Diabetic Complications Consortium

Application Title: **The epigenome maps of human diabetic kidney disease**

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1. Project Accomplishments:

Goals: Map chromatin modification patterns (H3K4me1/2/3, H3K36me3, H3K27me3, H3K27ac and CTCF) and gene regulatory regions in (A) **normal human** kidney cortical tubule cells (n=5) and (B) in patients with **stage 2 diabetic CKD** (n=5), DM (n=5) or HTN (n=5) but no detectable renal disease and (C) compare gene regulatory region in control and **stage 2 diabetic CKD** (GFR range 60-90 cc/min) (D) understand the **association between epigenetic modifications and transcript levels and downstream clinical and histological phenotype in patients.**

Accomplishments: We have collected more than 40 human kidney samples, including more than 5 from subjects with diabetes, 5 controls 5 from patients with hypertension and 5 with diabetic kidney disease. Samples have been cross-linked and sonicated into 200 bp fragments. Chromatin immunoprecipitation has been performed with 7 different histone tail antibodies. The precipitated DNA from the first sample has been submitted for Next Generation Sequencing analysis. We are in the process of analyzing the results. Our initial scan indicates that the results obtained with CTCF and H3K4me2 are not optimal, while the other5 antibodies indicated high quality ChIP enrichment.
At present we are examining different batches of CTCF and H3K4me2 antibodies and we are performing the ChIP analysis on the additional kidney samples using antibodies that already showed good quality results.

We have asked for a 1-year no-cost extension on this grant to complete the remaining ChIP experiments and analyze the results.

Specific Aims:

The hypothesis of the proposal is that epigenetic changes **play key role in diabetic kidney disease development. Here we propose to** map chromatin modification patterns (H3K4me1/2/3, H3K36me3, H3K27me3, H3K27ac and CTCF) and gene regulatory regions in (A) **normal human** kidney cortical tubule cells (n=5) and (B) in patients with DKD (n=5), DM (n=5) and HTN (n=5) but no detectable renal disease and (C) define differences in stage 2 diabetic

CKD (D) understand the **association between epigenetic modifications, transcript levels and downstream clinical and histological phenotype development in DKD.**

2. Publications:

None yet.