Anchored immunotherapy with intratumorally administered aluminum hydroxide-tethered IL-12 induces potent anti-tumor immune response

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Introduction: IL-12 is a potent cytokine that can promote innate and adaptive anti-tumor immunity. Its clinical development has been limited by toxicity when delivered systemically1. Intratumoral (IT) administration allows the therapeutic advantage of IL-12 and other cytokines but is limited by rapid systemic clearance and reduced retention in tumors.

We report the discovery and preclinical characterization of mANK-101, a novel IL-12-based therapeutic, which demonstrates enhanced antitumor activity compared to currently available IL-12 therapeutics through increased local tumor retention and persistent expression.

Methods: mANK-101 was designed to tether IL-12, packaged in an Alhydrogel® (Alum®) scaffold through a linker of 47 amino acids, to the tumor microenvironment to promote increased tumor retention and persistent expression.

Results: When compared to a buffer control, mANK-101 exhibited increased tumor accumulation when administered IT as a single dose in multiple syngeneic tumor models. Increased local cytokine expression was observed in tumors treated with mANK-101 when compared to IL-12-ABP and a tethered IL-12 protein (mIL-12-ABP). Increased tumor retention and reduced systemic exposure of mANK-101 was confirmed both by gene and protein expression analysis.

Conclusions: The enhanced local cytokine expression observed with mANK-101 demonstrates the potential for a new class of agents that can be localized to the tumor microenvironment to promote tumor-specific immune responses without systemic toxicity.

References: