**Novel therapeutic approaches for chondrosarcomas: the role of retinol-binding protein 1 (RBP1) and retinoic acid signaling**

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**Background:** Chondrosarcoma is a malignant bone cancer that produces cartilaginous matrix. Currently, surgery is the only available treatment option. Therefore, novel therapeutic approaches are urgently needed for patients with metastatic and/or unresectable tumors. A large percentage of chondrosarcomas carry a point mutation in the isocitrate dehydrogenase (*IDH*) 1 or *IDH2* gene. This leads to the production of the oncometabolite 2-hydroxyglutarate (2-HG), which promotes tumorigenesis through DNA hypermethylation and downregulation of tumor suppressor genes. Gliomas with *IDH1/2* mutations have been shown to downregulate retinol-binding protein 1 (RBP1), which is crucial in the metabolism of vitamin A to retinoic acid (RA). Importantly, treatment with RA can reverse this effect. RA induces the transcription of multiple genes that are important for tumor suppression, cell differentiation, and immune activation. Thus, this study investigates RBP1 levels in chondrosarcomas and the efficacy of RA as a potential new treatment strategy for patients with chondrosarcoma.

**Methods:** Human chondrosarcoma cell lines (HT-1080, SW1353, DK12) and control sarcoma cell lines (GIST-T1, GIST48) were treated with varying doses of RA. Quantitative PCR was used to assess gene expression levels of RBP1. Immunoblotting and luminescence-based assays were used to evaluate cell viability and apoptosis. DNA sequencing was used to assess *IDH1/2* mutations.

**Results:** HT-1080 and SW1353 have known *IDH1* and *IDH2* mutations, respectively. GIST-T1 cells were shown to be *IDH1/2* wildtype by DNA sequencing. RA treatment increased RBP1 expression, decreased cell viability, and induced apoptosis in a dose-dependent and time-dependent manner in *IDH*-mutant cell lines.

**Conclusion:** Our study shows that RBP1 levels increase upon RA treatment in *IDH*-mutant chondrosarcoma cells. Hence, RA is a promising new treatment strategy for *IDH*-mutant chondrosarcomas. Further studies will be done to confirm this result and investigate the mechanism by which RA acts to inhibit tumorigenic activity.