Immortal lines

The delicate frameworks for stem cell research sit uneasily between science, politics, ethics and religion. It's a brave new world carefully navigated by University of Sydney researchers, writes **Dr Kate Rossmanith**.

On a wall inside the University of Sydney's Centenary Institute of Cancer Medicine and Cell Biology hang neat snapshots of cheerful faces.

From a distance, molecular cardiologists, gene therapists and immunologists are indistinguishable, and the photos stuck together, running in rows, make it impossible to tell where one picture stops and another begins.

Conceived in 1982, the institute commemorates the centenaries of the University of Sydney Medical School and the Royal Prince Alfred Hospital. It is one of the few places at the University where scientists conduct human stem cell research, isolating stem cells from donors' bone marrow and umbilical cord blood, creating copies of the cells and analysing their potential use.

In February this year, the University of Sydney Senate approved a deal to pay St John's College $600,000 for land on which to build a medical research centre. In return for the rights to the land, the University agreed to the condition that the buildings should not be used for "human foetal stem cell medical research or any other procedures involving the termination or the artificial creation of human life".

Responding to criticism from some politicians and researchers about the University's decision, Vice-Chancellor Professor Gavin Brown explained that there were other facilities on campus where embryonic stem cell research could take place. "The conditions were purely a question of where certain things would be done, not whether they could be done," he said.

The University's agreement with St John's came three months after members of the federal Senate overturned the 2002 ban on human therapeutic cloning. While it continues to be illegal to grow an individual from a cloned cell, researchers in Australia will soon be able to harvest embryonic stem cell lines from the DNA of a living person: cell lines, argue scientists, which may lead to therapies for type 1 diabetes, cystic fibrosis and other diseases. The human stem cell research currently being carried out at the University, however, involves adult cells – cells derived from developed tissue – rather than those from embryos.

"We work with different types of stem cells found in bone marrow, specifically, the haematopoietic stem cells which form blood, and mesenchymal stem cells which form bone, cartilage, muscle and fat," explains Chuck Bailey, a research fellow in the Gene and Stem Cell Therapy Program at the Centenary Institute.

In the Centenary Institute laboratory, young researchers in white, ghostly gowns sit at metallic stations with microscopes, gloves and Petri dishes. They are studying effective ways to transfer haematopoietic stem cells into a recipient.

"It's one thing to introduce cells into a patient; it's another thing for the cells to multiply and survive," explains Dr Bailey. The survival of foreign stem cells in a patient depends in part on modifying those cells to enable them to grow and function properly. Part of the scientists' work at Centenary involves gene therapy, or stem cell modification. Researchers exploit the properties of viruses – their capacity to manipulate cells – in order to modify the stem cell.

Gene therapy breakthrough

Professor John Rasko, who heads the Gene and Stem Cell Therapy Program at Centenary, has recently reported a breakthrough in a gene therapy clinical trial performed with collaborators in the United States involving haemophiliac patients. By modifying the liver cells in haemophiliac patients, they observed a temporary improvement in clotting.

"We have tackled stem cells from two angles: by looking to improve gene delivery technologies, and by making steady progress in dissecting the subtleties of various stem cell types in the body," explained Professor Rasko. "Our lab is committed to the idea that gene and stem cell therapies will go hand in hand towards solving some of the big diseases of our time – including cancer, heart disease and diabetes."

