DEVELOPMENTAL TISSUE-SPECIFIC EXPRESSION OF THE PRORENIN RECEPTOR.

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The prorenin receptor [(P)RR] has two major roles: 1) Mediate specific intracellular effects of prorenin and renin and 2) Enhance their enzymatic activity on the plasma membrane. This study examined (P)RR gene and protein expression during mouse organogenesis. (P)RR mRNA levels were determined in the brain, kidney, lung and heart of CD1 mice on embryonic (E) days E12.5-18.5 and postnatal (P) days P1, P10 and P60 (adult) by quantitative RT-PCR. Cellular distribution of the PRR protein in the metanephros was mapped by immunohistochemistry and of (P)RR mRNA- by in situ hybridization (ISH). RT-PCR demonstrated that brain (P)RR mRNA levels are low initially, increase on E16.5 and remain unchanged thereafter until adulthood. Kidney (P)RR mRNA levels increase progressively during gestation, remain unchanged on P1, increase on P10 and decline in adulthood. Lung (P)RR mRNA abundance increases progressively during gestation, peaks on P10 and remains high in adulthood. In the heart, (P)RR mRNA contents remain stable during gestation to subsequently decrease on P10 and P60. The (P)RR protein is weakly expressed in the developing metanephros in inner tubular structures as early as on E14.5. On E16.5 and E18.5, (P)RR is present in the ureteric bud (UB) epithelia followed by glomerular mesangium. On P1 and P10, (P)RR is most abundant on the luminal aspect of collecting ducts followed by proximal tubules and mesangium. This expression pattern persists into adulthood. ISH revealed weak diffuse presence of (P)RR mRNA in the inner mesenchyme and UBs on E13.5. A significant increase in the intensity of (P)RR mRNA expression throughout the kidney was observed on E14.5. In summary, (P)RR mRNA expression increases with maturation in the brain, lung and kidney and decreases in the heart. (P)RR protein expression increases progressively during metanephric development. Spatially, (P)RR protein is restricted to UBs/collecting ducts followed by glomerular mesangium and tubules. During early metanephric development, (P)RR mRNA is broadly localized in the mesenchyme and UB epithelia. These results demonstrate that (P)RR gene is developmentally regulated in a tissue-specific manner. The enrichment of (P)RR in renal tubules and glomeruli suggests a novel function for the (P)RR in the regulation of nephron development.