

# Clinical research update

News from Southampton's clinical research teams

Issue 5, autumn 2015

[www.clinicalresearchinsouthampton.uhs.nhs.uk](http://www.clinicalresearchinsouthampton.uhs.nhs.uk)

## Meet Maddison

our first 100,000  
Genomes Project  
patient



In this  
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[Southampton's first 100,000  
Genomes Project patient](#)

[WISH lab feature](#)

[New screening test for  
Down's syndrome](#)

# In this edition...

...we're taking a closer look at genomic medicine, which is set to transform healthcare by tailoring treatments and care specifically to each of us as an individual.

## Southampton patients at the cutting edge

Six year old Maddison Cox is accessing cutting edge genetic screening for rare diseases through a national project, as her doctors and family hope to find answers to a range of unexplained health issues she has coped with since birth.

Maddison's story (page four) shows how researchers are studying the human genome – a three billion letter code containing all the information needed to make each of us – to identify the genetic factors underlying health and disease.

## An individual blueprint

Each of our body's cells has two copies of the genome, one inherited from our mother and the other from our father. Differences between us in this code either define (e.g. eye colour, blood type), or strongly influence (e.g. height, behaviours) much about us.

Genomic differences like these also underlie many medical conditions and our likelihood of developing a range of diseases, whilst damage or changes to the genome are the root cause of all cancers (see, targeting lung cancer, page eight).

## Unlocking the code

The genome's influence on health, illness, injury recovery and treatment is so critical that the NHS has invested £300 million in a world leading project to sequence 100,000 genomes. Targeting rare diseases and cancer, it is also paving the way for personalised genomic medicine.

Southampton is already decoding the genome's role in many areas of health and disease, from more accurate screening for Down's syndrome to better nutrition for pregnant mothers (pages five and 10), through to targeting lung cancer cells and using the body's own defences to fight cancer.

## See the future of your care

Finally, our centre pages take you through the doors of the WISH lab, which has the tools researchers need to understand individuals' genomes and bodies at a level of detail and speed previously unimaginable.

It gives a glimpse of the technology powering this research into the new personalised approach; cutting edge techniques that will be routine in the future.

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# Did you know...



Each of the millions of cells that make up our bodies has their own set of instructions, like a recipe book for the body – the genome.



Unravelled, the DNA from each cell would stretch to two metres – all of us contain enough DNA to wrap around the world 2.5 million times!



All humans in the world are 99.9% identical genetically, with just 0.1% of the DNA code accounting for our differences.



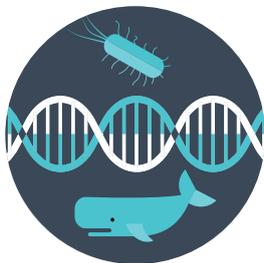
Organised into 23 separate sections known as chromosomes, our genome is a four letter code, 3.2 billion letters (or bases) long.



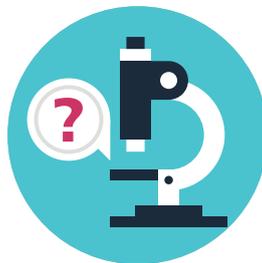
Just 3% of our whole genome contains all of the 20,000 genes used to make us...



Chimpanzees are our closest animal relatives – we share approximately 98% of our DNA with them.



It's made from a molecule called deoxyribonucleic acid (DNA), which is shaped like a twisted ribbon; all living organisms are made from instructions encoded in DNA – from bacteria to blue whales.



...researchers think the other 97% may be important, but are still working out what it does.



Gregor Mendel, a monk born 1822, is known as the father of genetics, after observing and changing patterns in colours, shapes and sizes of his pea plants across generations.



## Meet Maddison – our first 100,000 Genomes Project patient

**Born with a range of unexplained health issues, six-year-old Maddison Cox is our first patient to join the UK-wide 100,000 Genomes Project, with her family keen to pinpoint the genetic causes of her symptoms and find new treatments for Maddison and others like her.**



Maddison has been cared for and treated by doctors since she was born. Today, she lives with a number of health issues, including problems with her heart, bowel, kidneys, joints, eyes, hearing and development.

### **A real mystery**

Doctors knew before she was born that Maddison would have a heart condition, which was spotted at a routine pregnancy scan. Yet, although she had an exact diagnosis for this at two-years-old, the root cause of her other health issues has remained unclear to doctors.

