Osteoblast Exposure to Chordoma Exosomes Alters the Tumor Microenvironment

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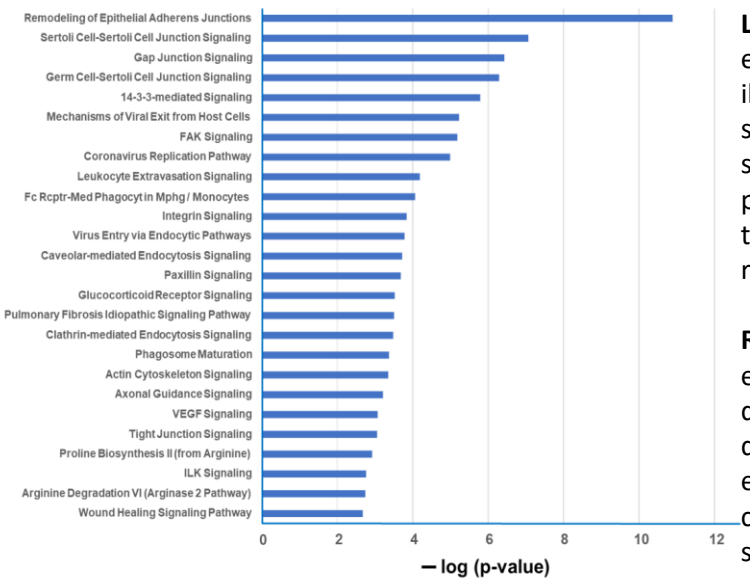
Introduction

Chordomas are extremely rare tumors of the sarcoma group; nonetheless, they are the most common tumor of the sacral and cervical spine. Within the tumor microenvironment, exosomes – secreted vesicles with multifaceted activities – are involved in tumor communication and material exchange. Our prior novel investigation showed chordoma exposure to chordoma exosomes resulted in different protein expression profiles for proteases, cytokines, and chemokines compared to control. Here, we investigated how chordoma exosomes influence osteoblasts, the normal cells within the tumor microenvironment. We hypothesize chordoma exosome-exposed osteoblasts will experience alterations to signaling, metabolism proliferation, and secretion of modifying material into the extracellular matrix.

Methodology

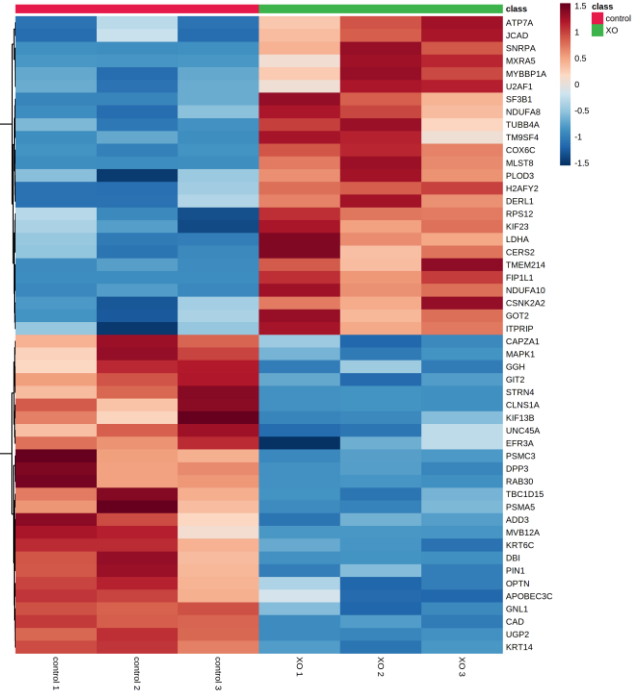
Phase I: ARF-8 chordoma cells were grown in DMEM+10% XO-Free (exosome-depleted) FBS. Conditioned medium was subjected to differential centrifugation, ultrafiltration, and ultracentrifugation to acquire ARF-8 exosomes.
Phase II: Purified ARF-8 exosomes were applied to osteoblasts (in triplicate) while control osteoblasts remained untreated. Both control and treated triplicates underwent proteomic and signaling pathway analyses.

Results



Left: Chordoma exosome-exposed osteoblasts illustrated modification of signaling pathways, specifically cell junction pathways, potentially for tumor microenvironment restructuring.

Right: Chordoma exosome-exposed osteoblasts demonstrated contrastingly different protein expressions compared to control, indicating significant changes.



Conclusions & Future Steps

Conclusions: From the results, it can be concluded:
1. Osteoblasts treated with chordoma exosomes expressed contrastingly opposite spectral counts of different proteins.
2. Osteoblasts treated with chordoma exosomes had modified signaling pathways, specifically pathways that affect cell junctions.

Limitations: Limitations of this project were the slow growth, low extracellular yield ARF-8 chordoma cells & osteoblasts.

Future Steps: Investigate how the different protein expressions alter the tumor microenvironment and chordoma metastatic potential. Investigate the mechanism as to how chordoma exosomes alter cell junction pathways.

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