Abstract

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Title of Diploma Thesis: Analysis of the molecular pathways and interactome of FUBP3

The far upstream element-binding protein 3 (FUBP3) has been recognized by genome-wide association studies to be associated with a higher risk of osteoporotic fracture. The knowledge about this protein and its role in bone biology is quite limited, though. Therefore, we aimed to broaden the horizons and created an overview of FUBP3 protein-protein interactors and possible pathway involvement.

The interacting proteins were gathered across multiple databases. Their association with osteoporosis (OP) and bone mineral density (BMD) was assessed using an online tool - OpenTargets Platform. Twelve hits associated with either were then used for qPCR analysis to investigate the influence of FUBP3 knockout. Among FUBP3 interactors were also proteins of cytosolic membraneless organelles – stress granules (SG). Stress conditions were induced and co-localization of SG markers PABPC1 and G3BP1 was carried out using immunostaining and fluorescence microscopy.

We were able to identify 75 protein interactors associated with either OP or BMD, out of which 8 were chosen as targets of interest for qPCR analysis. We report Osteocalcin, Collagen type I alpha 1 chain, and Transmembrane protein 64 to be differentially expressed in FUBP3 knockout human osteosarcoma cells. We were also able to successfully co-localize both SG markers with FUBP3 and conclude that it is a part of the stress granule proteome. Our results shall serve as a starting point for further studies of FUBP3's role in bone biology.