Consultant in clinical genetics, Dr Katherine Lachlan, first met Maddison as a newborn in 2008, and has since been part of a team trying to find answers for her and her family ever since.

“Maddison’s health is a real mystery. I’ve spoken with colleagues across the

world and not one has seen a patient with the same combination of issues.” Dr Lachlan explains.

### **Finding answers**

The Wessex NHS Genome Medicine Centre (GMC), based in Southampton is one of 11 centres delivering the £300 million national 100,000 Genomes Project.

It aims to identify the underlying genetic causes of rare diseases and cancer by comparing the complete set of genetic information (the genome) from 100,000 patients and their family members.

Dr Lachlan and her team hope that the project will deliver this information for Maddison, to give a better picture of what the future holds for her and how to best support her.

“When Katherine told us about this project we were really keen to join –

it’s a real honour that Maddison is their first patient.” Natalie Cox, Maddison’s mother, says.

### **Transforming healthcare**

“This project has the potential to transform the future of healthcare, and for some participating patients, there will be a conclusive diagnosis for a rare, inherited disease that was not possible before.” Explains Professor Karen Temple, co-lead for the Wessex NHS GMC.

Maddison’s family is hopeful this will be the case, but believe their involvement is about more than her individual care, as Natalie explains:

“Whilst we’d love a diagnosis for Maddison, we know this may not happen and it’s just as much about contributing to the bigger picture and hopefully being able to help other people and families in the future.”

# Revolutionising detection of Down's syndrome

**A new non-invasive genetic test for Down's syndrome could offer expectant parents a low-risk, accurate estimate of their baby's chances of being born with the condition.**



Screening for Down's syndrome is low-risk and offered in every pregnancy, yet confirmed diagnosis involves procedures with some risk of miscarriage. Local families have helped to evaluate a new screening test with the potential to reduce unnecessary diagnostic testing.

## **A genetic condition**

Involving some level of learning disability and distinctive physical characteristics, Down's syndrome is caused when an extra copy of chromosome 21 is present in the body's cells. People with Down's often lead full, independent lives; however the condition has lifelong implications for them and their families. Because of this screening is always offered, helping parents to understand the likelihood and implications of their baby being born with Down's.

## **Current screening for Down's**

Current screening estimates a baby's chances of having Down's, based on hormone levels in the mother's

**“Through this study, and with the accuracy the NIPT test has shown, we've seen women feel more confident in their screening results...”**

blood and the amount of fluid (nuchal fold) in the baby's neck at 11-14 weeks of pregnancy.

“The only way to diagnose Down's before birth is by taking a sample from the placenta – called chorionic villus sampling – or from the fluid from around the baby – called amniocentesis.” Fiona Walbridge, research midwife in Southampton, explains.

“Because both tests carry a risk of miscarriage, they are only performed for women with a high risk screening result, family history of certain conditions or when women want a confirmed diagnosis.” Fiona continues.

**A new, more reliable screening test**  
Mothers and midwives at our Princess

Anne maternity hospital have been part of a national study looking at a new non-invasive prenatal test (NIPT). It promises greater accuracy in predicting Down's by counting fragments of the baby's chromosome 21 in the mother's blood – with higher counts indicating Down's.

## **Immediate effects**

During the study, midwives saw a significant reduction in the number of amniocentesis and CVS procedures.

“Through this study, and with the accuracy the NIPT test has shown, we've seen women feel more confident in their screening results. And if introduced within the NHS, this test may lead to fewer unnecessary invasive procedures.” says Fiona.

And the results of the study, now closed for participation, will also help identify how NIPT, currently only available privately at a cost of between £350 and £900, might be offered by the NHS.

# The WISH lab

Bringing together the science and expertise needed to understand each patient's bodies and health in ever greater detail, our new laboratory is set to drive the next generation of treatments and care.

Uniquely tailoring treatment and care to the individual – personalised medicine is set to transform healthcare. This approach, and the research needed to make it happen, relies on understanding each person's biology in fine detail – which is where the Wessex Investigational Sciences Hub (WISH) lab comes in.

This new research-dedicated laboratory provides the tools, tests and expertise needed to

characterise an individual's genetic make-up, immune system, nutritional health and the bacteria living in or on us.

“With this level of detail, you can spot specific factors that mean a trial treatment works in person A, but not person B – critical for them, but may also prevent us dismissing otherwise promising trial treatments because they don't work in everyone.”  
WISH lab director, Professor

Tony Williams, explains.