Gene therapy and adult stem cell research is also being carried

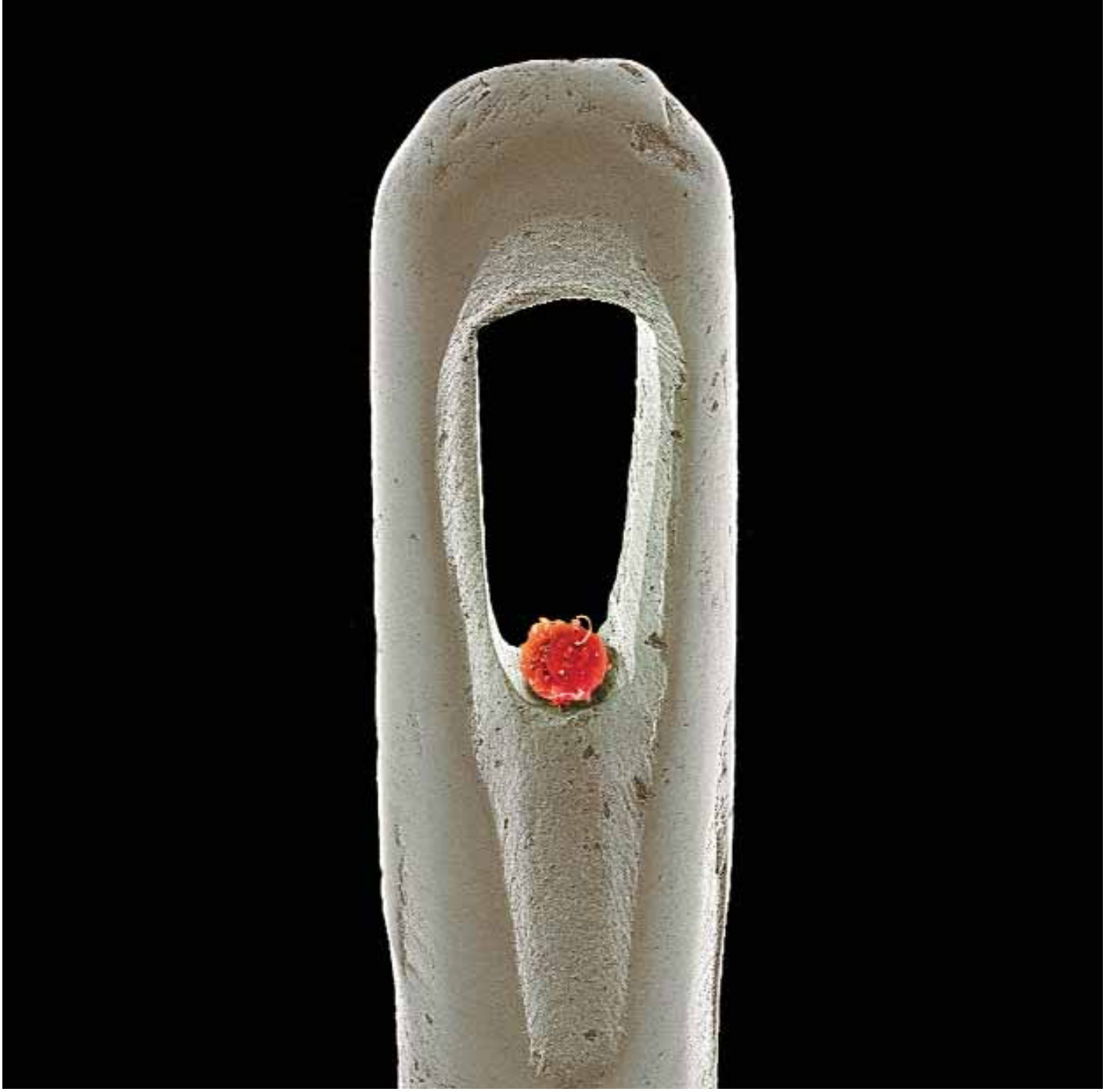

illustration: Photolibrary

In the eye of a needle … one tiny stem cell encapsulates an infinite world of possibility.

out at The Children's Hospital at the University of Sydney's Westmead Clinical School. Professor Peter Gunning, head of the Oncology Research Unit and chair of the Division of Research, is leading a cellular oncology group focussing on children with brain tumours.

"Chemotherapy is an effective approach for treating the actual tumour, but it simultaneously destroys the patient's bone marrow, often with fatal consequences," he says.

