

**ANTHONY  
NOLAN**

saving the lives  
of people with  
blood cancer

THE ANTHONY NOLAN  
NEWSLETTER FOR STAFF  
AND VOLUNTEERS

# INSIGHT



**WHAT  
MAKES**  
A PERFECT  
MATCH?

**GOING  
FOR GOLD**  
AT THE  
GAMES

**THE  
HERO  
PROJECT**  
IS HERE

ISSUE 27 |  
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# WELCOME TO INSIGHT

## WELCOME TO INSIGHT 27

Staff, volunteers and supporters have really been going the extra mile for our lifesaving cause this summer. We've signed up potential donors everywhere from army barracks in Germany to Essex Pride, pedalled thousands of miles to raise money at the Prudential RideLondon-Surrey 100, and celebrated life after transplant at the British Transplant Games.

And we're not stopping there - we've launched an exciting new education programme in time for the new school year, and we're marking Blood Cancer Awareness Month with an innovative event and a new phase of our advertising campaign.

This edition, we also talk to two of our world-leading scientists - James Robinson and Professor Steven Marsh - about how they are pushing the boundaries of our knowledge on the genetics of matching patients and donors. Plus a day in the life of one of our post-transplant Clinical Nurse Specialists, and how patients are helping to shape advice and information materials.

We were sad to hear that Bill Thompson, the former lead volunteer at our tea bar in Kirkcaldy Sheriff Court who featured in Insight 25, sadly passed away in June. Our thoughts are with Bill's family and friends.

**Ian Pithouse, Editor, Insight**

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Cover image: Tom Scott at the British Transplant Games

# ANTHONY NOLAN IN PARLIAMENT

**On Tuesday 18 July Anthony Nolan helped host the All-Party Parliamentary Group on Stem Cell Transplantation Summer Reception in Parliament.**

The event aimed to inform MPs - whether they were already engaged in our cause or new to our work - about the issues that matter to stem cell transplant patients and how they can help us save and improve more lives. It was also a chance to celebrate the progress made by the transplant community over the past year.

Anthony Nolan acts as Secretariat for the All-Party Parliamentary Group (APPG), helping to arrange meetings of the group and keep stem cell transplantation high on the political agenda.

Over 2,000 staff and supporters emailed their MPs via an e-campaign, which gave some statistics about people on the register in their constituency and encouraged them to attend the Summer Reception. We also invited patients, clinicians, partners and current and potential financial supporters along to the prestigious event in Parliament.

Henny Braund, Chief Executive of Anthony Nolan, said: 'There was a great turnout and a really convivial atmosphere. It's wonderful to have this opportunity to celebrate the achievements the transplant community has made in the past year. Anthony Nolan's pioneering research, dedicated nurses and patient-focused services mean we have increased the support patients receive at every stage of their transplant journey - but without the contribution of selfless donors and supporters, our vital work would be impossible.'

In September we'll host a reception at the Scottish Parliament - read all about it in the next edition of Insight.



Henny Braund and APPG Chair Mark Tami MP

# GOING THE EXTRA MILE FOR MYLES

**When British soldier Myles Brown was diagnosed with acute lymphoblastic leukaemia (ALL) and told he would need a stem cell transplant, the forces community rallied round - and enlisted the help of Anthony Nolan to sign them up to the register.**

27-year-old Myles is serving in the British Army, based in Germany with his fiancée and one-year-old daughter, and was diagnosed in April this year. His sister Sophie has been doing fantastic work rallying people to sign up to the stem cell register here in Britain, and the forces community wanted to do all they could to support Myles and his family. Myles' Medical Officer Major Sean Clarke - who was part of Marrow when he studied at Belfast University - invited Anthony Nolan over to Germany to recruit potential donors to the stem cell register.

The team from Anthony Nolan were hosted by Col Mike Cornwell of the 1st Battalion, Princess of Wales Royal

Regiment in the Officers Mess, and the Army also flew over all our supplies on a military flight to help keep costs at a minimum. The team were kept very busy, with a constant stream of soldiers wanting to join the register, and the Army medical officers pitched in to help sign up all those willing volunteers.

412 potential donors were recruited at Barker, Mansergh and Normandy Barracks over two days, with a further 160 promising to sign up when they returned from exercise. Barker Barracks also held a fundraiser at their Friday morning Physical Training session, with soldiers donating over £1,000 in a bid to avoid the hardest exercises!

Karen Archer, Regional Register Development Manager, said: 'The response and support we have received from everyone here in Germany has been incredible. It has been an amazing turnout and what everyone is doing is brilliant.'

