Title: The developmental origins of pediatric type 2 diabetes and early renal dysfunction

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Summary:

Childhood-onset type 2 diabetes (T2D) is associated with high rates of early-onset, progressive kidney disease. With increasing numbers of children diagnosed with T2D, more infants are born having been exposed to maternal pre-gestational T2D diabetes in the womb (in utero). Consequently, we now know that T2D exposure in utero is a potent risk factor for the development of childhood-onset T2D; however, it is not yet known how T2D exposure increases offspring risk or if it increases the risk of associated renal complications. Recent scientific advances have revealed that the maternal in utero environment can alter the expression of genes in the offspring via a process called epigenetic regulation, which impact important metabolic pathways needed to maintain health. In addition, a specific change in the DNA sequence (HNF1a gene variant) appears to be associated with childhood onset T2D risk. In this study, we aim to define the mechanisms by which exposure to T2D in utero and the G319S variant impact how the beta cells of the pancreas and the nephrons in the kidney develop and function and to determine the role of epigenetic programming in transmitting risk from in utero T2D exposure to b cell and kidney dysfunction.

Upon completion of this study, we hope to better understand how maternal diabetes exposure and the HNF1a gene variant impact the health of the pancreatic beta cells and the kidneys in the infants, to identify markers at birth that identify which children are at highest risk of developing T2D, and to inform the development of new treatments to prevent T2D and renal complications in exposed children.