Low back pain is a serious clinical problem and often related to intervertebral disc (IVD) degeneration. The mechanism responsible for this disease remains unknown. Interleukin-1 (IL-1) is a cytokine which plays an important role in inflammation and disc degeneration. β-catenin is a central molecule of canonical Wnt signaling and plays a key role in disc function. Chemokine (C-C motif) receptor 1 (CCR1) has been shown to interact with chemokines to mediate the migration of immune cells to the site of inflammation and is important for bone development. The purpose of this study is to investigate the roles of β-catenin and CCR1 in disc degeneration and inflammation. In our preliminary studies, we found that treatment with IL-1 in human disc cells caused an upregulation of chemokines, such as Ccl2, Ccl3, and Ccl5, and Mmp13. Using an in vitro cell migration assay, we demonstrated that one of the functions of the chemokines released by the disc cells is to chemoattract macrophages. It remains to be defined if CCR1 mediates chemokine signaling in disc cells. We have also found that IL-1 induced β-catenin nuclear translocation in chondrocytes and BIO (a GSK-3β inhibitor which activates β-catenin signaling) stimulated Ccl2 and Mmp13 expression in rat annulus fibrosus (AF) cells. In disc tissues from patients with disc degeneration, β-catenin protein levels are significantly up-regulated. To determine the function of β-catenin in disc cells and disc degeneration, we have generated and analyzed β-catenin conditional activation mice (β-catenin(ex3)Col2ER). These mice display severe defects in disc tissues, including extensive osteophyte formation, severe disorganized AF and nucleus pulposus (NP) tissues and up-regulation of MMPs in disc cells. These findings laid a strong foundation for further investigation of the roles of β-catenin signaling and CCR1 in IL-1-induced chemokine and MMP regulation and disc degeneration. Based on preliminary findings, we hypothesize that IL-1 causes disc degeneration and inflammation partially through the following signaling pathway: IL-1 → β-catenin → chemokines/CCR1 → MMPs in disc cells. To test this hypothesis, we propose two specific aims. In Aim 1, we will determine the roles of β-catenin and CCR1 in IL-1-induced chemokines and MMP regulation and macrophage migration. In Aim 2, we will determine if deletion of Ccr1 plays a role in the disc morphology and expression of marker genes involved in disc degeneration. Our proposed studies will provide novel insights into mechanisms of β-catenin and CCR1 in disc degeneration and inflammation.