Diabetic Complications Consortium

Application Title: A screen for transcription factors that can induce transdifferentiation of the stroma

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1. Project Accomplishments:

We have generated a library of lentiviral vectors for all of the transcription factors of interest and have begun screening for pools that are sufficient to convert fibroblasts to nephron progenitors. We have yet to identify a cohort of factors that are sufficient to reprogram the fibroblast cells to nephron progenitors.

2. Specific Aims:

Specific Aim 1: Identify pool of transcription factors that are sufficient to convert stromal cells into nephron progenitors.

Results: We proposed to infect mouse embryonic fibroblasts from Six2Cre;RosaYFP mice with different pools of viruses expressing 19 different transcription factors. We have cloned all 19 factors into lentiviral expression vectors and produced virus for all. In addition, we have obtained a vector for expressing the "Yamanaka reprogramming factors" Oct4, Klf4, Sox2, cMyc. We have also obtained a mouse line whereby we can express these factors in specific renal lineages to assist re-programming in vivo.

We have initiated our screen in Six2Cre;RosaYFP MEFS. To date, we have not identified a cohort that can re-program the fibroblast to a Six2 + lineage but w. We are now repeating the studies with the "re-programming" factors included with the hopes that these factors will make the cells more susceptible to conversion to the NPC lineage. These studies are ongoing.

We are also developing a protocol to directly inject the virus into living kidneys once we have identified a competent pool.

3. Publications:

None