Yang, C. K., et al. (2018). "C-terminus of Hsc70-interacting protein (CHIP) enhances stemness properties of human Wharton's jelly mesenchymal stem cell." Biotech Histochem 93(8): 632-639.

Mesenchymal stem cells are an attractive source of multipotent cells in part because they are easy to obtain. Several E3 ligases regulate the stability and functions of various factors in different adult stem cells through the ubiquitylation pathway. We investigated the C-terminus of Hsc70-interacting protein (CHIP) E3 ligase that regulates pluripotency of human Wharton's jelly mesenchymal stem cells (hWJMSC). We found that CHIP increases protein kinase B (Akt) phosphorylation by decreased expression of phosphatase and tensin homolog (PTEN), which suggests improvement of the survival pathway by CHIP over-expression. We also found that increased CHIP expression induced Sox2 and NANOG, which can promote stem cell self-renewal and prevent oxidative stress-induced senescence of hWJMSC by decreased p21. We found that CHIP could be used to enhance the multiple functions of hWJMSC.

Yang, R., et al. (2018). "Tet1 and Tet2 maintain mesenchymal stem cell homeostasis via demethylation of the P2rX7 promoter." Nat Commun 9(1): 2143.

Ten-eleven translocation (Tet) family-mediated DNA oxidation represents an epigenetic modification capable of converting 5-methylcytosine (5-mC) to 5-hydroxymethylcytosine (5-hmC), which regulates various biological processes. However, it is unknown whether Tet family affects mesenchymal stem cells (MSCs) or the skeletal system. Here we show that depletion of Tet1 and Tet2 results in impaired self-renewal and differentiation of bone marrow MSCs (BMMSCs) and a significant osteopenia phenotype. Tet1 and Tet2 deficiency reduces demethylation of the P2rX7 promoter and downregulates exosome release, leading to intracellular accumulation of miR-297a-5p, miR-297b-5p, and miR-297c-5p. These miRNAs inhibit Runx2 signaling to impair BMMSC function. We show that overexpression of P2rX7 rescues the impaired BMMSCs and osteoporotic phenotype in Tet1 and Tet2 double knockout mice. These results indicate that Tet1 and Tet2 play a critical role in maintaining BMMSC and bone homeostasis through demethylation of P2rX7 to control exosome and miRNA release. This Tet/P2rX7/Runx2 cascade may serve as a target for the development of novel therapies for osteopenia disorders.