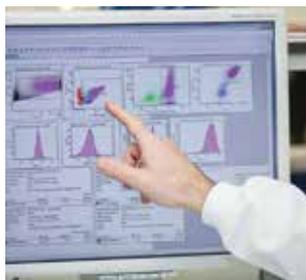
“WISH will also help us understand diseases better – it's central to our contribution to the 100,000 Genomes Project, which is going to reveal the genetic causes of rare diseases and cancers.” Professor Williams adds.

In fact all of the research in this edition is either supported by WISH right now, or will benefit from its work in the future.



## Understanding the body's defences

WISH can characterise the body's immune response to illness, treatments, diet and lifestyle. It's important in many areas of research – and critical to our work harnessing the immune system to fight cancer – see page eight for more.



## You are what you eat

What we eat and what we do have major impacts on our health and how we respond to illness, injury and treatment. WISH has the tests and techniques needed to understand this in studies such as our work with pregnant women featured on page 10.



## Microbiology

WISH can identify the exact species and types of bacteria present in or on our bodies to help develop new treatments for infectious bacteria and understand how the mix of 'normal' bacteria contributes to conditions like inflammatory bowel disease (see page nine).



## The blueprint for you

Your genome influences your lifelong health and chances of developing certain diseases or conditions. The WISH lab is already using genomics to help rare disease patients like six-year-old Maddison Cox and those with cancer find answers and treatments for their conditions (see page four).



**Twitterview**  
with Dr Ruth Challis



**Dr Ruth Challis is the laboratory operations manager in the WISH lab. We caught up with her to find out more about her job and what she enjoys outside of work – in 140 characters or less.**

**Hi @r\_challis, WISH lab operations manager sounds impressive – but what does it mean?**

Overseeing a busy & rapidly developing lab; this involves anything from costings, sorting equipment issues, HR & PR; each day is different.

**Busy then. What does a typical day look like for you?**

No day is typical! But perhaps email issues first thing and over lunch, operations meetings, dealing with lab & staff, assessing new work...

**What's the most interesting research going through the lab right now?**

Immunotherapy is hugely exciting right now. Getting the immune system to fight cancers for us? Amazing concept, brilliant current results!

**We know there's loads of hi-tech equipment in the lab but what's your favourite bit of kit to use?**

I'm a flow geek; our 3 laser FACS Aria can identify individual immune cells from patient blood samples to understand their immune responses.

**Righto! Away from the flow geekery what's your favourite thing to do at the weekend?**

Spend time with my young family and big dog! We love walking, or learning to cycle (my kids) in the New Forest.

**Give us an interesting fact about yourself...**

I am a fluent speaker of Italian. I love Italy and have lived or worked in Rome, Naples, Padova, and Foggia in the past.

**Eccellente! And finally, what's your favourite meal or thing to cook?**

I love cooking; making crazily iced cakes; check out #sciencecakes! Eating 'saltinbocca' that my husband has cooked for me is fantastic too!

# Targeting lung cancer

**Hard to spot and difficult to treat, lung cancer claims two in three lives within a year of diagnosis. Research teams here are using tumour samples to develop new treatments and improve chances of survival.**

40,000 people are diagnosed with lung cancer every year in the UK, often this diagnosis is made late because of few signs or symptoms in the early stages – making it difficult to treat and cure.

## Cancer - a genetic disease

“Most cancers start because of damage to genes, causing uncontrolled growth that forms tumours.” Professor Christian Ottensmeier, oncology consultant and researcher, explains.

“Genes also play a role in the body’s response to infection and disease, including cancer. That’s why we’re using samples from lung cancer patients to understand more about the genetics of the disease and how to better fight it.” Professor Ottensmeier continues.

## Personalised treatments

Because genetic changes causing cancer differ between patients, response to treatment also varies. The Cancer Research UK (CRUK) team in Southampton are identifying specific changes in tumour samples, to match patients with new trial treatments that may be more effective.

New experimental drugs are added to the list of options as they are created, and those showing no benefit are dropped, ensuring quick access to potentially more effective drugs.

Professor Peter Johnson, who is CRUK’s chief clinician and director of Southampton’s CRUK Centre, says



“These new medicines target very specific and often rare mutations; because of this we need to test the genes in many patients to find the few who might benefit when they otherwise have very limited treatment options.”

