



Insulin like Growth Factor Binding Protein 7 (IGFBP-7), a Novel Anti-Cancer Agent

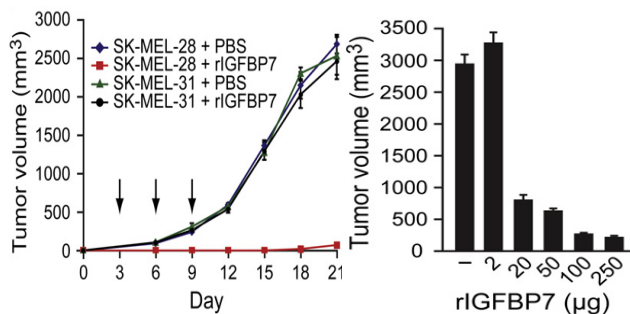
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US patent pending

Background

According to the *American Cancer Society*, cancer is the second leading cause of death in the US, behind heart diseases. Among cancer subtypes, melanoma will account for an estimated 62,000 new cases and 8,420 deaths in the US in 2008 (*National Cancer Institute*). *Activating vRaf murine sarcoma viral oncogene homolog B1 (BRAF)* mutations are found in 50-70% melanomas, 15% colorectal and ovarian cancers and 36-69% of papillary thyroid carcinomas. Activated BRAF-positive metastatic melanomas are very often refractory to conventional chemotherapeutic agents. Further, inhibitors of BRAF have unfortunately performed poorly in clinical trials. Hence, currently there are limited options for treatment of patients with this aggressive and often fatal disease.

Technology

UMass Medical School & Howard Hughes Medical Institute investigator Prof. Michael Green and colleagues have discovered that a secreted protein, IGFBP-7, can induce senescence and death in cancer cells and thereby can be used as a biological agent for cancer treatment. In an elegant study the investigators demonstrated the potent anti-cancer properties of IGFBP7 on melanoma cells (*Wajapeyee et al. (2008) Cell 132, 363–374*). This study identified IGFBP-7 in a genome wide-RNA interference (RNAi) screen designed to identify genes required for BRAFV600E, an activating BRAF mutation, to inhibit proliferation of human primary foreskin fibroblast. The anti-proliferative property of IGFBP-7 was confirmed in a secondary screen using primary human melanocytes. These results were substantiated and validated *in vivo* by robust suppression of tumor growth by recombinant IGFBP-7 in xenografted mice harboring human tumors containing an activating BRAF mutation.



Applications

Cancer therapy

Salient Features and Competitive Advantages

- **Novel Biological Agent for Cancer Treatment:** IGFBP-7 is a new class of cancer therapeutic and can be used for treatment of cancers expressing an activated BRAF or RAS such as melanoma, carcinoma or breast cancer.
- **Potent and Selective Tumor Suppression:** IGFBP7 induced robust apoptosis in melanoma cells harboring activated BRAF mutations *in vitro* and *in vivo* melanoma models.
- **Dual Effect:** Following transient exposure IGFBP-7 inhibits both BRAF-MEK-ERK signaling and irreversibly induces apoptosis.
- **High Tolerability:** When administered systemically to mouse models for human melanoma, the recombinant IGFBP-7 was well tolerated without apparent adverse effects even at doses higher than that required for tumor suppression.
- **Diagnostic Applications:** In addition to its therapeutic potential, the expression level of IGFBP-7 can be used for cancer diagnosis.
- **Market Potential:** US melanoma market is potentially valued at \$1.8 billion.

Business Opportunity

UMass OTM is seeking statements of interest from parties interested in licensing this technology.

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