'We'd like to thank everyone from 1st Battalion, Princess of Wales Royal Regiment, The Queen's Royal Hussars, 35 Engineer Regiment, 3 Armoured Close Support Battalion REME, 20th Armoured Infantry Brigade, British Army University Officers' Training Corps (UOTC) Southampton who signed up, raised awareness and helped us out with recruitment.'



# HEROES AND CHAMPIONS

Anthony Nolan's education programme for 16-18 year olds has a new name and approach, and young people themselves are helping us spread the word about blood, stem cell and organ donation.

Anthony Nolan has delivered the Register & Be a Lifesaver (R&Be) programme since 2009 as the legacy of journalist Adrian Sudbury, who died from leukaemia aged 27. Over the last eight years we have worked with volunteers in schools and colleges to reach over 280,000 young people and educate them about the importance of blood, organ and stem cell donation and inspire them to save lives. So far 22,000 young people have joined the Anthony Nolan donor register and 69 have been selected to donate stem cells to a stranger. In addition, more than 13,000 have registered as blood donors and over 6,000 as potential organ donors thanks to the programme and the amazing volunteers who have given up their time to speak so passionately about Anthony Nolan.

So why the change? Stephanie Drummond, Education Programme Lead at Anthony Nolan, explains:

'We need to adapt our education programme to make sure we are meeting the needs of our young audience and those supporting us to raise awareness in a flexible and sustainable way. So at the beginning of September we launched the Hero Project, offering shorter talks, new resources and follow-up materials as well as traditional presentations in schools and colleges where they work well.

'As we launch the Hero Project, Register & Be a Lifesaver will continue to deliver awareness-raising presentations about stem cell, blood and organ donation in schools and colleges in the East Midlands, run by Adrian's parents Keith and Kay as an Independent Charitable Trust. We wish the Sudburys the very best, and look forward to working with them on their new venture.'

The Hero Project aims to give young people opportunities to get more involved in Anthony Nolan's lifesaving work, and many are already going that extra mile by becoming 'Student Champions'. The champions help us to plan presentations and recruitment events in their schools, and play a key role in keeping conversations about joining the register going in that crucial time in between hearing about the Hero Project and potentially signing up at a recruitment event.

'We have found that where we have been able to work with Student Champions, schools and students have a much deeper sense of involvement and ownership and our events have been more successful and run much more smoothly.'

**Stephanie Drummond,**  
Education Programme Lead

'Some Champions have gone even further, organising fundraising events with impressive results. They do an incredible job of motivating their peers and generating support and we think they deserve a big thank you!'

The Champions get a lot out of it too, developing transferable skills including communication and event management, and exploring social and moral responsibilities. Anthony Nolan recognises their contribution by providing a letter of commendation, which can be useful in university and job applications.

Our partners in the Scottish Fire & Rescue Service (SFRS) have been working with Student Champions since they began delivering our partnership work in Scottish schools in 2013. Ally Boyle, founder of SFRS's partnership with Anthony Nolan, said of the approach:

'We decided to work with Student Champions as we were keen that SFRS, the schools and particularly the pupils get the most out of our events. We were also aware that there was a great opportunity to build on the requirements of the curriculum for excellence in Scotland with particular emphasis on active citizenship. The extended, peer led, conversation amongst pupils, with teachers and staff and with their relatives/carers greatly enhances the reputation of both the SFRS and Anthony Nolan and improves the success of our events.'

For more information on the Hero Project, visit [anthonymolan.org/heroproject](http://anthonymolan.org/heroproject)

# THE HERO PROJECT



Hero Project Student Champions

# TEAM ANTHONY NOLAN AT RIDELONDON 2017

On Sunday 30 July, 181 people took on the Prudential RideLondon-Surrey 100 cycle race for Anthony Nolan.

As usual, a huge team of staff and supporters was on hand to cheer our riders along the course and make them feel extra-special at our post-race party. They're on track to raise over £300,000 for our lifesaving cause.

We have had overwhelmingly positive feedback from all of our riders on the support from Anthony Nolan, and it's that personal touch that keeps many keen cyclists coming back to 'TeamAN' year after year.

For others - like Jason Branthwaite and Will Black - the cause comes first.

Jason Branthwaite's world was turned upside down in 2015 when the family received the news that their one-year-old son Freddie had severe aplastic anaemia, a rare bone marrow condition in which the body's bone marrow fails and stops producing new blood cells.

Jason said, 'When you hear that your little boy may not make it, it's like being hit with a sledgehammer - it's something that happens to other people.'

