The substrate for success

“I want to work in a way that allows my science to be translated into benefits for people, the potential to do this guides the kind of research I do. When thinking about returning to India, I felt, if I really wanted my science to contribute to human advancement industry would be the best place to do it. It’s been ten years and I have no regrets,” says cell biologist Dr Mabi Jaleel.

As an Associate Research Director for Aurigene Discovery Limited in Hyderabad, India, Dr Jaleel leads internal and collaborative drug discovery programmes in oncology and inflammation. She has translated the experience of kinase and phosphorylation research she gained as a postdoc at the Medical Research Council Protein Phosphorylation Unit (PPU) at the University of Dundee into drug discovery programmes.

Dr Jaleel’s team have just had a compound approved to go into a phase 1 clinical trial, the start of a path she hopes will lead to a new treatment for melanoma skin cancer. From there she hopes to see if it could work against any other kind of cancer. The compound is an inhibitor that works by targeting two kinases with the same molecule to stop skin cancer tumours from growing.

Following a path to new ideas

Dr Jaleel completed her PhD in the Department of Molecular Reproduction, Development and Genetics at the Indian Institute of Science in Bangalore in 2004. Her work on causes of childhood diarrhoea focused on finding potential molecular inhibitors. She met PPU Director Professor Dario Alessi at a research conference in Brussels, his innovative research encouraged her switch to seeking out the secrets of kinases.

“I was doing my PhD in India when I met Dario. He was working on phosphorylation in Dundee and I knew that he did path-breaking science. I could have gone to the US or anywhere else for my post doc but I chose Dundee because I could see how exciting Dario’s work was and I wanted to be the first person to discover something,” says Dr Jaleel. She did.

As a postdoc in Professor Alessi’s lab Dr Jaleel identified the first in vitro substrates for a kinase called LRRK2 that is mutated in Parkinson’s disease. This led to identification of a peptide substrate called LRRRKtide that led the way for an inhibitor that is now used as a Parkinson’s therapy.

“Every postdoc wants to achieve something within the short space of time they have. The way I approached it was to think ‘ok this is my best part whatever I can achieve in three or four years ok I’ll take it and just do it’. At that moment, in that short run I worked really hard. Identifying the substrate for the LRRK2 kinase thrilled me. When companies eventually started to use it to design Parkinson’s treatments it was really encouraging. That was when I first began to think about working in industry.”

Moving from academia to industry

“I was thinking about whether to stay in academia and I spoke to Dario. I wanted to come back to India. To me, building a career in academia meant working in the way Dario does at MRC PPU but I thought back home I may not have that sort of opportunity in a single place. So I thought if I really want to translate my science and make the most of what I had learnt in Dundee the best place I could do this in India would be to join industry. Once I’d made the decision I realised there was no point extending my time in academia - it’s best to get started.”

Dr Jaleel returned to India in 2007 where she joined the discovery research team at Dr Reddy’s Laboratories Ltd in Hyderabad. Dr Reddy’s was focused on kinase research at the time so responded quickly to her interest, she says: “I didn’t have any contacts or networks in industry in India. I just emailed Dr Reddy’s. Since I was working on AMPK kinases, and because Dundee is the birthplace of AMPK research, I think my email caught the eye of management and they immediately called. Since my CV showed that I was in Dundee working on AMPK kinases it was easy for me to get a job back here.”

The transition was smoothed by her experience in AMPK research, she says: “AMPK was one of the kinases people spoke about a lot and it was being implicated in different conditions. Moving from academia to industry can be a tough choice but because I had already been trained so well in AMPK research it was easy for me to settle into the job.”

Exposure to industry ways of working through MRC PPU’s ongoing industry collaboration, the Division of Signal Transduction Therapy (DSTT), also helped, she says: “When I was at PPU we regularly spoke to companies through the DSTT collaboration. I could see that basic research was being translated and that when companies were interested they could take it a step forward.”

At Dr Reddy’s she built a drug discovery programme to find new pain therapies, she says: “I didn’t want to be a very basic researcher. At PPU there is the opportunity to do bench to bedside work alongside basic research, I’ve brought that with me, it’s important to me that I can see how there could be a benefit to people from the work I do.”

