PROLYL-3 HYDROXYLASE EXPRESSION IN THE MOUSE KIDNEY AND DEVELOPING EMBRYO

Jennifer Lennington[1], Roy Morello[1], Ming-Ming Jiang[1], Dustin Baldridge[1], Terry Bertin[1] and Brendan Lee[1,2]

1 = Department of Molecular and Human Genetics, Baylor College of Medicine, 2 = Howard Hughes Medical Institute

All collagens undergo prolyl-3 hydroxylation post-translational modification. As specialized type IV collagen protomers are required for glomerular development, the purpose of this study is to examine which P3H isoforms are expressed in the developing mouse embryo, and specifically the kidney.

In-situ probes were amplified from S293 cDNA. The probes were labeled with S^{35} and hybridized to 6 micron thick sections at E12.5 – P1.

The kidney showed highest expression of P3H2 and P3H3 in distinct patterns from E16.5 onward. From E12.5 to E14.5, P3H3 was most prominent. P3H2 shows a glomerular specific expression pattern. In contrast, P3H3 shows highest expression in the interstitium and collecting system, but also is expressed in the central region of the glomerulus and the tubules.

Other organs also have non-redundant P3H expression. P3H2 only is expressed in pre-hypertrophic chondrocytes, and dominates in skeletal muscle, heart, and lens of the eye. Only P3H3 localizes to the periventricular region of the brain. P3H3 expression is also highest in the aorta and pulmonary veins. All three P3H's are expressed in the craniofacial mesenchyme, lung, and spine.

Because of the unique expression of P3H2 and P3H3 in the kidney, dysfunction of each may lead to distinct renal phenotypes. P3H2 could lead to abnormal glomerular basement membranes. Due to its early developmental expression and more diffuse expression, P3H3 may be involved in dysplasia, sclerosis, or cystic disease. Expression of the P3H isoforms in other tissues makes it likely that absence of any one of these isoforms would lead to multiorgan involvement. Lack of P3H2 could cause chondrodysplasia and myopathy. Lack of P3H3 may lead to a vascular phenotype, such as aneurysms. Further study to define the specific role of P3H's may lead to advances in diagnosis and management of chronic kidney disease.