Following his diagnosis, Freddie underwent regular blood transfusions but the family were told his best hope of a long term cure was a bone marrow transplant. His older brother Harry was tested but he wasn't a match, so the family turned to Anthony Nolan to find a match.

'Cycling 100 miles was a big challenge but I knew I'd get round no matter what. The training has been tough but the thing that gets me through is thinking about Freddie when my legs hurt.'

#### Jason Branthwaite

William Black took on RideLondon just days after success in the British Transplant Games (see opposite), where he won silver medals in the 5km Time Trial and the 10km Road Race cycling events.

Will had a transplant for a rare disorder of the immune system called Hemophagocytic Lymphohistiocytosis (HLH) in 2009, and has since taken on a series of gruelling cycling challenges to raise money for Anthony Nolan.

Will said: 'Ride London was amazing again this year! We absolutely love it, the support of Anthony Nolan and the events team is absolutely unbeatable.'



Jason, after completing RideLondon 2017



Will, (centre) receives his medal

# BRITISH TRANSPLANT GAMES

Team Anthony Nolan won a record medal haul at our third British Transplant Games, with 15 people who have received stem cell transplants winning 24 medals across a range of events

The Games, which took place in North Lanarkshire in July, saw people who have received lifesaving organ or stem cell transplants take part in a series of Olympic-style events. The annual event celebrates life after transplant and raises awareness of the need for more people to join the Anthony Nolan stem cell register and the NHS Organ Donation Register.

Chiara DeBiase, Assistant Director of Patient Services at Anthony Nolan, said: 'This was our third year taking Team Anthony Nolan to the British Transplant Games and it couldn't have gone better.'

'The Games are a testament to the incredible spirit and determination of people who have gone through such a difficult and complicated recovery.'

'Winning medals is brilliant, but what this event really demonstrates is how many stem cell transplant recipients can go on to live rich, healthy and fulfilling lives.'

And no-one demonstrates that better than Tom Scott. Tom, a sports coach from Edinburgh, received two stem cell transplants after suffering from Hodgkin's Lymphoma. He's really keen to raise money and awareness for Anthony Nolan - due to his mixed race background, it was more difficult for him to find a perfect match through Anthony Nolan and he's keen to raise awareness about stem cell donation among people from black, Asian and minority ethnic (BAME) backgrounds.

After a very difficult few years of treatment, Tom has made a remarkable recovery to win a Silver medal in the 800m, and a Bronze in the 1500m at the British Transplant Games.

Tom said: 'I almost did the British Transplant Games last year, but this year saw it was in North Lanarkshire and knew I should go for it. The weekend was amazing. At all of my events, there was the most positive and welcoming atmosphere and you could tell how much it meant to the crowd and participants to be there.'

He added: 'It's special for me to be part of Team Anthony Nolan because without Anthony Nolan and a 97kg man somewhere in the States... well, it might be a totally different story.'



Team Anthony Nolan



Tom, taking part in the British Transplant Games

# SAVING LIVES WITH PRIDE



**Anthony Nolan staff and volunteers have been getting loud and proud at Pride events around the country, spreading the word that sexuality is no barrier to becoming a lifesaving donor.**

This summer has seen our largest ever presence at UK Pride events, including marching in the Pride in London Parade on Sunday 8 July. 50 Anthony Nolan LGBTQ+ staff, donors and allies marched alongside more than 300 other charities and organisations.

The aim was to raise awareness of stem cell donation among the LGBTQ+ community, as well as celebrating our LGBTQ+ staff and showing that we are an inclusive employer.

Worryingly, in a YouGov survey Anthony Nolan recently commissioned, 50% of gay and bisexual men incorrectly believe that they are not allowed to join the stem cell register.

Jon Evans from Christchurch was one of that 50%, but joined the register after a chance encounter, and went on to donate stem cells in June. 'I joined the Anthony Nolan register about three years ago after talking to the sister of a friend of mine

who works for Anthony Nolan,' Jon explains. 'We were talking about blood donation, and how I'm not able to donate because I'm gay. She explained to me that gay men are able to sign up to the stem cell register. I was actually quite surprised to hear that gay men were able to sign up.'

Richard Davidson, Director of Engagement at Anthony Nolan, said: 'I am immensely proud to be part of the 44% of LGBTQ+ staff in senior leadership positions at Anthony Nolan.

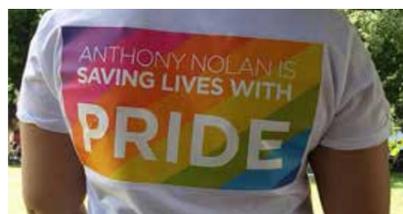
'Anthony Nolan encourages people from every background, identity or sexuality to sign up to our stem cell register as potential lifesavers - and that also applies to the people that we employ to deliver our lifesaving work. We have a rich and diverse organisation that draws strength and experience from a wide range of people, and we were delighted to join the Pride in London parade for the first time this year.'

