A journey along the double helix

While stem cell technology is a real and potential key to cures for inherited disorders, the watchword is caution, believes **Professor Jacquie Greenberg** – who is furthering the field in South Africa with care and consideration of the complex social issues surrounding her research.

> Stem cell prospects are the fuel of false promises. Many people want to hear they can be helped, but we must balance hype and hope.

"Stem cell prospects are the fuel of false promises. Many people want to hear they can be helped, but we must balance hype and hope," cautions Professor Jacquie Greenberg, co-head of the UCT Stem Cell Initiative.

Greenberg maintains that although much of the current thinking around genetic therapeutic intervention has been saddled with the baggage around the science and the ethics of culturing embryonic stem cells, new stem cell technology – induced pluripotent stem cells (iPSCs) – has changed that.

Careful progress

In 2012, Japanese scientist Shinya Yamanaka won the Nobel Prize for pioneering technology to turn cultured skin and other cells into iPSCs. Scientists can now take primitive and adult human cells and develop these into any type of cell in the body, even sperm. They are an ideal source of cells for the 'disease-in-a-dish' study of conditions affecting inaccessible tissues such as those found in the eyes and brain, which are the organs that are affected by the genetic condition that she researches.

Collaborating with researchers in Oxford and Japan, scientists from the UCT Stem Cell Initiative have established the first iPSCs from South African patients suffering from an inherited

neurodegenerative disease, spinocerebellar ataxia type 7 (SCA7). They are also in the process of deriving cells from patients with the neuromuscular disorder myasthenia gravis, chronic autoimmune neuromuscular disease characterised by skeletal muscle weakness.

But geneticists working with stem cells are not just "tinkering with cells", says Greenberg. Although iPSCs skip some of the ethical debate associated with embryonic stem cell research, the technology is still very new.

"What we do must be scientifically safe and ethically sound."

The burden of knowing

Greenberg wrapped up her PhD in 1990 in UCT's Division of Human Genetics, now part of the Department of Clinical Laboratory Sciences. The work stimulated an enduring interest in late-onset neurodegenerative diseases, such as inherited ataxias and Huntington's disease, a genetic disorder that affects muscle co-ordination and leads to cognitive decline and psychiatric problems.

Importantly, this research alerted her to the complex ethical considerations of genetic counselling – and the dilemmas of predictive testing. Typically, the onset of these diseases occurs between the ages of 30 and 50, and there's a 50% chance of a mother or father passing the disease on to their sons or daughters.

"It's a Sword of Damocles," says Greenberg. "Would one, as a child, *want* to know? Would one *need* to know? Should anyone be tested for a condition that is fatal, and devastating to both the patient and the patient's family?"

It's a complex area – both in terms of research and ethics – in which she's made a significant contribution. In 1996 Greenberg became one of the first genetic counsellors to register with the Health Professions Council of South Africa, and she served on the UCT Research Ethics Committees for both humans and animals for several years. She is also course convenor of one of only two master's programmes in genetic counselling in South Africa – a vital service in a country with numbers well below the World Health Organisation's recommended two genetic counsellors per million people.

The future is not yet now

Since 1990 Greenberg has worked closely with long-standing colleague Professor Raj Ramesar, head of the Division of Human Genetics, on a screening programme for retinal degenerative disorders. Currently, the registry has clinical and genetic data on a wide range of patients affected by inherited retinal degenerative disorders.

To date, this research – which is supported by Retina SA, and funders such as the Medical Research Council and the National Research Foundation in South Africa – has led to several advances in the identification of the genetic causes of the disease, specifically discovering retinal disease genes RP17 (CAIV) and RP13 (PRPF8). These genes were originally mapped uniquely to South African families in the 1990s.

As a result, the affected families are receiving better genetic management and will be able to track developments and, potentially, even participate in research towards future therapies for their disorders. An offshoot of this work is the ophthalmic genetic service now offered by four genetic counsellors trained at UCT.

As for their future work, the UCT Stem Cell Initiative is generating stem cell lines for other conditions. These will be used for future investigation into disease modelling, and possibly the development of therapeutic modalities.

"We do research not for the sake of science, but for the sake of patients – and to do what we do better. As excited as we are about stem cells, we need to restore balance. There are many people who hope it's a cure for the future; and yes, it is, but the future is not yet now."

We do research not for the sake of science, but for the sake of patients – and to do what we do better. As excited as we are about stem cells, we need to restore balance. There are many people who hope it's a cure for the future; and yes, it is, but the future is not yet now."

Professor Jacquie Greenberg gave her inaugural lecture, *A Journey Along the Double Helix: Around the human genome in 42 years,* on 17 April 2013.

Professor Jacquie Greenberg has been involved with molecular genetic diagnostic testing at UCT and Groote Schuur Hospital for over 40 years. Not only was she one of the first genetic counsellors to register with the Health Professional Council of South Africa, but she was also the first woman to be elected as chair of the Southern African Society of Human Genetics. Based in the Human Genetics Division in the Department of Clinical Laboratory Sciences at the Faculty of Health Sciences, Greenberg is also an affiliate member of the Institute of Infectious Disease and Molecular Medicine, and a National Research Foundation C1-rated scientist. She served on the committee of the National Department of Health team tasked with drafting regulations and guidelines for the new National Health Bill's section on human cloning and stem cell research.