## Harnessing our body’s defences

Southampton has specialised in cancer immunotherapy for a long time; priming the body’s immune system to identify and attack cancerous cells, and has had great success in melanoma skin cancer and blood cancers, like lymphoma.

“We believe this method holds much greater potential than current treatments to fight some cancers...”

“Although the immune system is good at recognising infections, like bacteria and viruses, it’s not so good at seeing cancer cells because they are rogue versions of normal cells and look very similar.” Professor Ottensmeier explains.

Professor Ottensmeier and his team are working with lung cancer patients to make lung cancer cells more visible to immune cells, stimulating them to attack the cancer.

“We believe this method holds much greater potential than current treatments to fight some cancers, offering patients better long-term protection against the disease. We hope these new approaches will give lung cancer patients many more options and a much better chance of survival in the future.” Professor Ottensmeier says.

# IBD: it's in our genes

**Southampton's paediatric inflammatory bowel disease (IBD) team is working with children with IBD and their families to understand how our genes contribute to this condition that has no known cure.**

IBD is a lifelong condition involving inflammation of the digestive system that can affect any of us. Crohn's disease and Ulcerative Colitis (UC) are the most common forms, with symptoms varying but including stomach pains and cramps, diarrhoea, vomiting and a lack of energy.

Those with IBD tend to experience periods of good health alternating with "flare-ups" when symptoms are particularly bad.

**“We've looked at hundreds of genes of about 150 children with IBD and their family members, allowing us to identify certain patterns and differences, proving that parents with IBD are more likely to have children with the condition.”**

## **What causes IBD?**

No one knows for sure what causes Crohn's and UC but research indicates that it's a combination of the genes we're born with and an abnormal reaction to certain bacteria in the gut, triggered by changes in our environment – such as diet or stress.

Researchers are working with local families to understand which differences in our genes matter, to tailor treatments to each person and better manage this debilitating condition.

“We've looked at hundreds of genes of about 150 children with IBD and their family members, allowing us to identify certain patterns and differences, proving that parents with IBD are more likely to have children with the condition.” Sarah Ennis, Professor of genetics, explains.

## **New, better treatments**

With no cure for IBD – treatment can only relieve symptoms – the team are now investigating whether individuals' genes



influence how they respond to different treatments.

“We know that every person's IBD is different so we'd like to move away from a 'one size fits all' approach to treatments.” Professor Ennis says.

“Up to now Crohn's and Ulcerative Colitis have been seen as two strict categories with different approaches to treat each condition, when the reality is that they have similar underlying genetic factors. By looking at patterns in the genes associated with IBD, we can identify patients who are more likely to benefit from a certain drug or method of treatment.” Professor Ennis continues.

## **Taking part**

We're still looking for children and families to take part in our study. If you're interested, or would just like to find out more, please contact research nurse Rachel Haggarty on 023 8120 3805.

# We are what we eat

**Local mothers are being asked to take part in an international study to see how their diet before and during pregnancy influences their babies' health and development.**

What we eat affects our health right now, our unborn children's health and our health later on in life. At the very root of this is a mother's diet – even before she's pregnant.

Diet before and during pregnancy plays a crucial role in children's health and development, and poor nutrition can increase the risk of developing diseases later on in life – like obesity, diabetes and heart conditions.

## **Long-term commitment to helping mothers**

Southampton has led research into better health through better nutrition, with a focus on mothers' diets and its impact on health throughout life.

"We know that a mother's nutritional state before and during pregnancy is important for their baby's health and development. We're now taking this to the next stage by looking at how

we can improve the health of mothers and their children." explains Professor Keith Godfrey, director of the NIHR Southampton Biomedical Research Centre and Professor of epidemiology and human development.

## **The NiPPeR study**

Southampton is one of three sites worldwide looking to see if a specific combination of nutrients, made into a drink, can improve the health of mothers and their babies. We'll be working with 600 local women who will drink the nutrients twice a day before and during their pregnancy.

"We'll be looking at the impact of blood sugar, vitamin and mineral levels of mothers on their babies' development and whether these supplements influence this. Mothers will be followed from pre-conception through pregnancy and their baby's first year of life."

Professor Godfrey says.