## OUT AND ABOUT

Our Register Development team also held recruitment events at Pride events around the country, here are some of the highlights:



Anthony Nolan staff/volunteers at Brighton Pride, where they recruited 24 people



Pallvi Senghani at Essex Pride

# SHARING TRANSPLANT EXPERIENCES

**Volunteers support Anthony Nolan's lifesaving work in many vital ways, and each has their own reason for getting involved. Kate Jones has shared her own experience of having a stem cell transplant in a new guide to help others in the same situation.**

Kate is one of the case studies in A young person's guide to the stem cell transplant journey, which aims to help prepare young transplant patients for treatment. The guide includes what happens after diagnosis, the effect of a transplant, taking control of recovery and dealing with your feelings, and features tips and comments from Kate and other young transplant recipients throughout.

Kate, who is now 17, had a transplant in 2015 to treat aplastic anaemia, a rare and serious blood disorder in which a person's bone marrow fails to produce enough blood cells.

'Being told that I needed a stem cell transplant was very scary,' says Kate. 'I was young but I was so supported that it was made a lot easier for me. I had a plan: get better, work through summer, and go back to school.'

'Having something that is relatable, and has been written and designed for young people, is great. It's easier to hear from someone who has been through it that is your own age.'

**'The guide is honest, genuine, truthful and realistic. It answers questions you may be afraid to ask older people or doctors. I would have found it really helpful, and hope it will help a lot of people.'**

Kate says that hair loss and fertility were big concerns for her when she was going through treatment, so she felt it was important to cover them in the guide. 'For me losing my hair felt like losing my femininity; it was really scary and it was like another mountain to climb. I had treatment from the age of 15 and was told that chemotherapy might affect my fertility. At the time, the transplant and hair loss was at the front of my mind. I have felt that I need to talk to my doctors about it - so having it mentioned in the guide is really important.'

Kate has also worked with her school to raise money for Anthony Nolan, and she's keen to do more to raise awareness around stem cell donation.

**'I work closely with Anthony Nolan because I feel unbelievably grateful a lovely man, I may never meet, saved my life.'**

**'The more people know about it the better, and if I'm going to take anything away from a horrible experience it's to make sure people learn about it in a positive way.'**

Chiara DeBiase, Assistant Director of Patient Services at Anthony Nolan, says: 'A blood cancer or disorder diagnosis can be devastating and to be told you need a stem cell transplant is, for many, the start of a long, turbulent and life-changing journey.'

'We've worked with young people, who have been through their own transplant journey, to let others know what they can really expect and provide tips so people can take control of their recovery.'

For more information, and to download or order the guide, visit [www.anthonynolan.org/patientinfo](http://www.anthonynolan.org/patientinfo)



Kate (right), pictured with her dad, Jack, and sister, Lucy

# MAKING BLOOD CANCER **VISIBLE**

September is Blood Cancer Awareness Month, and Anthony Nolan is working with eight other charities to shine a light on blood cancer through the Make Blood Cancer Visible campaign.

Artist Paul Cocksedge has created an installation representing the 104 people who are diagnosed with blood cancer every day through a 'typographic forest of names' in London's Paternoster Square. Each piece of the installation symbolises a person affected by blood cancer - including thirteen members of Anthony Nolan's patient panel - and perfectly matches their height.

The installation was unveiled on 4 September, and visitors have been interacting with the sculptures, reading the stories of those affected by blood cancer and sharing photos using #makebloodcancervisible.

The campaign is sponsored by Janssen UK and supported by nine charities - Anthony Nolan, Bloodwise, CLL Support Association, CML Support, Leukaemia Care, Lymphoma Association, MDS Foundation, Myeloma UK and WM UK.

One of Anthony Nolan's patient stories is nine-year-old Rory, who was diagnosed with AML (Acute Myeloid Leukaemia) six years ago and had a bone marrow transplant in 2012. Rory says:

'Being diagnosed with AML was scary. I was only three years old and was away from my home for a long time. I missed my brothers and my toys.'

'When I was diagnosed, I didn't know very much about cancer but my CLIC Sargent social worker, Macmillan family support nurse and my mum and dad helped me to understand what was happening.'

'I'm proud to have gone on to start school and make lots of new friends.'



