LIFESAVING SCIENCE: ANTHONY NOLAN’S RESEARCH STRATEGY
INTRODUCTION

Our story began in 1974. With her three-year-old son Anthony in urgent need of a stem cell transplant, Shirley Nolan set up the world’s first register; to match donors with people desperately in need of a chance of life.

Now, over 40 years later, the transplant landscape has changed – and we know we need to do much more. Patients are still dying from post-transplant complications, and we need to do more to address this.

In 2015 Anthony Nolan launched a new strategy, which reaffirms our lifesaving vision and sets out what we will do to further improve patient outcomes. Recognising that this vision will only be realised by keeping our groundbreaking medical research at the heart of everything we do, the Anthony Nolan Research Institute (ANRI) has developed a comprehensive research strategy. This sets out the research priorities that will contribute to the achievement of our ambitious longer-term goals.

By 2025, our research aims to:

- Improve overall survival for adults receiving a stem cell transplant for leukaemia from 44% to over half (55%)
- Increase survival for adults who receive a transplant for other blood disorders from 50% to 60%
- Halve the number of people with post-transplant complications such as graft versus host disease (GvHD)

Our research strategy has been informed by UK and international scientific and medical experts, who have used their insight to inform where we can make the biggest difference in three key areas:

- Before transplant – we will recruit and retain more donors, facilitate better matches and increase our understanding of what makes a genetic match
- After transplant – we will reduce the number of patients who experience debilitating post-transplant side effects such as GvHD
- In the research community – we will create a solid foundation for research and clinical trials throughout the UK and internationally by investing in world-class infrastructure

It’s a hugely exciting time in terms of scientific breakthroughs, advances in genetic technology and groundbreaking new treatments such as immunotherapy. That’s why it is vital for us to invest significantly in our research programme and focus on our work at the ANRI in areas that will make the biggest impact for patients.

By collaborating with other experts and partner institutions, both in the UK and internationally, we will share insight and bring the latest advances in science to patients through initiatives such as clinical trials.

Forty years since Shirley Nolan established the charity, patients remain at the heart of our work. And as we look forward, we know that funding the very best research will help us improve patient survival rates and their quality of life.

Henny Braund
Chief Executive
WHO ARE WE DOING THIS FOR?

Freddie

Freddie Branthwaite was diagnosed with severe aplastic anaemia in 2015 when he was just 15 months old. Doctors told his parents Laura and Jason that he’d need a stem cell transplant to survive; his older brother Harry was tested but sadly wasn’t a match.

When Freddie was diagnosed with severe aplastic anaemia it was a complete shock; he’d been born prematurely and had spent his first few weeks in hospital, but since then had been growing as normal. When we noticed he wasn’t well, we didn’t have a clue it would be anything as serious as this. It all happened very fast. The doctors explained that Freddie would need a stem cell transplant and that it was unlikely his older brother Harry would be a match. When this was confirmed I was worried that Harry would be upset as he was so desperate to step up and help his brother. We just had to hope that someone on the Anthony Nolan register would be the lifesaving match our little boy needed.

Thankfully Anthony Nolan was able to find him a donor. Freddie is so young; he hasn’t even started his life yet, so to know a stranger has given him a future is such an incredible thing. Harry is so happy to have his little brother back, he just wants to say a massive thank you to the selfless person who saved his brother and gave our family our lives back. We really hope that one day we meet him or her so we can give them the massive hug they deserve.

Lisa and Eugene

Lisa Wilson was diagnosed with acute myeloid leukaemia in 2004. Tragically she wasn’t well enough to receive a stem cell transplant and she passed away in 2005 aged just 22. Her dad Eugene has since run ten marathons for Anthony Nolan in honour of his daughter.

Lisa’s diagnosis of acute myeloid leukaemia in 2004 shocked us all. We live on the Isle of Man so we had to fly over to Liverpool for her treatment. The first round of chemotherapy was successful so doctors said it wasn’t necessary for her to have a transplant. We also found out that her sister Hayley was a 10/10 match. We knew this was relatively rare and we were lucky to have this option if she needed a stem cell transplant in the future.

However by February 2005 Lisa had relapsed and a stem cell transplant was now her only hope of survival. Unfortunately it was no longer possible for Hayley to be her donor as an imperfect match was needed to provoke a reaction from her immune system. As a result I was chosen to be her donor. I remember saying to her ‘I’m on this train with you and I’m not getting off. I’m here until the end.’

