Gene provides a link between lower birth weight and type 2 diabetes

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Two genes have been identified which are associated with lower birth weight.

New research uncovers two genetic regions that influence birth weight. One of the regions is also associated with type 2 diabetes, which helps to explain why small babies have higher rates of diabetes in later life.

A large international team of researchers, including scientists from several UK and international centres, has discovered two gene regions that affect a baby's size at birth. The research, published in Nature Genetics, is the first robust evidence that a well-known link between lower birth weight and susceptibility to type 2 diabetes has a genetic component.

The study was funded by the Wellcome Trust, the Netherlands Organisation for Scientific Research, the European Union, the Medical Research Council (UK), the Academy of Finland and the National

Institute of Health (USA).

The team analysed over 38 000 Europeans from 19 studies of pregnancy and birth. Two genetic variants showed strong associations with birth weight. One of the variants, in a gene called ADCY5, has recently been linked with susceptibility to type 2 diabetes. Individuals who inherit two risk copies of this variant are at a 25 per cent higher risk of diabetes in adulthood than those who inherit two non-risk copies. This latest study shows that they also weigh less at birth.

This is a key finding because it has long been known that lower weight babies are more at risk of type 2 diabetes in adulthood, but it was not clear why. Much research has focused on the role of the womb environment. It is widely believed that the mother's nutrition can influence both the growth of her baby and its later risk of disease, a process known as "programming". However, this latest research confirms that genes are also important.

Dr Rachel Freathy, a Sir Henry Wellcome Postdoctoral Fellow at the Peninsula Medical School, Exeter, commented: "Our study shows that genes are part of the reason why babies born with a lower birth weight are more at risk of type 2 diabetes 50 or 60 years later. It is now important for us to establish how much of the association is due to our genes and how much is due to the environment because this will inform how we target efforts to prevent the disease."

The combined effects of the two identified gene regions are quite substantial. Nine percent of Europeans inherit two copies of a genetic variant in each region and are, on average, 113g lighter at birth than the 24 per cent who inherit one or no copy. This effect is equivalent to the birth weight reduction caused by a mother smoking four to five cigarettes per day in pregnancy.

Mark McCarthy from the University of Oxford who was one of the leaders of the research, said "It was a surprise to see such strong genetic effects for a characteristic, such as birth weight, which is subject to powerful influences from so many environmental factors. These discoveries provide important clues to the mechanisms responsible for the control of growth in early life and may lead us to a better understanding of how to manage growth problems during pregnancy".

Dorret Boomsma, Professor in the Department of Biological Psychology at Vrije University, Amsterdam, commented: ""These findings illustrate that genetic research can help resolve the complex chain of causality underlying the association between early life course and later health outcomes.""

Marjo-Riitta Jarvelin, Paediatrician and Professor in Lifecourse Epidemiology at Imperial College London and one of the leaders of the research, said: "We have, for nearly two decades, tried to discover the factors which may explain why smaller fetal size associates with so many later life chronic conditions such as heart disease. We have known for a long time that fetal growth is genetically influenced on the basis of family and other population studies but the question has been where these markers are hiding? Also our own studies have demonstrated that a number of environmental factors influence fetal growth and that some fetuses are more vulnerable to those than the others. I believe that our genetic landmark discoveries will give us opportunity to answer these puzzling questions in the near future."

Dr Iain Frame, Director of Research at leading health charity Diabetes UK, said: "This research adds exciting further evidence supporting the idea that low birth weight and Type 2 diabetes are linked in some cases and will no doubt provide important clues about the development of Type 2 diabetes in the future. It is another excellent example of the importance of genetic studies in helping us understand complex

scientific issues and hopefully produce new methods to prevent conditions like Type 2 diabetes developing."

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