that a tyrosine kinase, PTK6, overexpressed in cancer promote apoptosis in response to DNA damage. The study showed that PTK6 promotes apoptosis *in vivo* by regulating pro- and anti-apoptotic members of the apoptotic signaling pathway. This finding highlighted how signaling can have context-specific and disparate functions.

Haegebarth A, **Perekatt AO,** Bie W, Gierut JJ, Tyner AL. Induction of protein tyrosine kinase 6 in mouse intestinal crypt epithelial cells promotes DNA damage-induced apoptosis. **Gastroenterology**. 2009;137(3):945-54. Epub 2009/06/09. doi: 10.1053/j.gastro.2009.05.054.

b) The intestinal epithelium has fast-cycling stem cells called Lgr5+ stem cells that maintain the intestinal epithelium. I found that the transcription factor Yy1 is essential to maintaining the Lgr5+ stem cells in the intestine. The findings of the research highlighted metabolic regulation of stem cell function. I played the lead role in elucidating the underlying mechanism by employing ChIP-seq and RNA-seq methods.

Perekatt AO, Valdez MJ, Davila M, Hoffman A, Bonder EM, Gao N, Verzi MP. YY1 is indispensable for Lgr5+ intestinal stem cell renewal. **Proc Natl Acad Sci** U S A. 2014;111(21):

c) I contributed to the research investigating the transcriptional mechanism underlying the etiology of inflammatory bowel diseases using a knockout study in the mouse model for inflammatory bowel diseases.

Chahar S, Gandhi V, Yu S, Desai K, Cowper-Sal-lari R, Kim Y, **Perekatt AO,** Kumar N, Thackray JK, Musolf A, Kumar N, Hoffman A, Londono D, Vazquez BN, Serrano L, Shin H, Lupien M, Gao N, Verzi MP. Chromatin profiling reveals regulatory network shifts and a protective role for hepatocyte nuclear factor 4alpha during colitis. **Mol Cell Biol.** 2014;34(17):3291-304.

d) How does enterocyte maintain the differentiated cellular identity despite the inherent plasticity of the intestinal epithelium? The study found that HNF4 regulates enhancers and co-operate with effectors of BMP signaling to maintain the enterocyte identity. I performed the ChIP experiments for Smad4, the transcriptional effector of BMP signaling, that elucidated the underlying mechanism.

Chen L, Toke NH, Luo S, Vasoya RP, Fullem RL, Parthasarathy A, **Perekatt AO**, Verzi MP. A reinforcing HNF4-SMAD4 feed-forward module stabilizes enterocyte identity. **Nature Genetics** 2019;51(5):777-85.

A full list of Dr. Perekatt's publications can be found at:
https://www.ncbi.nlm.nih.gov/myncbi/1JCua4CmJiAAD/bibliography/public/