Around this time Lisa’s boyfriend proposed, and we arranged the wedding in two weeks - they wanted to have it before the transplant. After the wedding Lisa went into isolation in preparation for her transplant. But she caught an infection and her condition worsened rapidly. She was no longer well enough for a transplant and on 1 August 2005 she passed away.

In October of that year I decided I wanted to give something back, so I signed up to run the marathon for Anthony Nolan in my daughter’s honour. I’ve since run ten marathons for the charity and every time I feel like I’m about to give up I think of Lisa and everything she went through. It’s so important for me to keep raising money and awareness, for Lisa and for everyone else affected by blood cancer.
Over the years our research has had a major impact on survival for people undergoing stem cell transplants worldwide.

We’ve pioneered new techniques for analysing the ‘compatibility genes’ (HLA genes) that determine whether a donor and patient will be a good match, and shared this information with transplant centres around the world. Now we’re studying how variations in other genes can affect how successful a transplant will be.

We’ve also carried out important studies into GvHD – a major complication that happens when transplanted immune cells attack the healthy cells in a patient’s body.

We’ve played a part in major studies developing and trialling lifesaving new approaches and guidelines for stem cell transplants. We’re looking forward to delivering on our ambitions and continuing to focus on the best possible outcomes for patients.

1971 Anthony Nolan is born with a rare blood condition, Wiskott-Aldrich syndrome.

1973 Anthony’s mother Shirley reads about a British boy with a similar condition, whose life was saved by the first ever bone marrow transplant from an unrelated donor.

1974 Shirley starts a register of potential stem cell donors in the hope of finding a match.

1977 Sadly, a donor for Anthony cannot be found and he dies aged just eight.

1978 Our first official laboratory opens in St Mary Abbots Hospital, west London.

1981 A database of variations in HLA compatibility genes that was begun by Professor Steven Marsh at the Imperial Cancer Research Fund (ICRF), is transferred to the ANRI.

1986 We’re part of a study showing that unrelated donors can provide transplants for blood conditions and leukaemia if there is no suitable related donor.

1988 We help to develop a technique to predict the chances of a transplant from an unrelated donor developing GvHD.

1990 Our new laboratory opens, housing 20 staff.

1996 The ANRI opens at the Royal Free Hospital under the direction of Professor Alejandro Madrigal.

1998 We develop an important new method for analysing variations in genes between people.

2000 We collaborate with a group in Spain to show that cord blood could be used with haploidentical progenitor cells to improve the outcome of cord blood transplantation.

2001 We discover the types of immune cells which are responsible for fighting chronic myeloid leukaemia in some patients who have received a stem cell transplant.

2002 We develop an important new method for analysing variations in genes between people.

2003 We develop a technique to read the entire DNA sequence of the HLA-B and HLA-C compatibility genes.

2008 We set up Anthony Nolan’s dedicated umbilical cord blood bank and develop a method for purifying special immune cells, called regulatory T cells, from cord blood.

2012 We study how immune cells respond to infection with cytomegalovirus – a major threat to stem cell transplant recipients. We celebrate one million stem cell transplants worldwide, many thousands of which have been possible thanks to our register and research.

2015 We bring Third Generation Sequencing to our SMARTLAB® at the ANRI, providing more detailed genetic information about donors and patients than ever before.

2016 We study the impact of variations in non-HLA compatibility genes on transplant success, providing important information for future matching. Our register now has more than 600,000 potential donors, and grows every year.

2017 Through a large study we discover that even ‘perfect matches’ have differences in certain immune cells, showing that there’s more to a match than the handful of genes that are usually considered.

2018 We confirm that younger, male donors are more likely to provide successful stem cell transplants than older and female donors, changing how we target people to join our register.

2019 We study how successful a transplant will be.

2020 We publish a major report updating and revising the classification of variations in the HLA compatibility genes.

2025 Our research aims: survival for people receiving transplants for leukaemia up by a quarter. Survival for people receiving transplants for other blood disorders up by a fifth. Levels of GvHD halved.

2030 We help to develop a new method for identifying variations in another gene, NOD2, involved in transplant success.
We're using the very latest technology to test DNA from thousands of patients and potential donors to work out exactly what makes the best possible match.

At four UK hospitals we collect stem cells donated from the umbilical cord and placenta after a baby is born. We're investigating how best to use these lifesaving donations and developing them into powerful new therapies.

Our register of potential stem cell donors is a lifesaving resource – the first database of its kind anywhere in the world. We're growing and developing it even further as well as making sure that donating stem cells is a positive, healthy and safe experience for all of our lifesavers.

Stem cell transplants can come from relatives, unrelated donors or umbilical cord blood. We want to work out the most efficient way of using these different sources, to provide the best options for patients.

