The Relationship Between Tumor-Induced Osteoclastogenesis and Osteoprotegerin

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Osteosarcoma (OS), a primary bone tumor, arises from an imbalance in the bone remodeling pathway which fosters metastasis. In healthy bones, the microenvironment supports balanced remodeling, crucial during growth to bear the body's mechanical load. Bone remodeling has two competing cells: osteoclasts (OC) promote bone degradation and osteoblasts (OB) promote bone synthesis. This process is orchestrated by RANK receptors on OC and its ligand RANKL from OB to initiate pre-OC to OC differentiation. Osteoprotegerin (OPG), produced by OB, acts as a decoy receptor, regulating bone resorption. In OS, excess RANK/RANKL interaction induces osteoclastogenesis which weakens bone integrity and leads to tumor metastasis. To model this state in vitro, U2OS, a RANK/RANKL producing OS cell line, was treated with TNFa, a cytokine inducing osteoclastogenesis. Exogenous OPG (1-1000 ng/mL) administered to TNFa-treated U2OS suggests decreased osteoclastogenesis thus inhibiting this metastatic pathway. ELISA showed a significant decrease in RANK/RANKL production with OPG treatment, supporting a decrease in RANK/RANKL interaction. Gene expression analysis revealed an upregulation in genes responsible for OB production and bone integrity, as well as a downregulation of WNT6 and NPC2 - genes indicative of metastasis, all due to OPG treatment. Diminished metastatic capability was shown through TRAP (Tartrate Resistant Acid Phosphatase) staining which showed a profound decrease in cells with an OC phenotype, an invasion assay which demonstrated reduced migration of OPG treated cells, and an ELISA which showed a significant decrease in MMP9 expression. Based on this research, OPG may have therapeutic potential in controlling OS metastasis and bone degradation, alongside current therapies.

Awards Won:

First Award of $5,000

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