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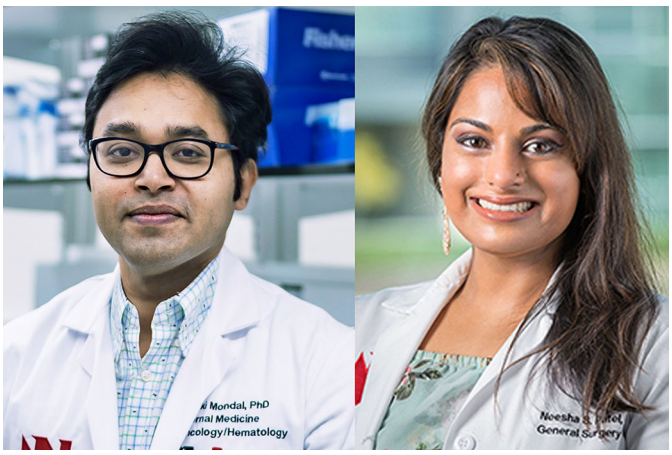
FIRST PERSON

First person – Pinaki Mondal and Neesha Patel

First Person is a series of interviews with the first authors of a selection of papers published in Disease Models & Mechanisms, helping researchers promote themselves alongside their papers. Pinaki Mondal and Neesha Patel are co-first authors on 'Induction of pancreatic neoplasia in the *KRAS*/*TP53* Oncopig', published in DMM. Pinaki is a research scientist, and Neesha is a surgical resident, in the lab of Mark A. Carlson at University of Nebraska Medical Center, Omaha, NE, USA, investigating pancreatic adenocarcinoma and reprograming of its complex microenvironment in therapy resistance.



Pinaki Mondal (left) and Neesha Patel (right)

How would you explain the main findings of your paper to non-scientific family and friends?

Until now, we needed to rely on mouse models to understand the mechanisms behind pancreatic cancer and to test new potential therapies before their approval. However, mouse models may not accurately predict human biology and response to interventions due to differences in the genome and body size. The fact remains that only a few percent of therapeutic anti-cancer drug candidates identified in preclinical studies ultimately get approval from the U.S. Food and Drug Administration. In this study, we induced and characterized pancreatic tumours in a transgenic pig model (the 'Oncopig'), and described similarities with human pancreatic cancer in DNA, RNA and protein levels. We also described a new surgical technique to enhance the possibility of cancer induction restricted only to the pancreatic ducts and not inducing all over the pancreas, to mimic the predominant ductal characteristics of human pancreatic cancer.

"[…] this pig model of pancreatic cancer could be useful for focused research and development of diagnostic and therapeutic technologies for pancreatic cancer."

What are the potential implications of these results for your field of research?

Pigs have greater similarity to humans than mice with respect to size, anatomy, physiology and coding sequences. With further optimization and validation, this pig model of pancreatic cancer could be useful for focused research and development of diagnostic and therapeutic technologies for pancreatic cancer. Such research and development would be difficult, if not infeasible, in a 20 g mouse.

What are the main advantages and drawbacks of the experimental system you have used as it relates to the disease you are investigating?

The main advantage is an improved surgical technique that we have described here, which enhances the restriction of adenovirus-mediated transgene induction to the pancreatic ducts. The main disadvantage is that the current dose of the adenovirus is making the induction of tumours extremely quick, in a range of 10-31 days. We need to optimize the induction conditions to obtain a more controlled induction of the disease.

What has surprised you the most while conducting your research?

We were surprised to see the fulminant cancer induction process. Pathologic analysis identified poorly differentiated pancreatic tumour cells, and all happening within a short period of time.

What do you think is the most significant challenge impacting your research at this time and how will this be addressed over the next 10 years?

The most significant challenge is the cost associated with pig research and the unavailability of genetically engineered pig models, which have transgene expression restricted to only the pancreatic ductal cells (the current Oncopig model can express transgenes in all somatic cells). More focused research from investigators on developing genetically engineered pig models that are specific for pancreatic cancer should be able solve this challenge.

"Greater availability of the grant mechanisms that enable scientists to test scientifically sound hypotheses with little or no preliminary data is essential."

What changes do you think could improve the professional lives of scientists?

Greater availability of the grant mechanisms that enable scientists to test scientifically sound hypotheses with little or no preliminary data

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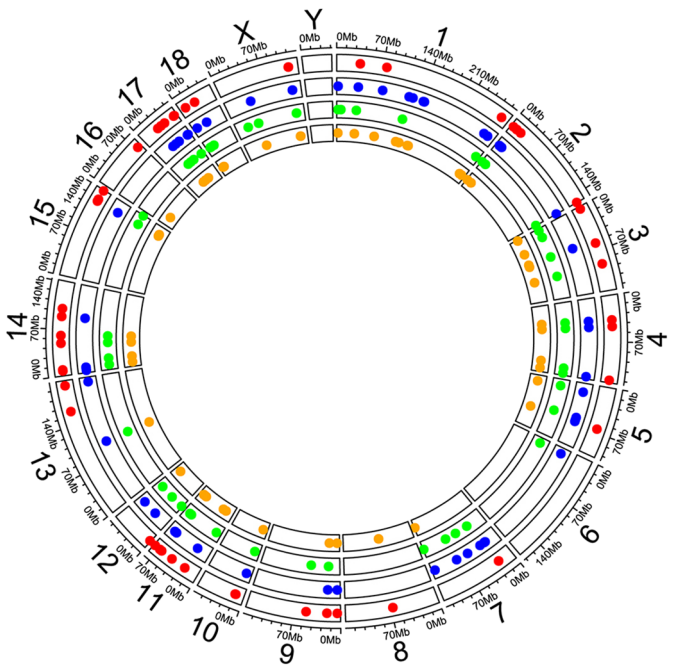

Genomic insertions in our porcine model of pancreatic cancer.

is essential. Such short-term funding will help scientists perform the most essential tests to develop a successful hypothesis and also ease the stress of not being able to apply for a grant due to non-availability of preliminary data.

What's next for you?

We are endeavouring to create a genetically engineered pig model for pancreatic cancer in which the neoplastic process is restricted to pancreatic ductal cells. We are introducing a specialized transgenic cassette into the pig genome with our genome and animal engineering collaborators.

Reference

Mondal, P., Patel, N. S., Bailey, K., Aravind, S., Cartwright, S. B., Hollingsworth, M. A., Lazenby, A. J. and Carlson, M. A. (2023). Induction of pancreatic neoplasia in the *KRAS*/*TP53* Oncopig. *Dis. Model. Mech.* **16**, dmm049699. doi:10.1242/dmm.049699