Once a match has been found, stem cells are taken from the donor and transplanted into the patient. But that's not the end of the journey…

This isn't a simple task; the HLA compatibility genes that govern matching are the most complex and variable regions of the human genome. We want to understand them in ever greater detail, to find the best possible match for every patient.

Every year thousands of people need a stem cell transplant. Finding a match for every single one of them is at the heart of our work.

Only a third of people will find a match within their own family; the rest will need an unrelated donor. Every year we recruit thousands of new potential donors to join our register.

We're working together with colleagues in the UK and around the world, sharing vital information as well as DNA and other samples to help find better matches, faster.

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AFTER A TRANSPLANT

A stem cell transplant is only successful for about half the people who receive one, and we need to find out why. Our research will make transplants increasingly effective so that even more lives are saved in the future.

STEM CELL TRANSPLANT

During the transplant process, a patient’s own stem cells are destroyed and replaced with donor cells. These stem cells engraft in the bone marrow, making healthy new blood cells.

BETTER CANCER CONTROL

Stem cell transplants are often used to treat blood cancers such as leukaemia, but sometimes the cancer can come back. We’re figuring out why this happens, and working to boost the effectiveness of donor stem cells.

BETTER TREATMENTS

We want to improve stem cell transplant processes, enabling older patients to receive transplants, as well as reducing side effects.

CUTTING COMPLICATIONS

Sometimes patients can pick up a life-threatening infection after their transplant, or donor immune cells can attack healthy cells in the patient’s body, causing GvHD. We want to find out why these complications happen, find new ways to prevent them and predict who is most at risk.

POST-TRANSPLANT CARE

We want to find out what kind of support patients need, whether physical or emotional, to help them return to their normal life after a stem cell transplant.

IMMUNOTHERAPY

We’re developing powerful new treatments based on the immune system – including special cells found in umbilical cord blood – to help make stem cell transplants more effective at fighting cancer.

GATHERING & SHARING DATA

By collecting and sharing information about the outcomes of every transplant, we can identify the best approaches for treatment and pinpoint areas where we need to focus our research and resources.

MORE CLINICAL TRIALS

We are working with other organisations across the UK on clinical trials that will help us to increase the success of stem cell transplants and reduce complications.

MORE LIVES ARE SAVED

All our research has one goal: improving the chances of survival for everyone who needs a stem cell transplant.
The Anthony Nolan Research Institute

The work carried out at the ANRI is aimed at understanding what makes a match between a potential donor and a patient, and improving the chances of survival for everyone who receives a stem cell transplant. For example:

- We're exploring how mismatches in individual compatibility genes can influence the risk of GvHD.
- We're identifying the variations in HLA compatibility genes that affect the potential success of a transplant.
- We're studying the genetic variations across our database of potential donors, and making it the best resource possible for finding matches.
- We're working with partners to establish a national platform for running stem cell transplant clinical trials, speeding up the translation of new discoveries into lifesaving advances for patients.
- We're exploring new treatments based on the immune system that can help transplanted stem cells to grow successfully in a patient and avoid common post-transplant problems.
- We're working with doctors in transplant centres across the UK to improve the collection, analysis and reporting of data about the outcomes of stem cell transplants, and using that information to improve outcomes in the future.

Meet some of our world-class scientists:

Our Scientific Director, Professor Alejandro Madrigal, is an internationally renowned scientist in the field of stem cell transplantation and donor matching, and Professor of Haematology at the Royal Free Hospital. His groundbreaking research has helped to change the way that transplants are carried out, including developing better techniques for matching donors and patients and finding new targets for treatments to fight viral infections and blood cancers. As Anthony Nolan’s Scientific Director for more than 20 years, Professor Madrigal’s leadership has been instrumental in delivering research with far-reaching impact and his role in teaching and training students is ensuring the next generation of scientists benefit from his expertise.

Information about variation

Professor Steven Marsh is a leading expert in bioinformatics and immunogenetics – using computer programmes to analyse and compare genetic variations. He established and continues to run several unique, gold standard databases containing tens of thousands of variations in the compatibility genes that determine whether a donor and patient are a good match. Professor Marsh has also been instrumental in developing a consistent naming system to describe each variation, so that data gathered from people around the world can be accurately compared. We want to expand this vital resource, which is used by the global community of transplant centres and researchers, by adding increasingly detailed information about more genes from more people to help make better matches. And we’re also using the data to find out more about the genetic diversity across the UK, so we can recruit potential donors with more unusual gene variations and increase the chances of finding a match for everyone that needs a transplant.

