Kidney Biology & Disease

The Batuman Lab: Chronic Kidney Damage & Disease

Multiple myeloma is one of the top ten most common cancer types. Of those living with this disease, more than half develop some sort of kidney comorbidity. These kidney issues can range from mild electrolytic imbalance to acute kidney toxicity necessitating dialysis or transplant. The lab of **Vecihi Batuman** was the first to discover and characterize one of the primary causes of this cancer-associated kidney disease.

Multiple Myeloma cells are malignant bone marrow cells that produce large quantities of antibodies. The lab discovered that these antibodies break down into heavy and light chain fragments and are then reabsorbed by the kidney, which can cause significant nephropathy over time.

Reabsorption of Antibody Light Chains

The Batuman Lab was the first to discover the specific way in which light chains can damage in kidney in multiple myeloma patients. Previously, it had been assumed that the light chains were filtered by the kidney and entered the cells of the kidney proximal tubule through passive diffusion.

The Lab surprisingly demonstrated that the light chains are absorbed into the kidney for recycling through receptor mediated endocytosis. This excessive light chain build-up in the kidney cells following endocytosis leads to the activation of the endoplasmic reticulum stress response. Part of this response involves the activation of assorted pro-inflammatory pathways – which then cause kidney cells to undergo an epithelial-to-mesenchymal shift, leading to fibrosis of the kidney.

By diminishing the expression of the specific light chain receptors on the kidney cells, we can prevent the activation of these pro-inflammatory pathways. The lab is actively pursuing ways to block light chain endocytosis in patients with multiple myeloma to prevent the kidney disease associated with this cancer.

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IL6: A Link Between Multiple Myeloma & Nephropathy

The IL6 signaling molecule is known to be important to multiple myeloma and kidney disease progression. The cellular response to IL6 is enhanced by the innate immune system through the toll-like receptor family. Currently, the research is focused on investigating whether the light chains absorbed by the kidney can activate these receptors. If so, the plan is to identify small molecules or RNAi-based treatments to modulate these receptors, helping to ablate IL6 signaling and the resultant kidney disease.

Environmental Lead and Cardiovascular Disease

The Batuman Lab also has significant experience studying the effects of environmental lead on human health. Of particular interest are the effects of body lead on kidney and cardiovascular health. In collaboration with colleagues in the Epidemiology department at Tulane, they have demonstrated a strong correlation between elevated levels of body lead and poor cardiovascular health and hypertension.

All of the afore-described projects and insights live within the larger framework of the Tulane Nephrology program, which places a strong emphasis on translating observations about the basic biology of the kidney to real-world human health applications.

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