

## Genome-wide Analysis Using ChIP-seq Reveals Novel Downstream Targets of Stat3

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Many cells are involved in the orchestra that is bone homeostasis--particularly osteoclasts and osteoblasts who mediate remodeling of bones. This creates a balance that must be kept in check, otherwise pathologies arise. The JAK-Stat signaling pathway is crucial to maintaining this balance. It has long been known that the transcription factor Stat3 has more profound effects on bone homeostasis than other members of the Stat family of proteins. Recently, a genetic condition called Job's Syndrome has been specifically linked to point mutations in the STAT3 gene. These patients present with severe bone abnormalities including prominent foreheads, broad nasal bridges, and abnormal eye spacing. Therefore, our lab has extensively studied conditional knockouts of Stat3 in all three types of bone cells in mice and observed severe deficiencies in numerous parameters of normal bone phenotypes. Stat3 seems to play a principal role in the signaling that takes place upon mechanical loading of bone tissues and calling cells into action where they are needed. Furthermore, STAT3 has been found to be up-regulated in the early-response gene cluster following mechanical loading. Our current approach to studying Stat3's effects on bone include employing available ChIP-seq data in order to elucidate the genome-wide binding patterns of Stat3. From the peak distribution, we can begin to uncover novel downstream effectors of Stat3 signaling that are responsible for the observed phenotypes in our mouse knockout model. A preliminary look at the ChIP-seq data reveals Wnt and Nrf2 signaling to be under the control of Stat3. In our further research we endeavor to experimentally confirm the ChIP-seq data for Stat3 with RNA-seq experiments in the hopes of finding potential therapeutic targets for bone pathologies.

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