



Genetics of Obesity Study

May 2019

GOOS Newsletter Spring-Summer 2019

How do I know it is time for another newsletter? The answer to this question tends to relate precisely to how busy we are as a Team, which inherently means it goes on a rather long list of “must do’s”!

I know we need to make sure you know what is going on here in Cambridge. Indeed you may have some idea already as Professor Farooqi has been talking to the media quite a bit lately. She was on TV and also speaking on lots of early morning radio slots (no need for the make-up artist for these) about our recent study into thinness. The main takeaway from this was that at last we could tell the world that weight is most certainly determined by our genes and not solely down to lack of self-control as many people would like to have us believe!

There was also quite a bit of press activity around our studies in semaphorins (read about this in our “Latest Research Highlights”) and about the time this newsletter is “published”, there will have been be some further press furore about another study featured in a very eminent journal called “Cell”. Because I know that Professor Farooqi loves a bit of media activity, I’m expecting her to refer to some of this in her spot: “News from the Professor”.

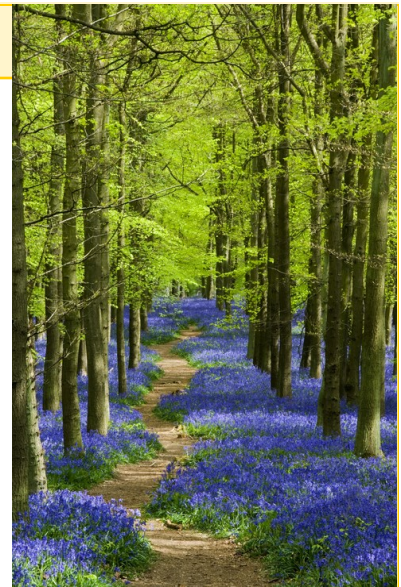
We do try to keep you up to date via our website (goos.org.uk). Actually, it came as a bit of a shock to me to realise that our website has been live for 7 years now and when I looked at it recently I thought it looked a bit dated and tired, rather like how I feel! So we are in the process of giving it a bit of a revamp, so keep looking and tell us what you think. Also, if you didn’t get to hear or listen to what our Professor had to say about thinness, just visit our “[media centre](#)”.

As you will see on the website, we have also taken rather a big step and joined the “Twitter” community. So keep looking at our website and let us know how you are doing!

As always, the message is “Keep in touch”!

That’s all for now

Julia



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News From The Professor

In the last few months we've managed to publish a number of research findings that have significantly advanced our understanding of why some people gain weight more easily than others.

Firstly, we published research on the genes involved in thinness, which showed for the first time that some people who find it easy to manage their weight, have particular genes that allow them to stay thin. They also have fewer of the genes that drive others to gain weight. Effectively they are lucky on two fronts! Some of you will have seen and heard a lot of the media attention that this research received. It was very hectic, but we were filmed by both the BBC and ITN for the News at 10. I took part in many radio programmes and spoke to many newspapers, including the Times, The Independent and the Daily Mail! The information was also rapidly communicated through Twitter which of course allows us to reach different audiences.

Overall I think the way the research was conveyed was really positive - people could readily identify with others that they know who seem to eat what they like and not put on weight. These research findings allowed us to show that this tendency is all about biology and not about greater willpower.



I really hope that this kind of research can help to change some of the attitudes that people have towards people who do suffer with their weight. Importantly we have communicated this to MPs in Parliament and people involved in tackling societal attitudes towards weight problems.

More recently there were two other major publications of research, one from our group and one from a group in the America. These research findings are based on a very large research study called UK Biobank, you may have heard of this. Essentially, a few years ago, a group of researchers in the UK worked together to recruit a cohort of people – in fact half a million people – who volunteered to give a blood sample and some information about themselves. By volunteering for this study, they have helped researchers all around the UK to make significant breakthroughs in our understanding of health and medical conditions.

News From The Professor (cont.)

We were able to look at the **MC4R** gene, a gene that we have shown can cause weight problems when it is not working or switched off. We were able to show that some people in UK Biobank have changes in this gene that seem to **protect them from gaining weight**. We then conducted some tests in cells which showed that these genetic changes keep the **MC4R** gene switched on.

Together these studies drive home the fact that genetics plays a major role in why some people gain weight while others are fortunate enough to have genes that protect them from weight problems.

Finding those genes and the pathways they control remains a major goal for us as we may then be able to find ways to help people. The work on the **MC4R** gene has opened up a new area of research for us and for many groups around the world. We are now pushing forward to see if we can use this information to design better treatments for the future.

One of the genes that we have discovered called **SRC-1** seems to dial up signals in the brain that tell you that you are full. If people have a faulty gene, they don't feel full and don't burn calories easily, so gain weight. A lot of people with a faulty **SRC-1** gene have recently been coming up to Cambridge for clinical studies. With their help we've been able to make some breakthrough findings which we are now trying to put together.

We'll keep you posted on our discoveries. We think this is an exciting time with a lot of new information to come and hopefully we'll be in a strong position to take some of this information forward to help people.

Professor Farooqi

Latest Research Highlights

Sending appetite signals in the brain

It is true that the increase in obesity worldwide has been driven by changes in how we live today. We have easy access to food, some loaded with calories, and on the whole we are far less active both in our work and in our leisure time. But we know that there is a wide variation in people's weight even when they live in the same environment, in fact, even between people in the same family. We have shown that this is down to a person's genes.

In this study, we showed that some genetic changes can actually disrupt connections in the brain that pass on messages or signals about our appetite. When these brain connections are disrupted by faulty genes, this can have an effect on body weight.

During the brain's development, over a 100 trillion connections are made between brain cells (neurones). Rather like a "roadmap" these connections follow a precise "route" and there are many "signposts" along the way. One group of such "signposts" in our brains are called **semaphorins**.



These semaphorins guide the "wiring" of the part of the brain that controls our appetite and metabolism (how we use the food that we eat), called the hypothalamus. We found rare genetic changes (variants) in the semaphorin genes and investigated their function in multiple ways in the laboratory. We could see that some of these genetic variants reduced the ability to guide brain cells precisely to their destination in the hypothalamus.

Currently we have no treatment for this condition and it will be difficult as the brain connections to their target areas (or destinations) are mostly made before we are born. However, if we can find out precisely which connections in the hypothalamus are wrongly wired, we will understand more about our brains and this will help us to work on future therapies.



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