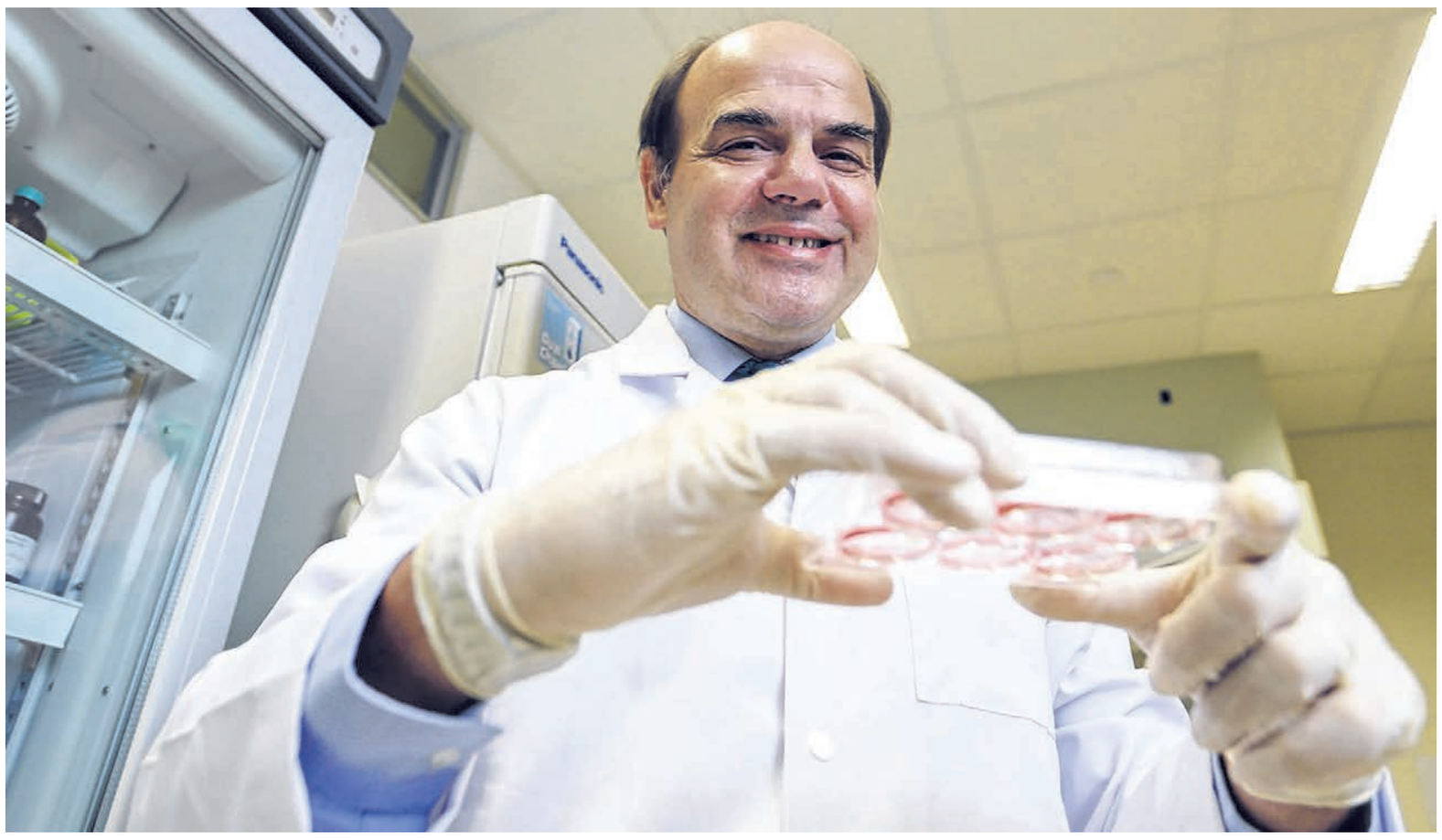
[I AM A SCIENTIST]

Sniffing out clues in Down syndrome

Condition could be key in treating ageing-related diseases and cancer, says Professor Dean Nizetic

Audrey Tan



ST PHOTO: ONG WEE JIN

Professor Dean Nizetic, 55, and his team recently discovered two genetic markers of acute lymphoblastic leukaemia that could aid treatment of the disease.

Q: You were involved in the Human Genome Project back in 2000 and mapped the human chromosome 21 – an extra copy of which causes Down syndrome. Was that what fuelled your interest in Down syndrome?
Yes. During that process, I became very intrigued in this complex phenomenon known as Down syndrome, and realised how frequent and prevalent it is. It happens once in about 1,000 live births worldwide, for instance, and there are about 4,000 people with Down syndrome in Singapore.

Q: What can we learn from Down syndrome?
I found it very fascinating that although Down syndrome is a condition where cells show accelerated ageing, some people who have it seem to be protected from some ageing-related diseases such as early memory loss and dementia, most types of cancer and Type 2 diabetes.