## SECOND WAVE OF #SECONDCHANCE

We are also launching a second phase of our #SecondChance advertising campaign. In June we ran ads featuring transplant recipient Hazel in London Underground stations and trains, aiming to raise awareness of what we do and that as a charity we need funding to provide lifesaving transplants.

This time we are sharing Ava Stark's story in her local area. Ava has already featured on targeted Facebook advertising to people who live near her in Fife, and we are rolling out ads on trains and bus shelters in Scotland in September.



**THIS IS WHAT A SECOND CHANCE OF LIFE CAN LOOK LIKE**

**THIS IS THE DIFFERENCE YOUR DONATION MAKES**

Ava, from Fife, was diagnosed with a serious blood disease when she was just three years old.

Anthony Nolan is a charity that works to cure blood cancer and blood disorders, like Ava's, when nothing else can. **But we can't do it without you.**

Your gift will be used to support Anthony Nolan's work to cure blood cancer. You will be charged £3 plus one message at your standard network rate. Anthony Nolan will receive 500%. If you wish to discuss this mobile payment call 020 3262 7863.

By texting CHANCE to 70123 you are agreeing to us contacting you by phone and SMS to tell you more about our lifesaving work and how you can support it. To give £3 without receiving further contact by phone or SMS, text CHANCE NO to 70123.

You can help save more people like Ava.

**Text CHANCE to 70123 to donate £3**



**saving the lives of people with blood cancer**

# A DAY IN THE LIFE OF A **CLINICAL NURSE**

Lorna Welsh is Anthony Nolan's newest Clinical Nurse Specialist, providing post-transplant support to patients all over Scotland from Queen Elizabeth University Hospital Glasgow.

Lorna started in the new role in July - the latest step in a long career in nursing, including 11 years in stem cell transplantation. Having cared for people in the transplant unit, Lorna says she became interested in what happened after people have had their transplant and leave hospital. 'I led a project last year to review and redesign how we follow up all haematology patients - not just those who have transplants - as part of Scotland's Transforming Care After Treatment (TCAT) initiative,' she says. 'So when I heard that this new post-transplant nursing role was being introduced at Glasgow I had to go for it.'

Since starting the role, Lorna has worked closely with hospital consultants and patients alike to find out the needs of the service as well as individual patients. 'A big part of my role is building those links between patients and medics to make sure they're getting the care they need,' explains Lorna. 'The aim is to offer personalised care to each and every transplant patient. I see them on the ward before they're discharged and talk them through what the next month will entail. We do a holistic needs assessment together one to two weeks after transplant, looking at what we can do to support all aspects of their recovery - physical, emotional, psychological, social... Once they've left hospital, they come into clinic once a week, where a clinician and I see how they're doing and address any concerns they may have.'

Lorna works three days a week, with clinics each morning and the rest of her time spent following up on patient care and looking for improvements to the service she offers. 'Because I'm here for patients across Scotland, I need to make sure they're getting the right care in their local area - whether that's following up with nurse practitioners at their local hospital or referring them to

dieticians, physios or psychologists,' she says. 'I also talk to patients about how they're settling back into everyday life with their family and local community, as those informal support networks have a big role to play in recovery.'

It's still early days for the Clinical Nurse Specialist role in Scotland, but Lorna has already started to identify improvements to people's transplant journey. 'There's a lot of information to take in when you're going through a transplant, and I've been looking at when that information should be prescribed - both pre- and post-

transplant - to make sure people are informed but not overwhelmed. I'm also looking at formalising GvHD [Graft vs Host Disease] assessments to improve care and give us better outcomes data.'

Lorna says she's seen a lot of improvements in stem cell transplants over the years, and she's excited to be part of people's ongoing care. 'When you're working on the wards you don't get to see the people who are doing well after their transplant. So it's lovely to see patients really thriving, and to be here to help keep them that way.'



# Q&A WITH PROFESSOR STEVEN MARSH

Professor Steven Marsh is Director of Bioinformatics and Deputy Director of Research at the Anthony Nolan Research Institute. Insight asked Steven what keeps him interested in immunogenetics after 30 years in the field.



**‘We can see tangible benefits from the work we’re doing: increasing the overall survival of patients, saving and improving lives.’**

## What keeps you focused in your research?

The patients keep me focused. As an organisation we provide a therapy for people with blood cancer and blood disorders, so our research is aimed at improving that therapy and improving their outcomes. There are lots of interesting questions that you may want to ask in research, but I think we need to keep the patient in mind at all times; be patient-focused. That’s why we’re here.

## What does your colleague James Robinson’s recent paper on HLA polymorphism add to our knowledge about HLA, and what could it mean for patients?

