Catching up with the FUTURE

Dr Zameel Cader, director of StemBANCC

Long Hanborough-based scientist and author **Dr Richard Corfield** reflects on an exciting time for medicine

In the climax to Ridley Scott's science fiction classic *Blade Runner*, replicant (artificial human) Roy Batty confronts the scientist who constructed him, reclusive billionaire Dr Eldon Tyrell, concerning his small problem with imminent death.

"You were made as well as we could make you, Roy," purrs Tyrell.

"But not to last . . ." replies Batty.

In the movie the replicants were all programmed with a four-year lifespan to ensure that they were never a threat to their human masters.

For those of us who arrived on this Earth by more conventional means, while life expectancy is increasing, broadly speaking our days are still three-score and ten. And lurking over all is the threat from diseases that are being intensively researched but which stalk our subconscious like nightmares from the id.

Cancer, Alzheimer's, Parkinson's, the degenerative diseases that are a simple function of growing old. We can cure most contagious diseases — hopefully even Ebola — but the consequence of ageing is a tougher nut to crack.

But science has a habit of catching up with science fiction and the breakthrough came from scientists John Gurdon and Shinya Yamanaka. For years it has been known that there are two types of cell on the body — standard cells and stem-cells.

The standard (or, as they are technically known, totipotent) organ and tissue cells were formed from embryonic (pluripotent) stem-cells during our development in the womb. These stem-cells themselves come in two flavours: those that do the initial construction in the womb and then shut down, and those that continue working throughout our lives, replenishing cells in all our organs that experience cell death (for example, the nervous system, the liver and the intestine).

For most of the 20th century it was considered certain that this differentiation process from stem-cells to body cells was a one-way street. But Gurdon and Yamanaka showed that ordinary body cells (totipotent cells) could be reprogrammed to become pluripotent stem-cells. This immediately raised the possibility that in the future aged — or cancer-ravaged — cells could be replaced with new cells.

It is impossible to understate the importance of this breakthrough in stem-cell technology. Professor Tony Hyman, Director of the Max Plank Institute for Cell Biology in Dresden said: "There is no question that the work of Yamanaka's, which was inspired by the pioneering work of Gurdon, represents one of the breakthroughs that comes at most once in a lifetime."

Gurdon and Yamanaka won the Nobel Prize for Biology in 2012

Oxford has been at the forefront of taking this research further. Dr Zameel Cader is director of StemBANCC, based at Oxford's John Radcliffe Hospital where his research focuses on neurological degenerative disorders, as well as a common but debilitating ailment that blights many lives — migraines.

Dr Cader explained to me how the process works. "The nervous system is not something that you can easily work on directly. You cannot just open up somebody's brain and start performing experiments. So how we use this new stem-cell technology is to take an ordinary cell that is easy to get at — a blood cell or a skin cell — and make it into a stem cell. From this we can generate the cell of interest — in our case a nerve.

"We can then perform tests on nerve cells from patients to see how it differ from a healthy cell.

"In someone who has a disease such as Alzheimer's we may find that the cell is malfunctioning, for example incorrect toxic proteins are being formed. In the case of disorders such epilepsy or migraine we have found that the channels in the cell membrane that are responsible for the movement of sodium and potassium in and out of the cell are not working correctly," Dr Cader said.

"We think this makes the nerves more excitable than they should be and may give rise to the disease that we see. To find better treatments for these type of conditions, we work with big pharmaceutical companies who have very large chemical libraries to run thousands of tests to find out which — if any — molecule improves the cell's function. This then is taken forward by the drug companies and developed into a new treatment."

Dr Cader said that a similar approach — producing stem-cells from patients, and then turning them into a cell of interest to test for abnormalities and develop treatments — is being used for a whole range of applications, including finding new cancer treatments.

So successful is this approach that Oxford is the centre for Stembancc, a consortium of ten giant drug companies including Roche, Pfizer and Astra-Zeneca, all of whom are using stem-cell technology for targeted drug design. "It is a very exciting time for medicine," Dr Cader said.

Dr Nicholas Irving, a Research Portfolio Manager at Oxford University added: "Induced pluripotent stem cells have the potential to significantly improve drug discovery for some of the most debilitating diseases, including diseases of the central nervous system. These have proved a particular challenge for the pharmaceutical industry in recent years and, with increasingly ageing population, this is likely to have a significant impact on society and the economy"

So if, within the next few years, you find yourself benefiting from the magic of stem-cell technology, spare a thought for *Blade Runner*'s Roy Batty whose eulogy is one of the most poignant in movie history.

"I have seen things you people would not believe, attack ships on fire off the shoulder of Orion, C-Beams glittering in the dark near the Tannhauser Gate — all these moments will be lost . . . like tears in rain."

Web: www.clneuro.ox.ac.uk/research/stembancc