This is despite them probably having accumulated errors in their DNA due to accelerated ageing, and many other risks, such as being overweight. In countries with developed health systems, most people with Down syndrome can survive into their late 60s.

There must be powerful cellular mechanisms that protect such people from ageing-related diseases. If we could understand what those mechanisms are, that could lead us to new ideas and approaches for the detection of such diseases, and their prevention and treatment in people, with and without Down syndrome.

Q: Can you elaborate on your current work?
The cells that give us the biggest clues to understanding Down syndrome are the brain cells.

But it is not possible to simply take them from live people. With modern technology, we can reprogramme hair cells, skin cells or blood cells back into an embryonic stem cell-like stage where they can transform into any cell and, from there, develop the patient's own neurons in that culture dish.

Last year, I co-initiated a project in London to study Down syndrome more systematically. It is a five-year, £2.5 million (S$5.1 million) project funded by the Wellcome Trust – the largest science charity in Britain – and includes geneticists, clinicians, psychologists and psychiatrists.

Once people gave their consent to take part in the study, we would take their cells and assess their intellectual function over a period of time, such as whether they have mild or severe Down syndrome, and whether this changes over time, and observe if they get dementia.

Q: How will you take the research further in Singapore?
First, there are already known differences within the ethnic sub-populations in Singapore in terms of the prevalence of vascular dementia and Alzheimer's dementia, and in risk factors linked to the incidence of Type 2 diabetes.

There is also bilingualism here. That is known to improve connections between brain cells and improve functional brain reserves.

All these features are specific to Singapore and are unexplored in people with Down syndrome. This is why we think the study here can provide us with extra clues.

One of the goals for my research here is to try to discover ways in which cellular defects could be corrected. Once done, pharmaceutical and biotech companies could come on board to work on drugs for ageing-related diseases.

Q: Last month, you and your team made a discovery that was published in science journal Nature Communications. You discovered two genetic markers of acute lymphoblastic leukaemia, a type of cancer of the white blood cells. Why is this discovery important?
We found that acute lymphoblastic leukaemia may be caused by mutations in one of the two key genes prevalent in children with Down syndrome. Children with Down syndrome are about 20 to 50 times more at risk of developing this leukaemia.

We discovered that in children with Down syndrome and leukaemia, cancer cells develop either the RAS or JAK gene mutations – never together. By knowing which gene has mutated, doctors would be able to prescribe treatment that will target the one gene.

Acute lymphoblastic leukaemia is the most common cancer in children, with 50 to 100 children diagnosed each year in Singapore. This discovery could benefit all children affected by the disease as clinicians would be able to offer more specific and less toxic treatments, which could reduce the side effects.

Q: You have done research in London and in Singapore. How would you compare both places?
Singapore has a very well-organised research environment in which interaction with other institutions and clinicians is straightforward.

London also offers its advantages, such as having a critical mass of people and researchers, but you need to go around to pull people together to achieve something.

In compact Singapore, that seems to be much easier to do, since many things are already pre-organised for scientists.

But one thing they have in common is that Down syndrome associations have been very supportive in this study.

Q: You have also taken to Singapore food?
Yes, it is absolutely brilliant and diverse! There are many dishes I enjoy. I especially like satay, while my wife Lidia enjoys chilli crab.

I also like the climate, cleanliness and vibrant culture of the place.

I have been to Singapore and South-east Asia many times before on holiday, but moved here for work only in February.

Q: You often work late into the night, and even through the weekend. Do you still find time to relax?
Yes, I enjoy reading, especially biographies of Sir Stamford Raffles.

I am now reading my third book on him. It was written in the 19th century, and my son got it for me in London.

During his lifetime, Sir Stamford Raffles was an underappreciated genius and visionary whose actions have transformed the connection between Europe and Asia.

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GROUND-BREAKING RESEARCH

Croatian-born Dean Nizetic, 55, is professor of molecular medicine at Nanyang Technological University's Lee Kong Chian School of Medicine.

His research interest in Down syndrome dates back more than 20 years, starting soon after he graduated from the medicine faculty at Croatia's University of Zagreb in 1982. Professor Nizetic then did research for his PhD thesis in molecular biology at the Max Planck Institute for Biology in Germany.

Since then, most of his work has been done in Britain, at the Imperial Cancer Research Fund, the University of London's Centre for Applied Molecular Biology, and Barts and The London School of Medicine.

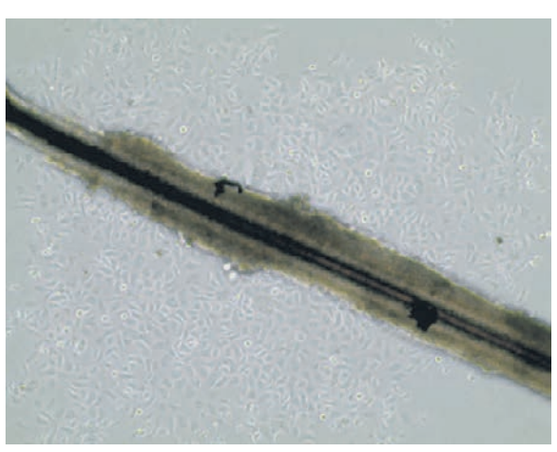
In 2008, Prof Nizetic and his team discovered the earliest molecular changes of Down syndrome in embryonic stem cells, which they found were triggered by the extra copy of a specific gene called DYRK1A on chromosome 21.