In 1989, we knew about just over 120 variants of the different HLA genes and we thought that we’d found pretty much everything that would be found. Almost 30 years later, there are over 17,000 different HLA sequences in our database.

James’s paper asked a couple of major questions. The first is how did we

get all this variation; is there a limited number of sequences from which all of this is derived? The other question is, based on the small proportion of the global population we’ve typed so far and the rate at which we discover new variants, how many could be out there? The answer is that all the variants we currently know about can be derived from a core of just 42, and there may be up to 3 million variants for each HLA class I gene – and this could in fact be an underestimate.

What this means for Anthony Nolan and other registers is that our typing techniques need to be able to detect both those sequences we know about now and all the millions of others that could be out there. We are using Third Generation Sequencing (TGS), which looks at every base in the sequence, for people joining the register. So we can be confident that we won’t miss anything new and we pretty much know if they are a match for a patient immediately, rather than having to wait for the results of confirmatory typing [further tests that are performed when a donor is selected as a potential match].

Knowing how much variation is out there reframes the question we and other researchers have been trying to answer for many years: what is a match, and do we know what the best match is?

## What research is currently underway to answer the question of what makes the best match?

Our Patient/Donor project looks at just that question. We published earlier this year on a cohort of 1,271 patients and donors, looking at the influence of HLA and CMV status matching on patient outcomes, and that included some very exciting findings about the importance of CMV status and donor age.

What we’ve been working on for the past two years now is re-typing as many people as possible from that cohort more accurately using Third Generation Sequencing, to understand what the real level of matching was in those patients and donors. We’ve typed 893 samples – some samples were too old to be typed using TGS – and we’re starting to do that analysis now.

## How do you think the role of unrelated donor transplants in treatment for blood cancer and other conditions will change in the next 5-10 years, and how will we adapt?

I suspect that things never move as fast as we think they might. I’ve worked here for over 20 years and over that time we’ve seen the number of adult unrelated donors increase year on year. I suspect that will continue for some time to come. There is an increasing role for haplo-related transplants [transplants from a partially matched related donor]. Obviously I don’t perform stem cell transplants myself, but I often ask transplanters what stem cell source they would choose for themselves, and I’ve had lots of people say they’d have an adult unrelated donor, some people would like a cord blood; I’ve only ever spoken to one transplanting who said they would like to have a haplo transplant themselves. But I think there’s probably room and need for all three options.



Professor Marsh (right) with Director of Engagement Richard Davidson at Pride in London

Every day you read more about the role of immunotherapy in treating different conditions and I’m sure that will have a big impact in the future. It may be that we could provide stem cells for therapies that we haven’t even considered yet, and I feel Anthony Nolan has a role in aiding this work.

## What did attending Pride in London with Anthony Nolan mean to you?

I thought it was a great day out – a large group of staff and donors represented Anthony Nolan at the march, and everyone enjoyed themselves. It was great to interact with people, and spread the message that sexuality is not a barrier to joining our register, as it still can be for gay men when it comes to giving blood. Some people recognised us, and said ‘yes I’m on your register’, so clearly that message is starting to get through. I hope it’s something we continue to do.

## What do you enjoy most about working at Anthony Nolan?

The ability to do something that I personally find very interesting that has an impact on people’s lives. I think we’re very lucky in that things that we do currently and have done in the past have directly had an impact on the outcomes of stem cell transplantation; on people’s lives. Many people working in research institutes don’t have that immediate link. The level of matching, the technology we and other people use in the world now, the sequence database, identifying new factors in matching – those are things that have happened here and have rolled out nationally and internationally and play a role in transplantation around the world. That’s what’s exciting – we’re able to do things and we can see tangible benefits from the work we’re doing: increasing the overall survival of patients, saving and improving lives.

# VARIATIONS ON A GENE

The Human Leucocyte Antigen genes, also known as HLA, are the most varied of all our genes, and for a stem cell transplant to succeed, the HLA type of the donor must match that of the patient as closely as possible. But just how varied is HLA, and where did all this diversity come from?

Those are the questions a new paper from the Anthony Nolan Research Institute aims to answer. Lead author James Robinson, Senior Bioinformatics Scientist, decided to tackle 'quantifying and qualifying' HLA diversity, as he puts it, as part of his PhD.

'Most genes have low numbers of variants, but we know there are over 10,000 for the class I HLA genes - HLA-A, HLA-B and HLA-C - alone,' James explains. The class I genes are the most functionally important when matching patients and donors, and each of us has two copies of a gene - one inherited from each parent. So when we talk about a 10/10 match, 6 of those 10 are class I alleles.