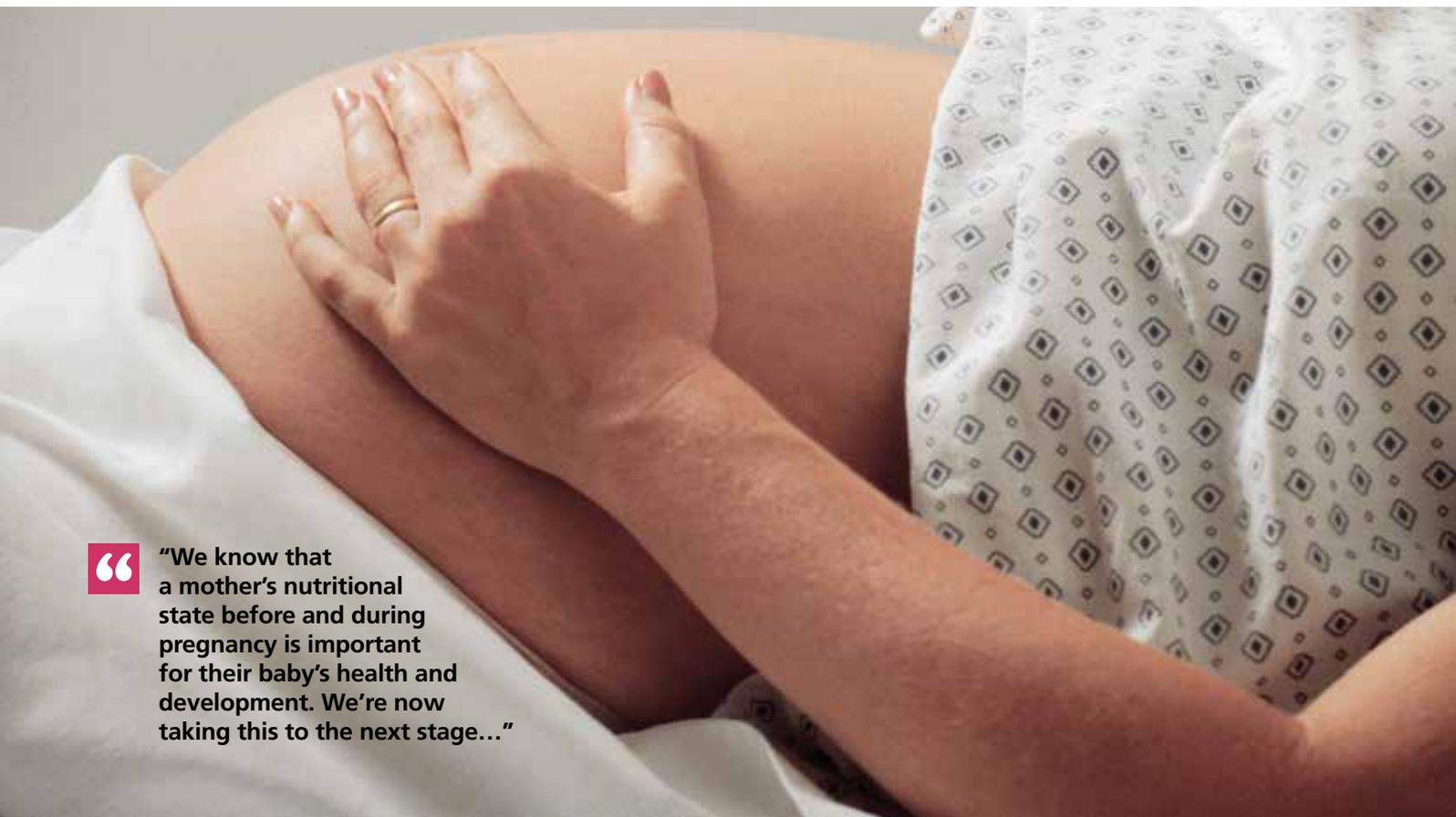
## **The best start in life**

This study also aims to look at how a mother's diet and lifestyle influences the expression of their baby's genes, and how this impacts the future growth and health of their children. By understanding this better the NiPPeR team aims to inform better nutritional advice before and during pregnancy so that babies start life healthier and are healthier throughout life.



## **Taking part**

**If you'd like to know more about the NiPPeR trial, or if you're interested in taking part, please contact the NiPPeR team on 0800 032 31 30 or email [nipper@mrc.soton.ac.uk](mailto:nipper@mrc.soton.ac.uk)**



**"We know that a mother's nutritional state before and during pregnancy is important for their baby's health and development. We're now taking this to the next stage..."**

# Help shape our research

**We want to improve our research process, our participants' experiences and make sure that our research provides maximum benefit to people's lives. We can only do this by involving people like you.**

Our patient and public involvement (PPI) officer, Kate Sonpal, works with patients and the public to soften the barriers between researchers and NHS service users to improve the process and outcome of clinical research for all.