Professor Gunning and his team are looking to introduce into the patient modified stem cells that will detoxify the chemotherapy in the patient's blood. And, like the research conducted at the Centenary Institute, one of the issues involves ensuring the patient's body takes up the new cells. "The cells we introduce are designed to be selectively advantaged by the patient. Gene therapy gives us an opportunity to advantage the incoming stem cells," he explains.

These University of Sydney researchers work with human adult stem cells. Only four organisations in Australia currently have licences to conduct embryonic stem cell research. Sydney IVF is one of them. There, researchers extract cells from days-old embryos that would otherwise be discarded and create stem cell lines. "Immortal lines", the scientists call them, for they divide and duplicate themselves indefinitely.

When magnified, embryonic stem cell colonies, minute flecks carrying a couple's DNA, look like fine paint sprays. The groups of cell droplets, no bigger than five thousandths of a millimetre, are bounded patches of life. And they're "pluripotent".

"Unlike adult stem cells, they have the potential to transform into a wide range of other cells," explains Teija Peura, the principal scientist at Sydney IVF's stem cell lab.

Unsurprisingly, the delicate frameworks for stem cell research, in Australia and elsewhere, sit uneasily between science, politics, ethics and religion. "The most viable source of stem cell lines is human embryos. Hence, stem cell technology brings with it controversies around the embryo, the foetus, the right to life and so forth," explains Professor Catherine Waldby, an