Dr Jaleel recommends switching your thinking along with the move from academia if you choose to move into industry, she says: “Project time frames can be short and you have to deliver on them or they get shut down. When you are in academia you are trying to bring research to a conclusion and publish papers. Sooner or later I learnt that you cannot have that academic mindset in industry so the earlier the better, when you change career, to let go of your attachment to the project and have a business perspective on it.”

In 2009 from Dr Reddy’s she moved to Aurigene as a Principal Scientist where she became a Senior Group Leader in 2012 and was promoted to the current Associate Director role in 2015.

At Aurigene, Dr Jaleel’s role as a project team lead means she is learning about the way other companies work too, she says: “Here our collaborations mean that I’m not just stuck on one pathway. I work with chemistry, toxicology, biology, cloning and pharmacology groups and sometimes with clinicians too.”

Encouraging her team is important, she says: “My team is made up of really energetic young people who are keen to learn. I’m always trying to tell them all my learning was in my PhD and postdoc. I still remember when we generated data and presented it to Dario. I learnt so much about how to make sure I captured the answers from experiments and how to design them so that I could get a useful answer. That learning was incredible for me.”

Dr Jaleel is keen to pass on the skills she learnt at PPU: “I train the people working here in the same way I was in Dundee – to generate high quality, reproducible data. The challenge in industry is that people are not working towards a PhD or publication so you have to find other ways to keep motivating your team. You have to show them that the data they are collecting is good and explain why,” she says.

Final word

“Drug discovery is such a hit or miss project. You never know when a drug will fail, it could because of toxicity, or lack of efficacy or even a company decision to stop a project. My ambition is to see a molecule I’ve worked on transition into a therapy for cancer patients. That is my dream and motivation,” Dr Mabi Jaleel.

Top publications

Dr Mabi Jaleel picks her top three papers and tells us why she has chosen each one**.**

1) *LRRK2 phosphorylates moesin at threonine-558: characterization of how Parkinson's disease mutants affect kinase activity.*

Biochem J. 2007 Jul 15;405(2):307-17.
Jaleel M[1], Nichols RJ, Deak M, Campbell DG, Gillardon F, Knebel A, Alessi DR.

“This paper during my post-doctoral work is close to my heart, since my aim to identify something new was fulfilled. After a lot of effort and using the KESTREL approach, we identified LRRKtide peptide substrate for LRRK2. Further work was done in the lab to improvise the substrate and to develop robust kinase assays. This is being used by companies working on Parkinson’s disease**.”**

2) *ASN003, a unique B-RAF inhibitor with additional selective activity against PI3K and mTOR kinases, shows strong antitumor activity in multiple xenograft models*
DOI: 10.1158/1535-7163.TARG-15-B100 Published 1 December 2015
Abstracts: AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics; November 5-9, 2015; Boston, MA
Scott K. Thompson, Mahaboobi Jaleel, Vijay Kumar Nyavanandi, Murali Ramachandra, Hosahalli Subramanya, Aravind Basavaraju, Vaibhav Sihorkar, Roger A. Smith, Niranjan Rao, Sandeep Gupta, Sanjeeva P. Reddy.

“Identified highly selective kinase inhibitor and dual targeting of the B-RAF and PI3K pathways which has the potential to overcome the acquired resistance to selective B-RAF inhibitors. After doing three projects, this is my first discovery program to complete preclinical development.”

3) *ODM-207, a novel BET-bromodomain inhibitor as a therapeutic approach for the treatment of prostate and breast cancer.*
AACR 2016: April 16-21
Mari Björkman 1, Elina Mattila 1, Reetta Riikonen 1, Chandra Sekhar 2, Mahaboobi Jaleel 2, Sivapriya Marappan 2, Tarja Ikonen 1, Daniel Nicorici 1, Juha Rantala 3, Susanta Samajdar 2, Murali Ramachandra2 Pekka Kallio 1, Anu Moilanen 1. 1Orion Corporation Orion Pharma, Espoo, Finland, 2Aurigene Discovery Technologies Limited, Bangalore, India, 3Misvik Biology, Finland

"In this study we identified a novel, potent and highly selective BET bromodomain inhibitor with excellent efficacy in preclinical models of prostate and breast cancer as well as in patient-derived tumor cell cultures from various tumor types."

Dr Mabi Jaleel LinkedIn Profile

This PPU alumni profile was written by Hazel Lambert of sciencestory.com