**The Wellcome Trust Type 2 Diabetes Genetics**
**Case-Control Collection-A Study of Lifestyle and Genes**

## WHY DO PEOPLE GET TYPE 2 DIABETES?
## A STUDY OF LIFESTYLE & GENES

**Professor Andrew Morris** , who led the Wellcome Trust Study, said "*The research has put Tayside on the map in becoming a flagship collection for the treatment of diabetes and related conditions and it was recently cited in the House of Lords Report on Genomic Medicine to be an example of best practice."*

Welcome to our newsletter.

The Wellcome Trust Study team was set up in 2004 to create an international resource to help define the genetic and environmental causes of diabetes. We would like to thank you for all your invaluable help and continued support. We would also like to take this opportunity to update you on the progress of the Resource and our plans for the future.

**Study Recruitment Update:**
Recruitment for the Wellcome Trust Case Control study is now complete and the systems are also in place to manage this invaluable Resource. Tayside is an ideal location for this study because of the advanced system of computer based long-term follow-up of patients. This system is underpinned by the use of the unique patient identifier, the Community Health Index number, the CHI, for healthcare activities in Tayside. As well as the information gathered at the time of participation, we have consent from each participating patient to anonymous follow-up using this system.

Recruitment started in October 2004 and since then we have enrolled an amazing 16,000 volunteers. Half of the people who helped us out have type 2 diabetes and half are free of diabetes. Over the last 4 years, our team of research nurses has been working hard recruiting volunteers throughout the region and the help and support that we have received from the hospital clinics, general practices and work places has been tremendous. The response from the people in Tayside has been very positive and the comments that we receive show that there is a great willingness from both patients and healthy individuals to help with research into diabetes. Every volunteer recruited has made an invaluable contribution to this international resource.

**International Resource**
Subject to appropriate permissions and regulations, researchers from institutions world-wide have access to this anonymous resource produced from this population study. There is nothing comparable in the rest of Europe and US, and researchers from as far as Spain, Sweden, Japan, Denmark, France, and Harvard and Chicago in the US supported its creation, in recognition of its unique properties.

**What do people say about the study?**
*"The outstanding longitudinal tracking you have in place will add considerable information once susceptibility variants are described. There is no doubt that a resource like this is desperately needed as the absence of robust large case controls is holding back progress in defining the genes in Type 2 diabetes. I would be very keen to use this resource."* - **David Altshuler, Professor of Genetics and Medicine at Harvard Medical School Boston**

*"Your programme of work is at the forefront in the UK demonstrating the power of the academic and clinical use of electronic data from patients. The work you have undertaken on diabetes is outstanding and enabled your key contribution to the recent work on the genetics of diabetes, as a participant in the Wellcome Trust*

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*Case Control Consortium. The papers recently published from this study have been widely applauded."* - **Mark Walport, Director and Chief Executive, Wellcome Trust**

**Bridget Shepherd**, who led the research team said "*the comments that we receive from participants show that there is a great willingness from both patients and healthy individuals to help with research into diabetes. Every volunteer recruited has made an invaluable contribution to this international resource."*

**What Have We Found?**

This high quality international resource is already helping to define and characterize genetic factors related to type 2 diabetes and a rapidly growing number of published papers are leading to other research being carried out on diabetes and related conditions.

A good example is the discovery of a common variant in the FTO - fat mass and obesity associated - gene (dubbed the "fat gene" or "pie gene" in some tabloid papers!) which is associated with BMI – Body Mass Index - and predisposes to childhood and adult obesity. The initial discovery of this gene for obesity and type 2 diabetes resulted from an international collaborative effort which included the Tayside Case Control Study as a pivotal component and was published in *Science* in 2007. Professor Palmer's latest study of the FTO gene, published late last year, provoked widespread media interest when it found that Tayside primary-school children with the common form of the gene ate 100 more calories in an eating test than other children. The research, which was published in the prestigious *New England Journal of Medicine,* measured the metabolism, fat composition, exercise and eating behaviours of 100 primary school children in Tayside. It found that children with the FTO gene were more likely to choose higher calorie food. The results suggested that the FTO gene seemed to affect what the children were choosing to eat. More work needs to be done to find out why this is the case.

A further example is a study also involving the Tayside Case Control Study which has found a genetic link between sleep patterns and type 2 diabetes. Too little sleep has been linked with susceptibility to type 2 diabetes. Melatonin is an important hormone involved in determining sleeping patterns and is used to treat jet lag, but has never been previously linked to type 2 diabetes. In a recent edition of *Nature Genetics*, we have described how changes in the melatonin receptor affect susceptibility to type 2 diabetes.

Work on pharmacogenetics, the study on how genetic information may be used to personalize medicine, has shown that people with a particular gene variant respond poorly to one of the most common types of diabetes treatment, sulphonylureas. Although this genetic test has now been made commercially available by other groups further investigation is needed to determine how we might improve the test using much more genetic information before we use it in clinical practice in the UK.

The Tayside Diabetes Genetics Research Team is also investigating the genes involved in defining whether an individual can tolerate the use of statins. The research has already shown that there is a gene which predisposes individuals to having complications such as muscle pain and damage. The initial results have led to a large-scale effort to find these genes in statin response and intolerance.

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**Professor Colin Palmer** who co-ordinated the laboratory team said *"We have been overwhelmed by the support and enthusiasm of the people and their willingness to help out – the response has been unprecedented. I am delighted that we exceeded our target of working with 15,000 people in Tayside."*

Over the last few years, the anonymous data and samples that have been collected from willing volunteers in Tayside are contributing to major new insights into genetic factors involved in diabetes susceptibility, outcomes in diabetes such as cardiovascular disease and how people with diabetes respond to a wide variety of drugs. This increased knowledge will undoubtedly contribute in the future to improved management of patients with diabetes. The resource is enriched by the availability of anonymous detailed long term clinical follow up that is available in Tayside. The Genetics Consortium oversees and manages access to this resource. Already 24 papers have been published using the data collected.
Details can be found on our website. .http://diabetesgenetics.dundee.ac.uk

**The Way Forward:**
This international resource will continue to be invaluable over the years and indeed will become more powerful with time. It will help us to discover how to reduce the risk of complications, how we can use existing treatments more effectively, and how to shift the emphasis away from the current one medicine for all approach to medicines tailored to treat the individual. Combined with the staggering pace of technological progress we are excited about the potential for revealing new genetic tests for drug response.

The ethics committee has approved continued collection into this invaluable resource so we will be out and about in Tayside and Fife again soon.

**Study Website:**
Our study website includes contact details of the team, information on the data collected, our Standard Operating Procedures, the access policy and links to papers published to date.
https://crs.dundee.ac.uk

Any queries or comments please contact:


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