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UMass CCTS Research Retreat
Poster Abstract Submission

Identification of GDF-6 blocking antibodies as anti-melanoma therapeutics

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#Co-corresponding authors and Co-PIs for NHMPP award

Through comparative oncogenomic studies and functional analyses, we have identified the bone morphogenetic protein (BMP) factor GDF6 as a new melanoma oncogene. The secreted, carboxy-terminal portion of GDF6 is the active form that binds to cell-surface receptors to initiate BMP signaling. Targeted antibodies directed against secreted proteins are a proven therapeutic modality in several diseases.

To develop therapeutic antibodies against the active form of GDF6, we generated a panel of monoclonal antibodies. Due to the high similarity of human and mouse GDF6 proteins, the C-terminal GDF6 protein was expressed as bacterial recombinant protein with fusion tags to enhance immunogenicity. The Expresso Screening System (*Lucigen*) was used to select fusion tags, and MBP and SlyD were chosen for optimal protein solubility and purification recovery. Ten CD1 mice were immunized with GDF6-MBP fusion protein and robust immune responses were observed in all animals after 5 immunizations. Animals were sacrificed for hybridoma fusion, and hybridoma clones were screened by ELISA using GDF6-SlyD fusion protein to select clones with specific binding activity to GDF6. Over 70 monoclonal antibodies were identified with strong reactivity to GDF6, and a subset has been shown to recognize the endogenous, secreted form of GDF6 via western blot. These antibodies will be screened for their activity to block GDF6 binding to melanoma cells and ability to inhibit downstream signaling using both *in vitro* assays and *in vivo* xenograft models.



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