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The impact of maternal obesity and weight loss during the periconceptional period on epigenetic regulation of insulin signaling in liver and skeletal muscle of the offspring

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We have used an embryo transfer model in the sheep to investigate the effects of exposure to either maternal obesity or to weight loss in normal and obese ewes preceding and for one week after conception on the expression and abundance of insulin signalling molecules in the liver and skeletal muscle of the offspring at four months of age. We found that exposure of the oocyte/early embryo to maternal obesity and/or dietary restriction and weight loss resulted in differential effects on expression of molecules involved in these metabolic networks in these insulin sensitive tissues. Importantly, maternal dietary restriction in obese ewes was mostly unable to abolish the effects of maternal obesity. Moreover, dietary restriction itself resulted in a suite of changes, which could negatively impact metabolism in the offspring. We also found that some of these changes were potentially the result of underlying epigenetic modifications, which occurred in the oocyte/developing embryo and persisted into postnatal life. In conclusion, we have shown that the periconceptional period is a developmental window that is sensitive to programming by the maternal metabolic milieu. Both a high and low maternal pre-pregnancy weight as well as the maternal metabolic response to dietary restriction each appears to increase the risk for development of insulin resistance and potentially Type 2 Diabetes Mellitus in the offspring. Importantly, we have shown that weight loss in overweight/obese women prior to becoming pregnant is not a straightforward solution to stopping the 'intergenerational cycle' of obesity and insulin resistance.

Biography

L M Nicholas recently obtained her PhD from the University of South Australia. Her research focused on the impact of maternal obesity and weight loss during the periconceptional period on development of the metabolic system of the offspring with a particular focus on the insulin signalling and insulin-like growth factor systems in liver, skeletal muscle and adipose tissue. She also determined the possible epigenetic mechanisms that are recruited in the oocyte/early embryo, which contribute to changes in these systems. She is currently a post-doctoral researcher at the Lund University Diabetes Centre in Sweden.

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