Ms. MeiLan Han

LTRC Concept Sheet # 08-03-0001

Role of Relaxin in Idiopathic Pulmonary Fibrosis

ABSTRACT

Gender discrepancies in idiopathic pulmonary fibrosis have been noted for some time. The incidence and prevalence of disease have been reported to be higher in men than in women, and several retrospective studies have reported female gender to be associated with improved survival in IPF. We have recently reported significant gender differences in the rate of physiologic progression of disease with ambulatory hypoxemia progressing more rapidly in men with IPF than women. Relaxin is a peptide hormone most well known for its role in the preparation of the female body for parturition. While levels are higher in women, it is also expressed in men. Mounting evidence suggests that relaxin plays a key role in collagen regulation in both men and women. Expression of the primary receptor for relaxin, LGR7, has been identified in lung tissue. Mouse models of pulmonary fibrosis indicate that relaxin inhibits the development of pulmonary fibrosis, while animals that are relaxin deficient develop more extensive fibrosis. Furthermore, the combination of estrogen and relaxin deficiency appears to be synergistic with respect to the development of fibrosis suggesting a possible mechanism for the less rapid rate of disease progression in women. In other fibrotic diseases, serum relaxin has been noted to be significantly higher in females than males and it has been hypothesized that relaxin represents a defensive response against the fibrotic process. We propose to obtain lung tissue and serum from IPF patients and controls from the LTRC as pilot data for a K23 application. Specifically, we seek to determine whether relaxin is measurable in serum via ELISAs. We also seek to determine if we can detect the relaxin receptor, LGR7, can be detected via immunohistochemistry in lung tissue from IPF patients. If we are able to accomplish these aims, we will then seek to obtain larger sample sizes from the LTRC in order to be able to look for gender differences