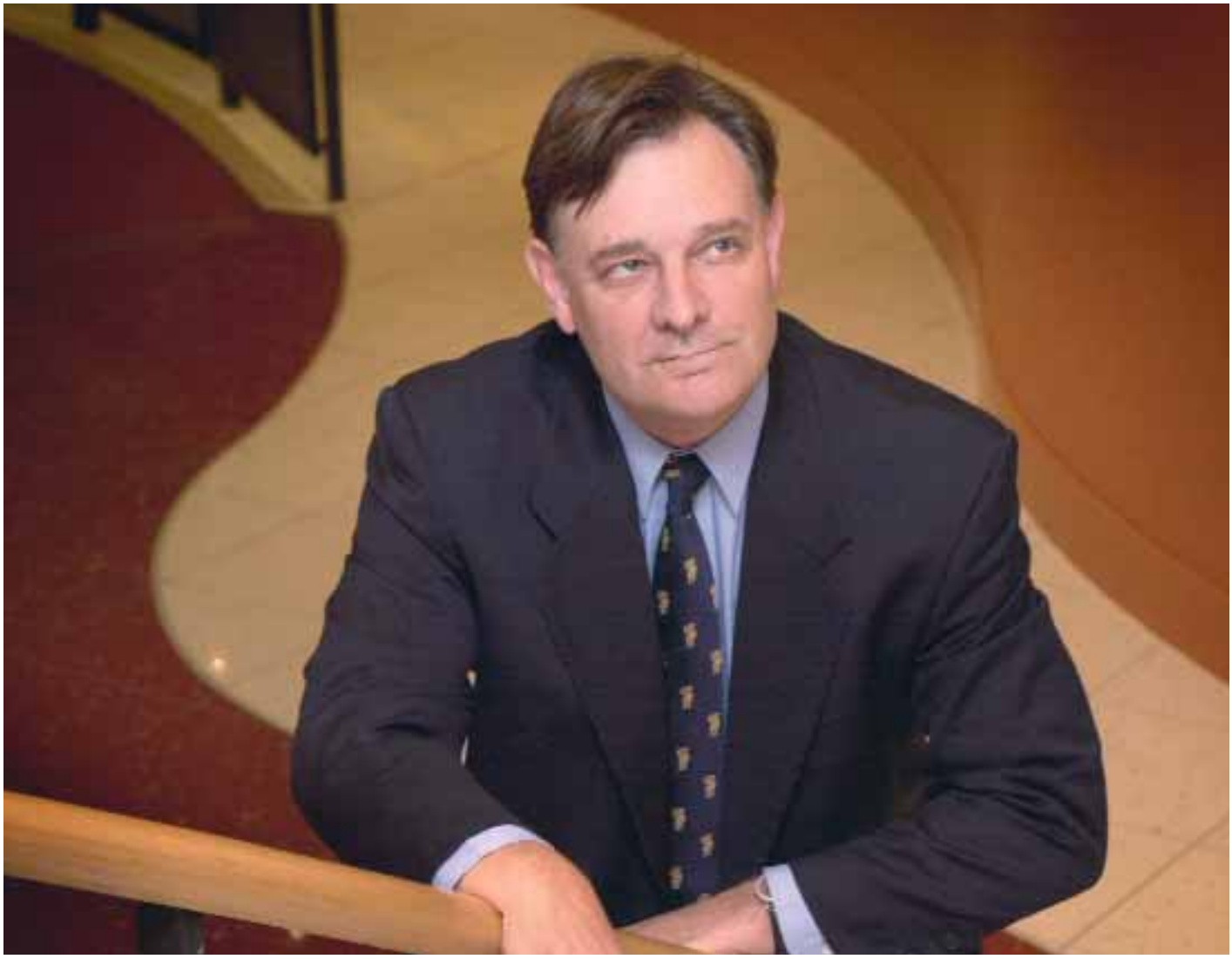

photo: newspix

Professor Peter Gunning from the University of Sydney's Westmead Clinical School … investigating ways to use modified stem cells to detoxify chemotherapy when used on cancer patients.

international research fellow from the University of Sydney's Department of Sociology and Social Policy.

Therapeutic cloning

A five-day-old ball of cells may or may not be a person, but it is human life, with its innate intent to be and grow. It's not extinguished when the stem cells are extracted; it becomes more alive than ever, producing sprawling copies of our cells.

"For opponents of therapeutic cloning, the life of the embryo is biographical, the beginning point of a human narrative that should be allowed to run its social course. For advocates, the life of the embryo is a form of raw biological vitality," says Professor Waldby. Part of the discomfort we might have towards therapeutic cloning is not that something dies, but that something lives, and can be repeated infinitely.

That colonies of our flesh – identical copies of our DNA – might multiply beyond the boundaries of our bodies questions a fundamental principle governing Western self-consciousness: our uniqueness.

Enchantment with our own uniqueness remains central to the Western imagination of the self. Therapeutic cloning not only shakes that idea; it also confronts our notion of ourselves as circumscribed individuals both spatially and temporally.

In cell therapy, an individual's cells might be used some day to heal someone else's lungs, our separateness collapsing irrevocably. While this transgression already happens with organ transplants and blood transfusions, cell therapies stretch the reality further still.

"Stem cell technologies involve a reorganisation of the boundaries and elements of the human body. Bodies become materially implicated in each other," says Professor Waldby. Through an indefinite fusing of bodies, what disappears are the safe, certain lines where one body stops and another begins.

At the same time, cell therapy involves complex temporal configurations, disrupting our idea of ourselves as ageing uniformly and chronologically. "Stem cell lines reconfigure biological time as scientists arrest the development of human tissue – by freezing cells – before immobilising and deploying it at a later stage," explains Professor Waldby. "The dream of stem cell technologies is the dream of a regenerative body," she says.

The contemporary sense of ourselves as separate beings, following a uniform time trajectory, is not universal. Throughout the Middle Ages, the carnivals which dominated European popular culture suspended the distance between bodies: revellers drank, ate, sweated, spat, copulated, and defecated together, merging individuals into a corporeal mass in

suspended time. And in many cultures today, there exists a latent connective tissue between people and their world. For the Warlpiri people in the Northern Territory, person, country and time coalesce, fusing the body and the environment in an internal physiology. "Thus, a sacred site is a womb, the odour of a person's sweat may evoke the aromatic sap of a particular species of tree, and a deposit of white clay may be said to be the semen of a Dreaming ancestor," the anthropologist Michael Jackson has observed.