'We know why this area of the genome is so diverse - it's involved in immune function, so the more variation we have, the more weapons we have against viruses and the spread of infection within.'

'It's like an arms race between us and disease! But all that diversity becomes a problem when you're trying to put one person's stem cells into another person and avoid an immune response. So first of all we wanted to put a number on the scale of diversity - how bad could it get?'

Those 10,000 Class I alleles - which are recorded on the IPD-IMGT/HLA database that James and his colleagues maintain - have been discovered by scientists all over the world submitting sequences to the database. New variants are currently being discovered

at a rate of roughly one in every 2,000 people that are typed. Based on this, James' paper predicts that there could be up to 9,000,000 class I alleles in the global population. 'That's useful to know, because it gives us the scale of what any allele-level typing system - such as our Third Generation Sequencing pipeline - needs to be able to deal with. It also means people are less likely to write new alleles off as errors in their typing - if you see something different, it may well be something new.'

Next, James wanted to know how and why all those alleles have been created. 'If you think of all the alleles we see today as children, we wanted to trace their family tree as far back as possible to the 'original' alleles.'

There are two main ways that new alleles are created: Single Nucleotide Polymorphism (SNP) and recombination. In SNP, the new allele differs from an existing one by just one letter in the DNA code - if you compare DNA to music, the new allele is the same song with one different note. In recombination, whole chunks of one strand of DNA get copied into another - like a DJ mixing two songs. James created some software to trace back through all the SNPs and recombinations - all the bum notes and remixes - and identified 42 'core' HLA Class I alleles. All 10,000 alleles discovered so far can be derived from these 42.

'This allows us to start to cut through the noise of all that variation and look at which variations are likely to be functional,' says James. 'Eighty percent of variants are just one base pair [or letter in the DNA code] away from

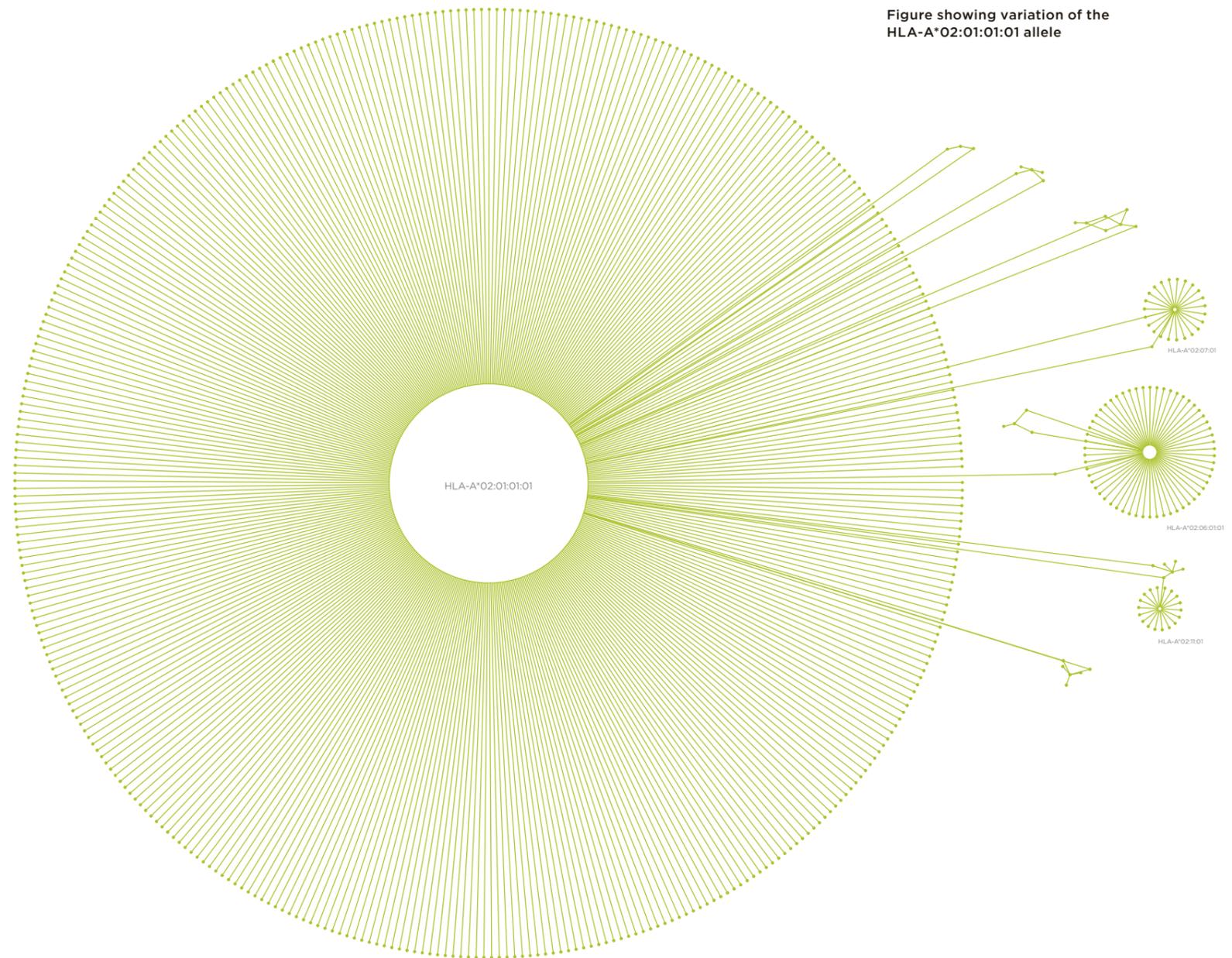
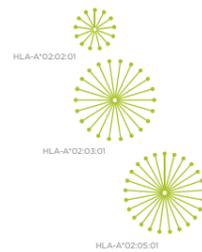


