

Article in *The Times* Thursday 29.12.05

Why our fatty diet leads to diabetes

By Sam Lister, Health Correspondent

FATTY diets that involve large amounts of meat and dairy products encourage diabetes by disrupting the work of a single gene responsible for insulin production, scientists have found.

Researchers at the University of California, San Diego (UCSD) School of Medicine have pinpointed for the first time a molecular link between the high-fat diet common in the West and type 2 diabetes. They hope that it will offer new ways to treat the condition.

The number of people with diabetes in Britain has risen in the past decade from 1.4 million to more than two million. Of these, the vast majority — about 1.7 million — suffer from type 2 diabetes, the most common form of the disease, which is thought to be linked to lifestyle. A further million people are estimated to be living with the chronic condition, as yet undiagnosed.

Type 2 diabetes is often associated with insulin resistance, when the body ceases to react properly to insulin. It can increase greatly the risk of a host of serious and potentially life-threatening conditions, including heart disease, stroke, nerve damage and damage to organs and eyes.

The new study, published in the journal *Cell*, shows that a single gene responsible for encoding an enzyme known as GnT-4a is a key to enabling beta cells in the pancreas to detect blood glucose levels and trigger the production of insulin when appropriate.

The researchers demonstrated in tests on mice that this enzyme is suppressed by a high-fat diet. Without enough GnT-4a enzyme, pancreatic cell failure occurs, resulting in type 2 diabetes.

Western-style diets, followed by most people in North America and Europe, consist mainly of processed foods, red meat, dairy products, refined carbohydrates, food additives, junk foods, fast foods and snacks with a high sodium, sugar and saturated fat content. By contrast, the Asian diet is relatively low in meat and dairy foods. Protein and iron are obtained from nuts, seeds and legumes, iron through vegetables such as dark leafy greens, and calcium from soy products, nuts, seeds and leafy vegetables.

More than 200 million people worldwide have been diagnosed with type 2 diabetes, close to 20 million of them Americans. In Britain, doctors' leaders have given warning that one Briton in ten can expect to have diabetes by 2010, mainly as a consequence of the growing obesity problem.

While it is widely recognised that type 2 diabetes is related directly to a high-fat diet and excess weight, until now researchers had not been able to discover why.

Jamey Marth, UCSD Professor of Cellular and Molecular Medicine, and researcher with the Howard Hughes Medical Institute, said that the discovery could have a significant impact on future research. "We have discovered a mechanistic explanation for beta cell failure in response to a high-fat diet and obesity, a molecular trigger which begins the chain of events leading from hyperglycaemia (elevated blood glucose levels) to insulin resistance and type 2 diabetes. This finding suggests new approaches to the prevention and treatment of diabetes."

The research team made the discovery by studying glycosylation, the process that controls the linkages between sugars, proteins and enzymes such as GnT-4a. The key role of the GnT-4a enzyme is to maintain glucose "transporters" in place on the surface of the pancreatic cell to sense glucose levels in the blood. When glucose is elevated after a meal, the transport of glucose by these transporters triggers the beta cell to secrete insulin. Proper insulin secretion is essential to enable the rest of the body to metabolise glucose and convert it to cellular energy.

"Our findings suggest that the current human epidemic in type 2 diabetes may be a result of GnT-4a enzyme deficiency," Professor Marth said.

A spokesman for the charity Diabetes UK hailed the research. "One thing we do know is that the main factor driving type 2 diabetes is lifestyle — diet and lack of exercise," he said. "If we are able to pinpoint what's behind the diet element then this would be a significant breakthrough."