On her computer screen at Sydney IVF, Dr Peura brings up a photo of a five-day-old human embryo. It takes this viewer a beat to recognise what's being shown, and then it becomes clear: it's a perfect earth. It looks like the images of earth that NASA send from space. "Embryos for almost every organism look exactly the same at that stage of development," Dr Peura says.

Grown from tiny earths, we are already more a part of one another, part of our world's flesh, than we can imagine.

Kate Rossmanith is a lecturer in Performance Studies at the University of Sydney. She also works as a writer, with her essays appearing in *The Monthly* and *The Australian*, and she writes regularly for Sydney University's *UniNews*. An earlier version of this article appeared in *The Monthly*, February 2007.

Understanding the science of stem cells

Stem cells are the foundation cells for every organ, tissue and cell in the body. As undifferentiated, or 'blank' cells, they do not yet have a specific function, and therefore have the ability to act as a repair system for the body because they can divide and differentiate, replenishing other cells.

Stem cells are derived from embryonic and adult tissues, although those from embryos are considered more malleable as they can generate every cell type of the body.

"Stem cells can be found in blood from the umbilical cord, and from some adult tissues such as bone marrow, but these do not appear to be as flexible or active as tissue derived from embryos," explains Associate Professor Catherine Waldby, an international research fellow from the University of Sydney's Department of Sociology and Social Policy.

Widespread controversy exists over stem cell technologies, especially embryonic stem cell research. Starting an embryonic stem cell line – where stem cells divide and duplicate – requires the destruction of a human embryo and/or therapeutic cloning.

In Australia, researchers develop embryonic stem cell lines using spare IVF embryos donated by couples. Each embryo from which stem cells are derived is less than a week old; it's a hollow ball of 100 cells, a speck smaller than a grain of sand. Scientists extract stem cells from the centre of the ball, the inner mass cell, and allow them to grow in culture dishes incubated at body temperature.

Now that the 2002 federal ban on human therapeutic cloning has been lifted, researchers will be able to produce 'embryos' with the sole purpose of creating stem cell lines. In therapeutic cloning, scientists take the nucleus of a human cell – for example, the DNA of a donor's skin cell – and inject it into a woman's unfertilised egg whose nucleus has been removed. The egg is stimulated in such a way that it begins to divide. If it were then implanted in a woman and left to grow, it could, theoretically, produce an individual with the donor's genetic coding, a person who looks almost identical to that donor. Dolly the sheep was born this way.

Human reproductive cloning, however, continues to be illegal across the world. Instead, the egg cell grows for five days before the inner cell mass is removed and used to create a stem cell line with the donor's genetic make-up.

photo: Ted Sealy

Associate Professor Catherine Waldby ... concerns over global oocyte trade.

Therapeutic cloning, however, requires large numbers of oocytes, or egg cells, and some researchers are concerned that exploitative procurement networks could be used to obtain them.

"There is a growth in a global market for oocytes, where transnational IVF clinics broker sales between generally poor, female vendors and wealthy purchasers, beyond the borders of national regulation. These networks have already been used to procure oocytes for stem cell research," explains Professor Waldby. She is also concerned about the medical procedures involved in retrieving oocytes, as there are risks, even for women in first world hospital systems.

"For poorer women involved in the global oocyte trade, an approach to oocyte supply that combines issues of safety, consent and clinical conditions with those of workers' rights, organised representation for vendors and regulated negotiation of conditions, may yield benefits in terms of harm minimisation and transparency," she says.

– Kate Rossmanith

Professor Lord Robert Winston Lecture
Thursday 12 July at 1pm
In the Great Hall, University of Sydney.
Lord Robert Winston, best known for the *Human Body* TV series, will deliver a public lecture on stem cell research. All alumni are invited to attend this free lecture, followed by refreshments. To rsvp, phone + 61 2 9036 9278, email rsvp@usyd.edu.au or visit www.usyd.edu.au/alumni