From meeting up to discuss study ideas, to reviewing participant information and feeding back ideas on how to promote trials and their outcomes, PPI is key to underpinning future treatments and health technologies.



Kate Sonpal

## Meet a member

One of our NIHR Wellcome Trust Clinical Research Facility PPI group members, Daniel Russell, explains what made him want to take part in clinical research and why he thinks it's important to shape research in Southampton.

"I became a fully fledged PPI group member in November 2014 – so almost a year ago now – having seen a poster in the clinical research facility reception area when I was waiting for another appointment.

"My involvement has a slight asthma and respiratory disease slant to it. I live

with asthma and care for someone with the condition so I thought this could be a good way to help myself and others and find out more about asthma and respiratory diseases. And who knows, my participation could potentially help find a cure one day!

"I'm currently on a steering group for the WATCH study and I'm also involved with the myAirCoach study that will hopefully lead to new and better ways for self-managing asthma – which could benefit so many people.

"I think it's important to be able to

influence clinical research, and it's great we have the opportunity to do this in Southampton. You get to interact with senior researchers and clinicians, but most importantly, I feel my views and opinions are both listened to and welcomed by all those involved in PPI.

"If someone is thinking of getting involved, I'd say "do it". As well as having a voice and playing a part in the direction of research, you find out so many new things and hear about ideas and studies that could make a huge difference to people's daily lives and quality of life."



If you're interested in finding out more about PPI or becoming part of one of our PPI groups, please contact Kate on 023 8120 4989 or at [kate.sonpal@uhs.nhs.uk](mailto:kate.sonpal@uhs.nhs.uk).

# Trials and studies recruiting now

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## Babelfish

We're developing a new headphone-like tool for measuring pressure on the brain and need the help of healthy volunteers to identify a normal range of brain pressures before we use the headset with patients. To find out more, please contact Shannon on **023 8120 3370** or Gabriella on **023 8120 3713**, or email [ICPstudy@uhs.nhs.uk](mailto:ICPstudy@uhs.nhs.uk).

## NiPPeR

We're working to better understand how diet before and during pregnancy affects the health and development of babies, and how we can improve the health of mothers and their children – see page 10. If you're interested in taking part, and are aged between 18 and 38 and thinking of getting pregnant in the next six months, please contact the NiPPeR team on **0800 032 31 30** or email [nipper@mrc.soton.ac.uk](mailto:nipper@mrc.soton.ac.uk).

## LASER

The LASER trial, which is open for recruitment till November 2015, will assess whether a new treatment device, which operates as they sleep, will help patients with allergic asthma to reduce the frequency of asthma attacks. Anyone interested in finding out more about the study in Southampton, and how to participate, can contact the research team by calling Rachael Collings on **023 8120 8427** or emailing [rachael.collings@uhs.nhs.uk](mailto:rachael.collings@uhs.nhs.uk).

## NTHi004 COPD

For people aged between 40 to 80 years with moderate to severe Chronic Obstructive Pulmonary Disease (COP), the NTHi004 COPD study is testing a vaccine that could reduce the number and severity of chest infections and exacerbations. If you're interested in finding out more about the study, or would like to take part, please contact Sarah Bawden on **023 8120 4479** or email [sarah.bawden@uhs.nhs.uk](mailto:sarah.bawden@uhs.nhs.uk). This study will close for recruitment in November 2015.

## Synairgen Respiratory Tissue Bank

Synairgen is looking for volunteers to learn more about asthma and other chronic lung diseases to test, identify and develop new, targeted treatments. If you have mild asthma (use a blue Ventolin inhaler only) and think you may be allergic to house dust mites, and are interested in taking part, please email Joanna Samways at [joanna.samways@synairgen.com](mailto:joanna.samways@synairgen.com) or call **023 8051 2800**.

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# Let us know

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We want to hear about your views and experiences of clinical research in Southampton as well as answer any questions you may have.

To let us know what you think, to find out more about our work or to register interest in any of our research activities you can email [uhs.southamptoncrf@nhs.net](mailto:uhs.southamptoncrf@nhs.net) or call **023 8120 4989**.