

The novel techniques of stem cell research

Professor Alejandro Madrigal has been an integral component of the Anthony Nolan Research Institute's success throughout his twenty years as Scientific Director. He spoke with *Research Features* about his time in the role and the direction he sees stem cell research going in the future.

Anthony Nolan really do put the stem in stem cell research. Since becoming established as the Anthony Nolan Register back in 1974, the charity has pioneered vital research into stem cells in the hope of curing leukaemia and developing haematopoietic (blood-derived) stem cell transplantation techniques.

Not only that, but Anthony Nolan have played a massive role in getting stem cell disorders recognised and gathering public support for their UK stem cell register. As of today, they currently have over 620,000 stem cell donors on their UK register – but there is always a need for more.

With this in mind, Professor J Alejandro Madrigal – Scientific Director of the Anthony Nolan Research Institute – recently sat

down with *Research Features* to discuss the charity's newly-released research strategy, while highlighting the areas of stem cell research in need of further consideration.

Hello Alejandro! How would you describe your role as Scientific Director of Anthony Nolan?

I've been the Scientific Director of Anthony Nolan since 1996, and my main mission has been to lead research to improve donor provision and outcomes of haematopoietic stem cell transplantation through innovative research. ▶

Anthony Nolan was born in 1971 with Wiskott-Aldrich syndrome. Thanks to his legacy, the number of registered stem cell donors has grown to 28 million people around the world ”

Could you tell us who Anthony Nolan was and why the foundation was set up in his name?

Anthony Nolan was a young boy born in 1971 with Wiskott-Aldrich syndrome – a rare blood disorder. He needed a bone marrow transplant but at that time there was no register of unrelated donors. His mother Shirley set up the world's first register to match people in need of a transplant with people willing to donate their bone marrow. Sadly, no donor was found in time to save Anthony, but thanks to his legacy the Anthony Nolan register has grown to over 620,000 people in the UK, with 28 million people on registers around the world.

What impact has Anthony Nolan had on stem cell research since it was first established? What accomplishments are you particularly proud of?

We've seen dramatic improvements in donor provision, HLA matching and immune cell therapy. We, at the Anthony Nolan Research Institute, are extremely proud to have been very involved with each of these areas and to have contributed by performing research and collaborating with world leaders in the field.

Back in the early 2000s, Anthony Nolan pioneered new techniques for analysing compatibility genes (HLA genes). Could you tell us more about this and the effect this has had on stem cell research?

HLA typing has been one of the most challenging aspects in donor provision, since these genes are extremely variable (polymorphic) and have thousands of variations on the same gene. Since they were discovered, we've been hitting a moving target and have had to invent several techniques. Around the year 2000, we invented an innovative technique, published in *Nature Genetics*, called RSCA; it allowed for high resolution matching for HLA types to identify more accurate matches than conventional methods.

This year we became the first register in the world to introduce Third Generation

Sequencing, which we believe is the optimum and most efficient approach to typing all these genes, with no uncertainties. By doing this we can provide patients with the best possible donor.

Stem cells are often an area of ethical dispute. How does Anthony Nolan recognise this in its research? And how have the ethics surrounding stem cells changed since the institution was first founded?

We work with blood stem cells from living adults or with umbilical cord blood. We do not conduct research into embryonic stem cells. Anthony Nolan places the welfare of donors and patients at the heart of our work. All of our research is ethically approved and Anthony Nolan abides by the Human Tissue Act 2004, the Human Tissue Regulations 2007 and associated Codes of Practice. We do not use animals in experiments at the Anthony Nolan Research Institute and, in terms of our umbilical cord blood programme, we comply with all the requirements of the Human Tissue Authority. A major feature of the Human Tissue Act is that it makes consent the fundamental principle for the lawful removal, storage and use of human tissue. As medical science progresses, new ethical questions will arise and we will approach these in the same way – by complying with best practice and putting the wellbeing of donors and patients first.

Anthony Nolan has recently released its research strategy and aims for future work. Are there any areas of stem cell research that you are particularly focused on studying?

At the Anthony Nolan Research Institute, we perform translational research. We are focusing on developing innovative techniques for donor provision but we also have a strong component on immune cell therapy. This aims to select specific immune cells that can target tumour cells or modulate immune responses to decrease complications, such as graft versus host disease or infections.



Why is researching into what happens following a stem cell transplant so important?

We need to understand how immune systems and engraftments recover post-transplant. Unfortunately, approximately 50% of transplant recipients die due to relapse or because of post-transplant complications. Studying the reasons behind this will help us to prevent them and improve the survival rates and quality of life for many patients.

How do you see the landscape of stem cell research changing over the next ten years?

Genomics and immune cell therapy are very promising tools that are already changing the way we treat patients. Pharmacogenomics and personalised medicine will no doubt help us extend

the benefit of haematopoietic stem cell transplants to many other conditions, such as autoimmunity.

Anthony Nolan has seen a massive rise in the number of stem cell donors over recent years. Is there still an urgency for people to donate their stem cells and, if so, how should they go about it?

There is always a need for people to register as donors as we are only able to find the best match for 60% of patients. However, rather than just adding more people, we are focusing on finding the right people – and that means diversifying the register.

There is a shortage of black, Asian and ethnic minority donors, which means it is a struggle to find a match for patients from these backgrounds. They have just

a one in five chance of finding the best donor match. We are also urging more young men to join the register; they are the preferred donors, yet make up just 15% of the register. Joining the register is very easy – if you're aged 16–30 and in good health, simply visit our website and request a free spit kit. We'll then send you a kit in the post to collect a saliva sample. We'll add you to the register and notify you if you are ever a match for someone in need of a transplant. Ninety per cent of donations take place via peripheral blood stem cell collection, which is similar to platelet donation.

• *If you would like to find out any more information about stem cell research, or how to become a registered stem cell donor, visit www.anthonynolan.org.*

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