

# A complex story behind genes, environment, diabetes and obesity

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While it is well known that there is a strong genetic basis to both diabetes and obesity, and that they are linked, Australian researchers say that there are many rare genetic variants involved, which will pose a significant challenge in the quest to develop effective therapies.

Type 2 diabetes is a [metabolic disorder](#) that occurs when the body becomes less able to produce and use insulin effectively, a hormone essential for maintaining normal metabolism of food. The disorder is commonly associated with a high-sugar, high-fat diet combined with lack of exercise.

A new study by Professor Lesley Campbell, Director of Diabetes Services at St. Vincent's Hospital and a senior member of Garvan's Diabetes and Obesity Clinical Studies group, in collaboration with Dr Arthur Jenkins and coworkers from the University of Wollongong, shows that many different defects in overweight or obesity [genes](#) are involved, most of which are very rare. The findings are published in *PLOS ONE*, now online.

Over the last 25 years, Professor Campbell has gathered detailed information about over 300 healthy people with a family history of type 2 diabetes, including their [body shape](#), size and composition (using Dual-energy X-ray absorptiometry to obtain [accurate measurements](#)). Specifically, her research looks at people who are genetically at risk of developing type 2 diabetes and are overweight or obese before they get the disease.

The information gathered by Professor Campbell was analysed by Dr Jenkins using a specially constructed mathematical model. He concluded that many genes are responsible for obesity, with each affected family likely to tell a slightly different genetic story.

"We can see that there are many, many different ways in which the system can go wrong, with more variety than commonality," said Dr Jenkins.

"In my opinion, the current quest to develop a single anti-[obesity drug](#) is misguided – because there are too many potential problems to be targeted by a single drug, or indeed any small number of drugs."

"It's likely that the same is true of [type 2 diabetes](#). The underlying cause is genetic and the genetic causes are very rare, but there are many differences between people."

"Rare genetic defects account for something like 95% of the total problem. That is a very unwelcome fact for most people, who would like to think an easy solution is close at hand."

Professor Campbell stresses that genes bring out underlying predispositions, and there are fairly predictable interactions between genes and environment. So if people are predisposed to a strong appetite, large amounts of easily available, highly palatable, food are likely to make them fat.

"The reason we see so many people getting fat is that they carry strong hunger genes while the environment is maxed; it's an obesogenic environment that rewards eating," said Professor Campbell.

"People no longer have to go fishing, or hunting and gathering in order to eat. They just go to McDonalds, or KFC, or the freezer. The point is

that people don't have to expend any energy to get an abundance of food, often high in fat or sugar."

"We have shown in previous studies that people with [diabetes](#) in the family tend to be hungry more often, are able to eat more at a sitting, and will generally opt to eat high calorie foods. This does not mean they are 'greedy', it just means that their bodies are genetically driven to eat more."

"The same genes would serve these people well in times of food scarcity or famine. They would survive, while their leaner neighbours would perish."

Provided by Garvan Institute of Medical Research

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