



Genetics of Obesity Study

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GOOS Newsletter

Summer 2015

I really hope that when you read this newsletter, the sun is shining and we can all look forward to a wonderful summer! It seems that a lot of people are now looking at our website which is very gratifying.

We recently added a further information leaflet for our patients and families who have a problem with the SIM1 gene. Hopefully you will find it helpful. We welcome your thoughts and views as it is quite difficult to know if we have covered the things you want to know about.

We are always asking you to keep in contact with us and it has been great to hear from many of you, especially those of you who were children when you first came to see us here in Cambridge. Some of you have come back to help us with further studies, others have told us about weddings and babies. Sometimes of course, the news is not so good. So thank you, it is important that we know where you all are, how you and your family are getting on.

For some time now, people have been trying to persuade us that "social media" is the way forward. We have been hesitant, concerned that many people have such negative views about people who have weight problems, thinking that it is all down to the individual and they need to change their ways! You know the sort of people I'm talking about! Excitingly, one of our MC4R patients has set up a Facebook group for patients and families with an MC4R gene problem. It is a "private" group, you will need to request to join but you can now search for the group on Facebook or use the link below:

<https://www.facebook.com/groups/>

[MC4Rpatientandfamilysupport/](https://www.facebook.com/groups/MC4Rpatientandfamilysupport/)

Quite a few of you have let me know that you have joined the group and have appreciated the chance to talk to others. I would personally like to use this opportunity to say a big thank you to a rather special MC4R patient of ours who went to the trouble of setting this up for others. You know who you are! We have been in touch for a good many years now and you have supported our work in many ways throughout that time. Let's keep on working together, all of us, supporting and informing each other.

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SPECIAL POINTS OF INTEREST

Facebook Support Group

Update on Trial of Treatment for MC4R Deficiency

We don't have any further news with respect to this Trial at present. Disappointing as this is, we realise that a "treatment" is what you want to hear about and what underpins our future work. This is why Professor Farooqi wanted to use this opportunity to update all of you on where we are going with our research and the challenges ahead, so please read on!

News From The Professor

Finding new medicines for weight loss

I thought I would take this opportunity to update you on one of the major things we are working on - the search for new medicines to help people lose weight.

We know there are a lot of people who struggle with their weight. Whilst diet and exercise can help those with a small amount of weight to lose, it can be very difficult to lose a lot of weight in this way. So medicines or surgery are often an option for people with a lot of weight to lose. But, there are only a few different medicines available and they don't work for everyone. Why is that the case? What can we do about it?

The Challenges - finding the right targets

To make effective treatments for any medical condition, you need to know quite a lot about the underlying problem. For example, to find good treatments for diabetes, doctors and scientists had to first work out how the body makes insulin and how insulin works in the body to handle sugar levels during the day and night, when people eat different foods and when they exercise. Researchers were then able to find out which of these steps were not working properly in people with diabetes. These studies led to the discovery of suitable "drug targets". Researchers continuously publish their work in scientific and medical journals so that information is shared and so people can build on the work of others. Pharmaceutical companies then pick up on these targets and see if they can use existing medicines or design new medicines that will switch off/switch on/fine tune the process underlying the medical condition. This final step - making a medicine that is effective and safe without too many side-effects - can often take years of work even if you know the right "target". Once a drug is made, the companies seek permission from National and International regulatory bodies to perform clinical trials in healthy volunteers to work out the right dose and then in patients with the condition.

