ABSTRACT
Chordomas are rare tumors seen along the spine and skull base. Chordomas are locally destructive and chemoresistant, with poor prognosis and limited therapeutic options. Since there is no cure for the disease, molecular discoveries are needed to elucidate mechanisms behind chordoma initiation and progression. This study compared the expression profile of miRNAs in chordomas to that of healthy nucleus pulposus samples to gain insight into the molecular pathogenesis of chordomas. Selected miRNAs were transfected to chordoma cell lines, followed by viability assay, apoptosis assay, and cell-cycle analysis. miR-31 decreased cell viability in all chordoma cell lines after 72 hours. Although each miRNA had a similar pattern, miR-31 had the most effective S-phase arrest. Important genes for cancer progression were found to be targeted. The level of miR-222 in chordoma cell lines U-CH1 and MUG-Chor1 correlated positively with EMT markers. Furthermore, pro-inflammatory cytokines leukemia inhibitory factor and tumor necrosis factor were found to increase the aggressive traits of chordoma cells and lead to a poor prognosis in patients. Treating chordoma cells with these cytokines resulted in increased migration, invasion, tumorosphere formation, colony formation, epithelial-mesenchymal transition, and chemoresistance accompanied by a dramatic activation in pro-inflammatory pathways. LIF was associated with tumor size and a poorer overall survival. Results indicate that tumor promoting inflammation plays a role in elevation of aggressiveness related functions and genes in chordomas in vitro. Overall, this thesis presents important molecular findings which contributes to molecular knowledge about chordoma.

BIOGRAPHY
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