Oxalosis and Hyperoxaluria grant title: ***"Regulation of Renal Epithelial Cell Surface Calcium Oxalate Crystal Binding Molecules".***

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Final Non-Technical Report:

Oxalate is a small molecule that is contained in certain plants humans eat. The liver also generates oxalate as a by-product of metabolism. When excessive amounts of oxalate are found in the urine, it can combine with calcium to form calcium oxalate crystals. These crystals can deposit in the kidney and produce stones, or when the hyperoxaluria is marked, massive crystal deposition can result in renal scarring, and potentially kidney failure. Therefore, understanding the processes that allow calcium oxalate crystals to deposit in the kidney of patients with PH is very important in order to prevent kidney failure and possible death.

The funded proposal was designed to determine which molecule, Annexin II (AxII) or Hyaluronan (HA), is the most important crystal binding molecule on the surface of kidney cells, by genetically manipulating expression of each on surface of cultured cells.

We were able to generate a number of **stable inducible cell lines** in culture by transfecting plasmid vectors expressing siRNA against either AxII or HA into renal cells. *In response to tetracycline*, cells expressed siRNA against either AXII or HA thereby decreasing the expression of these molecules on the renal cell surface. These cells expressing decreased amounts of either molecule bound significantly lower amounts of Calcium Oxalate Crystals *in vitro*, suggesting both of these molecules being important in crystal binding to renal cells. Decreased expression of AxII and HA both led to decreased proliferation of renal cells which was on expected lines since both these molecules have been shown to have role in cell proliferation.

These results confirm the *in vitro* importance of AxII and HA as crystal binding molecules. These **stable**, **inducible cell lines** are an excellent *in vitro* model to assess the relative importance of candidate CBMs under various stimuli, and could be exploited to develop novel therapeutic agents.

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