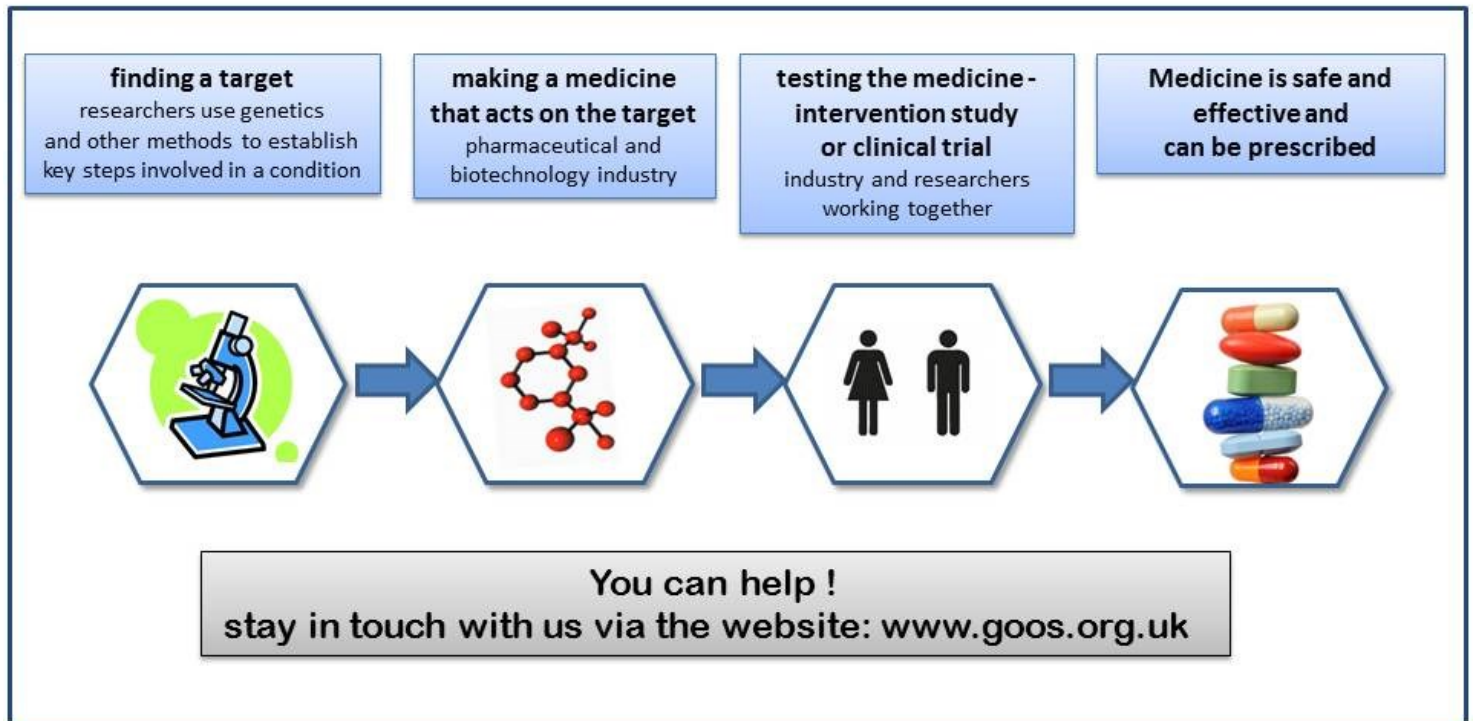


So how much do we know about weight problems and potential targets?

Well, we know quite a bit. The first discoveries were made 20 years ago with the discovery that the hormone leptin regulates our body's system for controlling weight. Since that time we and others have identified more than 100 potential targets that seem to be important. We have played a major role in this International effort by proving that some of these targets are especially important, as disrupting them causes people to gain weight. We have published our findings and now many groups around the world are working on these targets. They keep in touch with us regularly, updating us on their progress, asking for our input and advice. Sometimes, their researchers come to Cambridge to work with us and to strengthen ties between groups working towards a common aim.

So when will these discoveries lead to new treatments?

It is difficult to know the answer to this question, as this work can take a long time. But there is a lot of work going on and the advent of new technologies and more cooperation between researchers and the Pharmaceutical industry certainly helps to move things along. We are in regular discussion with several of the World's leading companies so we can influence this work.



Is there anything else we can do to help with the development of new treatments?

Yes, there is. Over the last couple of years, the more we talk to companies, the more we have learned about what they need to take a target and make it into a safe medicine. They need information about weight problems, particularly when they are caused by specific genes and there are several things that we can do to help with that:

1. How do certain genes lead to weight problems when they are faulty?

Many people come to Cambridge to help with our studies. These studies have been vital in teaching us how genes work and how targeting these genes could help weight loss. This work can also tell us about possible side-effects that companies need to look out for.

