

How poor maternal diet can increase risk of diabetes -- new mechanism discovered

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Researchers have shown one way in which poor nutrition in the womb can put a person at greater risk of developing type 2 diabetes and other age-related diseases in later life. This finding could lead to new ways of identifying people who are at a higher risk of developing these diseases and might open up targets for treatment.

The team, from the University of Cambridge and the Medical Research Council (MRC) Toxicology Unit at the University of Leicester, publish their findings today in the journal <u>Cell Death and Differentiation</u>.

The research shows that, in both rats and humans, individuals who experience a poor diet in the womb are less able to store fats correctly in later life. Storing fats in the right areas of the body is important because otherwise they can accumulate in places like the liver and muscle where they are more likely to lead to disease.

Professor Anne Willis of the MRC Toxicology Unit at the University of Leicester explains "One of the ways that our bodies cope with a rich modern western diet is by storing excess calories in fat cells. When these cells aren't able to absorb the excess then fats get deposited in other places, like the liver, where they are much more dangerous and can lead to type 2 diabetes."

The team found that this process is controlled by a molecule called miR-483-3p. They found that miR-483-3p was produced at higher levels in individuals who had experienced a <u>poor diet</u> in their mother's wombs



than those who were better nourished.

When pregnant rats were fed low protein diets their offspring had higher levels of miR-483-3p. This led to them developing smaller <u>fat cells</u> and left them less able to store fats in adulthood. These rats were less likely to get fat when fed a high calorie diet but were at a higher risk of developing diabetes. Rats are known to be a good model for studying human dietary diseases and the team also found that miR-483-3p was present in elevated levels in a group of people who were born with a <u>low birth weight</u>.

Dr Susan Ozanne, a British Heart Foundation Senior Fellow, who led the work at the University of Cambridge, adds "It has been known for a while that your mother's diet during pregnancy plays an important role in your adult health, but the mechanisms in the body that underlie this aren't well understood. We have shown in detail how one mechanism links poor maternal diet to diabetes and other diseases that develop as we age."

Dr Ozanne and Professor Willis and their team found that miR-483-3p works by suppressing a protein called GDF3. When they studied a group of adult humans who were born with a low birth weight, they found that GDF3 protein was present at around only thirty percent of the levels found in people born at a normal weight.

Professor Willis, Director of the MRC Toxicology Unit, adds "Improving people's diets and encouraging exercise is clearly the best way to combat the epidemic of diabetes and diet-related disease which is sweeping through our society. However some people are at particular risk of these diseases, despite not looking visibly overweight. This research will hopefully allow us to help these people to take precautionary steps to reduce their likelihood of developing type 2 diabetes."



Professor Douglas Kell, Chief Executive of BBSRC said "People are continuing to live ever longer and healthier lives thanks to improvements in nutrition and healthcare. However modern diets and lifestyles are posing new challenges to which our bodies sometimes seem poorly adapted – and this has caused unforeseen health problems.

"If we are to remain healthy throughout our lives and into old age it is vital that scientists work to understand our fundamental biology in the context of social and environmental changes. By identifying a mechanism that links <u>maternal diet</u> to diabetes this research has made an important contribution to the fight against a growing epidemic of metabolic diseases."

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