

**Number & Title** 11475 - Forced Induction of Differentiation in Osteosarcoma Tumor Initiating Cells

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## Abstract

**Background:** Osteosarcoma (OS) is a highly malignant form of bone cancer that is defined histologically by the secretion of immature osteoid. OS is believed to originate from mesenchymal or osteogenic committed progenitors, involving disruption of extracellular matrix synthesis in favor of proliferation.

**Purpose:** During skeletal formation, Bone Morphogenetic Proteins (BMPs) play key roles in osteogenic maturation. Because their lineage of origin suggests an innate sensitivity to BMP proteins, we hypothesize that BMP stimulation will force the induction of differentiation in OS Tumor Initiating Cells (TICs) and will impair the ability of these cells to initiate and maintain tumor growth. There is an urgent need for more effective therapies and a better understanding of OS biology.

**Methods:** BMP receptor expression was analyzed using Flow Cytometry. Immunoblotting was used to determine if the BMP signaling cascade was able to be activated upon BMP stimulation. Cell cycle analysis was performed using DAPI staining of nuclear content, and our xenograft mouse model was used to determine the effects of BMP stimulation on tumor formation.

**Results:** TICs express BMP Receptors, are capable of activating the BMP signaling after BMP stimulation, and display changes in their cell cycling. Furthermore, stimulated TICs showed reduced tumor formation in xenograft studies.

**Conclusions:** This data suggests an inhibition of OS tumorigenicity due to a *BMP 4/7 induced differentiation based response*. Such a differentiation-based therapy could become a much more effective and safer alternative to cytotoxic chemotherapy.