2. What sort of problems do people with these gene problems have?

We need to know how gene problems affect people over many years. Some people don't have any problems, others develop diabetes or high blood pressure. Some problems can be apparent from a young age, but others become clear later on in life. By understanding these conditions, we can make a case for developing treatments. Ultimately, the companies and the regulatory agencies want to know how new medicines will help people. It seems pretty obvious, but we need to provide the facts and figures and for that we need your help. We need to know how you are getting on and if you have any new medical problems or have had major operations.

3. How do people with gene problems respond to specific diets, or to exercise, or when they have surgery or are treated with certain medicines?

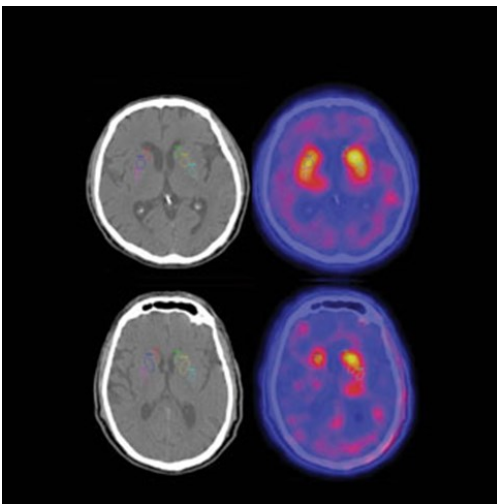
This is an area we haven't looked at much as yet, but something we are planning to do. We will be approaching people to see if they want to take part in longer "intervention studies" to help weight loss. These studies might last for several days or weeks and could involve a trial of a new medicine, or a particular type of hormone. By testing people before and after giving them the "intervention", we want to learn how peoples' bodies respond and why some people respond better than others. This kind of information is invaluable as it will inform the design of new "smarter" medicines based on real knowledge about people (rather than predictions).

So, there is lots going on and we are right at the heart of new developments into weight loss medications. As always, we continue to need your help and active involvement, so do keep in touch, let us know if you move, and let us know if your medical condition changes.

We will keep you posted on our research and will let you know about new studies!

Latest Research Highlights— Dopamine and food choices

One of the things we are interested in working out is how certain chemicals in the brain are released when we are hungry or when we see food we like. One of these chemicals is dopamine, which has been linked to sensations of pleasure or reward. We wanted to see whether the release of dopamine in the brain is related to our food choices.



For this study, Nenad Medic, one of our young scientists studying for a PhD, used functional magnetic resonance imaging (fMRI), a technology we have talked about in one of our previous newsletters. This enables us to see which brain regions are activated, or 'light up', when people are asked to do a specific task while they are having a brain scan. We know from the research of other groups, that when people are asked to make choices (do you like the iPad more than the book?) when lying inside the MRI scanner, certain brain areas light up. The more you like something, the more these brain areas light up. So our brains 'compute' how much value we place on things which then influences what we choose to do.

In this study, we looked at how the brain processes the value of foods and whether the chemical dopamine might have a role in regulating our food choices. We asked some volunteers to take tablets which briefly increased or decreased the effects of dopamine on brain activity, which we monitored while they were lying in the MRI scanner. At the same time, people were presented with pictures of foods and asked to rate how much they valued them. In this way, we were able to study the effects of dopamine on the ability of the brain to compute the value of certain foods (how much would you pay for a bar of chocolate, for example?). Interestingly, we found that increasing dopamine levels resulted in a more accurate estimate of the values of foods, whereas, reducing dopamine in the brain led to a more variable response. It seems that dopamine give us a clearer picture (like increasing the resolution of a photo or fine tuning the radio reception) of which food option is more valuable to us, which might then influence our food choices.

We hope that these kinds of studies, which lead to a better understanding of how our brains control food choices, will reveal some strategies that we can use in helping people with weight problems.

Let us know what you want to see on our website and in our newsletters.

Visit GOOS at www.goos.org.uk to meet our team and learn more about our work.

Or email us at info@goos.org.uk to stay up-to-date with what we're doing and how you can get involved.

If you would like to know more about our new studies, contact us at info@goos.org.uk



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