Molecular match-making

Dr Neema Mayor is studying the genetic makeup of more than 2,500 pairs of stem cell donors and their recipients, gathered over 20 years from more than 40 UK transplant centres. A stem cell transplant is most likely to succeed if the donor and the patient are as genetically similar as possible, and we currently match people by assessing the degree of relatedness between the donor and patient. Sometimes we can find a donor that looks like a good match, yet the transplant still fails. But in other cases, a transplant will still work despite not being a ‘perfect’ match. It’s clear there must be other factors at play; by delving into detailed genetic makeup of these donor and patient pairs we hope to discover exactly what makes a match.

Harnessing the power of the immune system

Immune cells are a crucial component of a stem cell transplant. They can rebuild a patient’s damaged immune system and fight cancer cells or infections in their body. But they can also cause harm by attacking healthy cells and causing GvHD. Dr Aurore Saudemont is developing exciting new therapies based on immune cells and molecules found in umbilical cord blood. One type of treatment, using so-called ‘natural killer’ cells, is aimed at helping the transplanted stem cells to settle into the recipient’s body and destroy any remaining cancer cells. Another approach involves using special regulatory T cells to damp down the overactive immune response that causes GvHD. We want to push forward the development of these potentially lifesaving new therapies and take them into clinical trials so that patients can benefit as soon as possible.

Smart thinking, SMARTLAB®

Over the years our scientists have developed essential methods for analysing the genetic makeup of donors and patients, so they can find the best possible match for a stem cell transplant. Dr Katy Latham and her SMARTLAB® team have taken the next step in this journey by adopting Third Generation Sequencing (TGS) – a pioneering technique that can read long sections of genes without stopping. We will use this technology to gather more information than ever before about the variations in compatibility genes between people, leading to better matching and more successful transplants.

The work done at the ANRI is a collaborative effort between expert teams of scientists, all working together in pursuit of a shared and enduring goal; to save and improve the lives of all those who need a stem cell transplant.
Our donor register and pioneering research have already made a huge impact in improving survival from blood cancer and other disorders. But we still have a long way to go to meet our goals, and we can’t do it alone.

If we’re to save more lives, we need to build a strong research environment in the UK, bringing together partners and collaborators to push forward with research that will make a difference.

As part of our research strategy, we will create a nationwide platform for running clinical trials, providing vital information about how best to provide stem cell transplants as well as preventing and treating complications such as infection or GvHD.

We are working with partners across the transplant community to make sure detailed information about outcomes and survival for UK transplant recipients is gathered and analysed, so people are getting the very best treatment and care.

All of the work carried out at the ANRI is performed under strict ethical approvals.
28 MILLION
potential stem cell donors worldwide.

1,268
patients in 2015-16 were given the chance of life by Anthony Nolan through the provision of stem cells.

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100
donors are on our panel who can actively advise on the services we provide – including how we arrange medicals and involvement in research trials. This is in order to ensure we are listening to our donors and retaining them on the register.

600,000+
potential lifesavers on the Anthony Nolan register as of July 2016.

£2.2M
is the annual budget for ANRI in 2015/16. This figure includes £451k received from external grants and £1.75m provided by Anthony Nolan.

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patient/donor pairs have been accrued from the long-standing Patient/Donor Project. This will help us to understand the impact of genetic factors on the outcome and potential complications of stem cell transplants. With the help of TGS, we aim to develop robust methods for sequencing non-HLA genes in order to demonstrate their role in transplants.

06.01.16
the date Anthony Nolan launched Third Generation Sequencing (TGS) for HLA typing. The technology means that when we’re tissue typing donors, we can examine an entire gene in one go.

800
donors have been recruited to our Phenotype project in 2015-16, a pioneering initiative aimed at providing increasingly accurate data on a selected donor’s blood tissue type. By identifying the donors most likely to provide a match, the project enables transplant centres to more readily spot them.

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of people that go on to donate have been selected from the Phenotype project. They form a panel of ‘super donors’ and are 40 times more likely to be chosen as donors.

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Our Research in Numbers

The number of research staff at the ANRI during the last five years has increased from 28 (2010-2014) to 36 (2015-16).

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OUR LIFESAVING DONORS

Rajan

Rajan Goel joined the Anthony Nolan register in December 2013. He donated via peripheral blood stem cell (PBSC) collection in May 2015. Later that year he received a letter from his recipient, who is recovering well.

I was motivated to join the register after my brother-in-law was diagnosed with acute myeloid leukaemia. Around this time I also became aware of the lack of ethnic minority donors on the register, and as an Asian-Indian man I knew it was even more important that I joined. I think the reason people can be reluctant to join the register is down to myths about donating being painful, and I wanted to break down those barriers.

