Andrew Walker, Biochemistry

University: University of Missouri-Columbia
Year in School: Senior
Hometown: Springfield, Missouri
Faculty Mentor: Dr. Charlotte Phillips, Biochemistry
Funding Source: Life Sciences Undergraduate Research Opportunity Program

Relations between matrix metalloproteinase (MMP) activity, type I collagen accumulation, and glomerular sclerosis in the oim mouse

Andrew L. Walker, Anna M. Roberts-Pilgrim, Amanda C. Brodeur, and Charlotte L. Phillips

A novel type I collagen glomerulopathy was identified in oim mice [proα2(I) collagen (COL1A2 deficient)], which synthesize exclusively homotrimeric type I collagen, [$\alpha1(I)_3$]. Type I collagen exists predominantly as a heterotrimer [$\alpha1(I)_2$ α2(I)], although the homotrimeric form is present in small amounts in skin, embryologic tissues and would healing. However, the functional role of this homotrimer is unknown. In the oim mouse kidney the homotrimer accumulates in the glomeruli. Under normal physiologic conditions type I collagen is not present in the glomeruli; its accumulation is pathologic. In the following study we use an innovative perfusion technique that utilizes magnetic beads to isolate the glomeruli from surrounding tissue to investigate whether the accumulation of homotrimer is a result of either increased synthesis or a decreased degradative function of glomerular MMPs. We demonstrate through RT-PCR amplification that wild type and oim glomerular cells do, in fact, produce transcripts for MMP-1, MMP-2, MMP-9, and MMP-13. Furthermore, preliminary studies from collagen gel zymography suggest that glomerular MMPs cleave heterotrimeric type I collagen preferentially.