Identifying Functional Disease Drivers in Lupus Nephritis Associated with Glomerular Remodeling

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Lupus Nephritis (LN) is an autoimmune disease that leads to chronic inflammation of the kidney and excessive proteinuria. Current methods of treatment involve management of symptoms and slowing the progression toward renal failure, but these anti-inflammatories have been proven to degrade kidney function. An alternate method of treatment, precision medicine, may be more effective when targeting the genomic drivers of LN. However, while the genes linked to LN have been identified, limited research has highlighted which specific genes may be driving the physical changes causing proteinuria in this disease. Thus, the purpose of my study was to identify the specific morphological changes within the glomerulus that led to protein leakage, and then to use qPCR to identify the specific genes that are driving this conformational change. Using banked serum samples and Masson's Trichrome-stained slides from NZB/W female mice, my study has revealed, for the first time, that a significant expansion of the Bowman's capsule within the LN group may correlate with excessive protein leakage. In addition, by correlating my qPCR expression results with the increase in Bowman's space, my research has also revealed that ROCK2, ICAM, cMET, TGFß, acox, and Col1 may be driving the morphological change of LN. The next step for this research is to determine whether inhibition of these specific genes can slow, or even reverse, the morphological changes of LN. And by better understanding the underlying mechanisms of LN, precision medication can eventually be tailored to each patient's genotype, thereby increasing the effectiveness of treatment.

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