When I got the call to say I was a match, I was at work. As an accountant I don’t get the chance to save lives so I knew this was my chance to give something back. The great thing was that it inspired a few of my family and friends to sign up too, so hopefully more lives will be saved in the future.

The donation process itself was a lot easier than I thought it would be. I passed the time chatting with my family and I was back at work the next day feeling absolutely fine. It’s honestly the easiest process, and it’s great to know that what you’ve done could have a positive impact on someone else and their family. Just by signing up, you can hold your head up high and know you’ve done something good.

Alison and Ada Mae

Alison Hulme gave birth to her daughter Ada Mae in August 2015 at King’s College Hospital. She donated her cord blood in the hope it could save someone’s life.

I heard about the cord blood donation programme quite early on in my pregnancy. I decided to do it because I couldn’t see a reason not to. My attitude was that it was a part of me that I didn’t need (I definitely didn’t want to take it home and have it made into tablets!) but that it could mean so much for someone else. When it became apparent during my pregnancy that I was going to need a C-section it seemed to make even more sense, as the cord would be cut immediately.

The process was so easy. The Anthony Nolan team talked me through everything and I just had to sign a form.

I felt, and still do feel, brilliant about donating my cord blood. What an amazing thing, that a little newborn baby could already be helping to save another person’s life.

I absolutely loved the ‘Born Lifesaver’ Babygro that Anthony Nolan sent for Ada Mae to wear. I’ll definitely keep it and show it to her when she’s older so she knows what an amazing thing she’s done. I wouldn’t think twice about doing it again if I have another child.
Saving more lives and making more matches has been the bedrock of our work for more than four decades, and we are incredibly proud of what we’ve achieved so far. However, we cannot become complacent. There are still too many people dying from relapse or complications, and too many people living with debilitating post-transplant side effects.

Science holds the key to delivering our lifesaving work in the 21st century and our research strategy reaffirms our commitment to put research at the heart of all that we do. It is only by being at the forefront of scientific discovery that we can realise our vision; to save and improve the lives of all those who need a stem cell transplant.

We work closely with fellow researchers, academics and clinicians in the field of stem cell transplantation, as well as increasing our own expertise at the ANRI to understand how we can best help patients. And over the coming years we will strive to involve patients as we design, prioritise, execute and evaluate our research.

We will continue our long-term work to curate and develop the unique gold standard databases that are used internationally to facilitate HLA typing using DNA-based technologies, thus allowing better-matched transplants. We will also continue to expand the retrospective analysis of the impact of immunogenetic factors on the outcome of stem cell transplantation. This research will increase understanding of what level of HLA matching is necessary to achieve the best possible outcomes.

Over the next five years and beyond, we will further enhance our understanding of what makes the best possible patient/donor match, and explore how we can reduce incidences of post-transplant relapse, infection and GvHD. We will continue conducting translational research that complements the development of the Anthony Nolan Cord Blood Bank by understanding the unique properties and therapeutic potential of cord blood immune cells. This exciting field of research has the potential to significantly improve stem cell engraftment and to prevent post-transplant complications.

It’s vital that we continue to bring pioneering ideas from our laboratories to clinics faster than ever before, including supporting early stage clinical trials. Our plans for the future will hopefully result in new approaches and treatments that have the potential to change the face of the transplant landscape. While we have set solid foundations and goals for the next five to ten years, we will keep listening to researchers and experts in the UK and internationally, to ensure we remain leaders in our field.

The strategy will only succeed if we work in partnership with the very best people and invest in the infrastructure to facilitate lifesaving research. In a dynamic and evolving research environment, it is vital that we are able to identify and harness new opportunities to drive improvements in clinical practice and patient outcomes.

From international experts who’ll collaborate on and contribute to our work, to our staff, donors, and supporters who make this possible; we can only achieve our goals with your help. With our blueprint for research to drive our ambitions, and the support of the wider Anthony Nolan community, we will deliver a better future for patients.
Anthony Nolan has been saving the lives of people with a blood cancer or blood disorder for over 40 years.

We know that keeping groundbreaking science and research at the heart of what we do is crucial in ensuring we remain leaders in our field and, most importantly, that we succeed in saving more lives than ever before.

This booklet explains how the Anthony Nolan Research Institute’s new strategy will help us to reach our long-term goals by investing in world-class science and research.

With this ambitious research strategy in place, we know we can make the greatest difference and realise our vision: to save and improve the lives of all those who need a stem cell transplant.