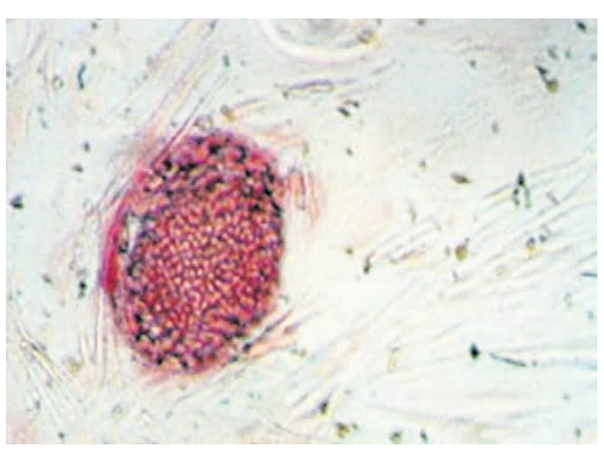
Prof Nizetic's work has also led to breakthroughs. He found certain chemical compounds could potentially be used to treat cognitive deficiencies in people with Down syndrome. Clinical trials are ongoing.

Prof Nizetic and his wife Lidia, a housewife of "about the same age", have two sons, aged 20 and 28, who are studying and working in London. The couple moved here in February.

Audrey Tan

Beautiful Science





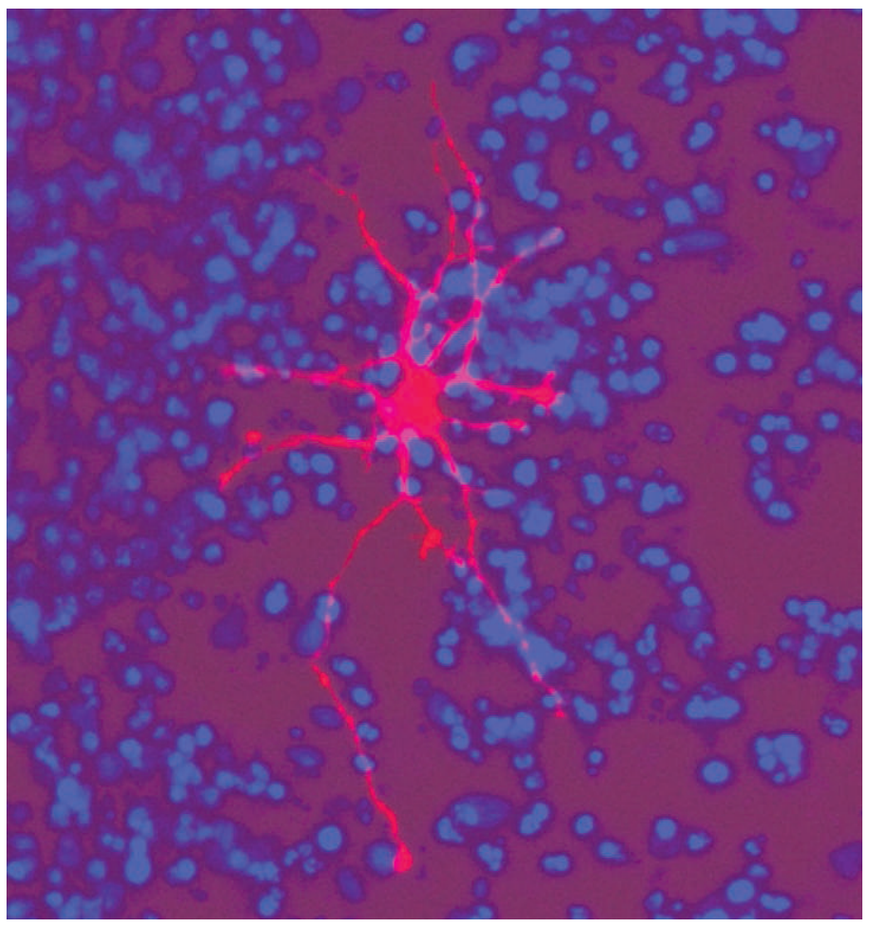
Studying brain disease or monitoring how the brain cells of individual patients respond to treatment no longer calls for invasive procedures to extract the cells.

Instead, scientists can simply use cells from a strand of the patient's hair (above left).

Researchers in Singapore have been able to reprogramme such hair cells to become induced pluripotent stem cells (above right).

These cells are similar to embryonic stem cells, which have the ability to become any type of cell in the body.

The cells are then placed in a petri dish and cultured into the patient's own brain cells (right).



PHOTOS: DEAN NIZETIC