068-LIPS

Elucidating the role of sFRP2 in modulating kidney fibrosis

Introductory Statement

Despite the widely known function of urine production, kidneys' role in human physiology is much more complex and as vital as the heart and lungs. In addition to excretion and filtration, kidneys are responsible for maintaining acid-base homeostasis, working in tandem with several organs and forming several endocrinological relationships. Tubular epithelial cells line the kidney tubules and are primarily responsible for urine formation. When these cells are damaged, they signal to nearby fibroblasts to produce collagen and other regenerative proteins. Secreted frizzled-related protein (sFRP2) has been identified as a mesenchyme derived factor that partially down-regulates fibrosis. Yet, the molecular mechanism that regulates sFRP2's effect on fibroblasts in modulating tissue fibrosis is incompletely understood. We have generated a transgenic mouse model in which we can temporally and spatially regulate the expression of sFRP2 in injury-induced activated fibroblasts. Based on our preliminary observation, we hypothesize that sFRP2 inhibits fibrosis by modulating the pro-fibrotic signaling pathways in post-injury activated myofibroblasts. To test this hypothesis, we analyzed the pro-fibrotic pathways activated in response to injury in sFRP2 and Cre mice at multiple time points. These pro-fibrotic pathways were analyzed via semi-quantitative RT-PCR, Western Blot Analysis and IF staining.

Methodological Approach

sFRP2 expression was induced post unilateral urethral obstruction (UUO) following tamoxifen treatment in mice expressing sFRP2 under the FSP1 promoter. Following Cre activation by tamoxifen, sFRP2 gets expressed, instead of GFP, in FSP1+ cells. Bone marrow transplant (BMT) animals were generated to ensure sFRP2 expression in fibroblasts, since FSP1 is also expressed in hematopoietic cells. The animals were fed tamoxifen for five consecutive days prior to injury.

Findings

Masson's trichrome blue staining of injured kidneys following UUO shows an increase in collagen deposition suppression in sFRP2 mice compared to Cre mice.