Figure showing variation of the HLA-A\*02:01:01:01 allele

another allele, and some of these don't make any difference to the protein that's created when the DNA is 'read'. But there are clear regions of the code where we see many more variations, which suggests they have a functional role - the variations have been passed down through the generations because they give a different immune response to a particular disease.'

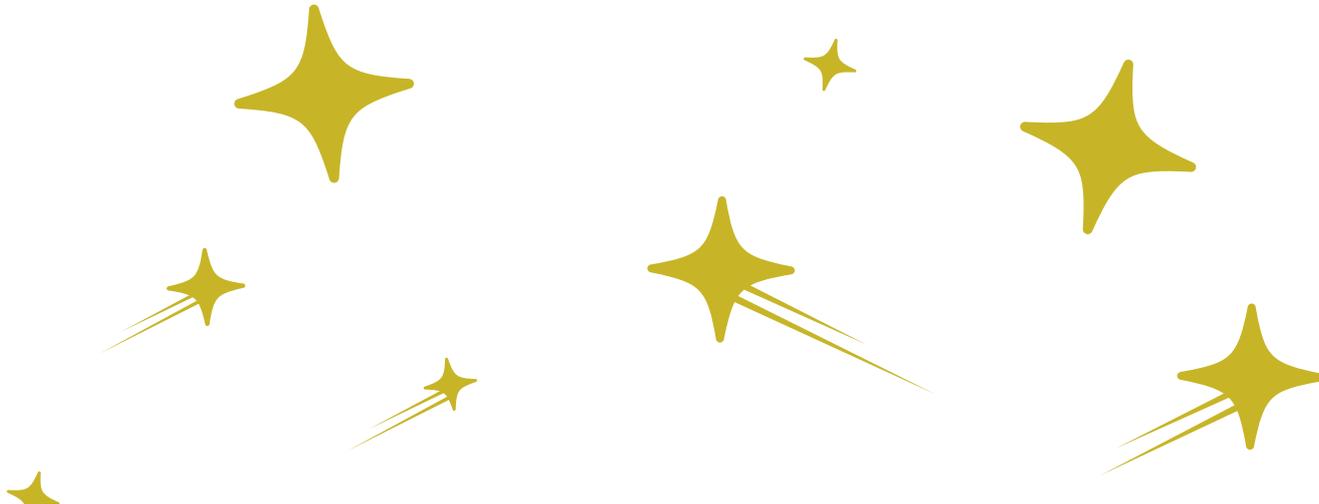
So what does all this mean for the future of matching patients in need of stem cell transplants with donors? With an estimated 3,000,000 possible alleles for each gene, will finding that 'perfect' match become almost impossible?

James hopes that with more research it could be quite the opposite - and his paper is the starting point.

'Understanding how the sequence varies, and where the variation lies, may be the key to understanding what makes a successful match', he says. 'This paper allows us to begin to understand the level of variation and the potentially important regions. In some regions variation is just noise - the function of the allele is still the same or similar enough that you won't get an immune clash - in effect a 'permissive mismatch'. So we may then be able to match on more targeted regions of the gene and not just the whole sequence. Together with our TGS typing and the research on the Patient-Donor project, we should begin to better understand how and where allele variation impacts on the success of a transplant.'



'This paper may ask more questions than it answers, but it puts us in a better position to ask the right questions.'



*Anthony Nolan  
Christmas Carols*

6 DECEMBER

★ 2017 ★

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