



#### research project

Targeting the mRNA processing machinery in cancer

# project summary

Dr Vihandha Wickramasinghe's paradigm-shifting research focuses on understanding the fundamental biology of gene expression and how it is altered in the development of cancer cells. His goal is to find new ways to intervene when normal quality control processes within the cell go awry.

At the world class Peter MacCallum Cancer Centre, Dr Wickramasinghe leads the RNA Biology and Cancer Laboratory where he investigates the molecular basis of how mRNA is selectively processed and exported from the nucleus into the cytoplasm and its emerging links to cancer.

Dr Wickramasinghe's research will use state of the art genomic, molecular and cell biological approaches developed during his time at the University of Cambridge with some of the most renowned experts in molecular biology and cancer research.

One of Dr Wickramasinghe's key projects, researching the mechanisms of selective messenger RNA (mRNA) export, is seen as a critical step in the gene expression pathway, which is altered in cancer. Through this research, Dr Wickramasinghe and his team have demonstrated that mRNA export is not constitutive, but is highly selective and can regulate distinct biological processes through poorly understood mechanisms.

His second project is researching the effect of alternative mRNA splicing on the human proteome, which has emerged as a key mechanism for enabling biological complexity within the human genome. However, the extent to which this increased genomic complexity contributes to the generation of proteomic diversity is largely unknown. Dr Wickramasinghe and his team have identified this fundamental biological question as one of critical importance to human health, given the recent identification of perturbed RNA splicing as a causative factor in cancer.

The establishment of Dr Wickramasinghe's RNA Biology and Cancer laboratory at the Peter MacCallum Cancer Centre offers opportunities for new and expanded industry collaborations. The Oncogenic Signalling and Growth Control division, which Dr Wickramasinghe joins, has strong links with the pharmaceutical industry. This collaboration saw the development of the world's first selective inhibitors of RNA Polymerase I transcription, a new class of therapeutic. As an integrated member of this team, Dr Wickramasinghe will access these collaborative industry networks with a view to progressing his discoveries to the clinical arena.

#### personal history

Dr Vihandha Wickramasinghe moved to Australia from the UK in 2016 to become a **veski** innovation fellow at the Peter MacCallum Cancer Centre.

He grew up in Canberra and was awarded a highly prestigious Melbourne National Scholarship to undertake his undergraduate and honours degrees in Biomedical Science at the University of Melbourne.

At the successful completion of his Honours degree, he was awarded a Medical Research Council pre-doctoral fellowship - one of around 10 awarded annually in the UK - to undertake his PhD studies at the University of Cambridge with Professor Ron Laskey, FRS and CBE.

During his subsequent post-doctoral studies at the MRC Cancer Unit in Cambridge with Professor Ashok Venkitaraman, he established his current research program investigating the molecular mechanisms that regulate selectively of the mRNA processing machinery and their emerging links to cancer. This research demonstrated for the first time that selective mRNA export from the nucleus can regulate a fundamental biological process, namely DNA repair.

Vihandha's research into the mechanisms of mRNA splicing and export published in top tier journals

### Dr Vihandha Wickramasinghe

"Investing in fundamental biological research is critical to ensure that scientific breakthroughs can be directly translated into novel therapeutics for a disease as prevalent as cancer."

# other innovation fellowship recipients

has challenged previous dogma on the obligate steps in gene expression. This body of work has been recognised by the premier review journal in molecular biology, Nature Reviews Molecular Cell Biology, along with Molecular Cell, who have both commissioned review articles on selective mRNA export, and RNA processing and genome stability, respectively.

During his PhD in Cambridge, Vihandha met his Scottish wife Melanie. After working in the homelessness and community sector in the UK, Melanie is now using her experience to make a difference here in Australia.

Both Vihandha and Melanie have settled into life in Australia and are enjoying all the benefits that Melbourne provides.

Dr Wickramasinghe's identical twin brother, Rochana also did his PhD and postdoctoral studies in Cambridge. He now works as a Director of Oncology Evaluation for the multinational pharmaceutical company AstraZeneca.

Dr Wickramasinghe is a committed mentor of young scientists, nurturing their passion for science and ensuring that they realise their potential. Professor Andrew Holmes AC FRS FAA FTSE
Professor Marcus Pandy
Adjunct Assoc. Professor Gareth Forde
Associate Professor Alyssa Barry
Professor Michael Cowley FTSE
Professor Sarah Hosking
Professor Ygal Haupt
Associate Professor Ross Dickins
Dr Mark Shackleton

Professor Edwin van Leeuwen FTSE

Dr Matthew Call

Associate Professor Christopher McNeill

Dr Seth Masters

Professor Tiffany Walsh

Professor Cameron Simmons

Dr Luke Connal

Professor Colette McKay

Dr Ethan Goddard-Borger

Professor Mark Dawson

Professor Kenneth Crozier

Associate Professor Roger Pocock

Professor Richard Sandberg

Professor Colby Zaph

Professor Jon N Shah

## background information

veski delivers a range of Victoria's most prestigious science and innovation programs including the veski innovation fellowships which bring world-leading scientists and researchers back to Victoria.

Since 2004, 25 **veski** innovation fellows have returned to Victoria. Active innovation fellows have secured more than \$68m in research income to date delivering an 18.4:1 economic return on investment. Their research covers semiconductors, epigenetics, audiology, optics and nanotechnology, enzymes, dengue, malaria, cancer, inflammatory diseases, musculoskeletal health, geothermal energy, obesity, computational fluid dynamics and bio-medical imaging.

**veski** is supported by the State Government of Victoria.

# further information

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