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Novel targeted non-RGD cyclic peptide drug conjugates for treatment of human metastatic melanoma

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Metastatic Melanoma (MMel) is the most deadly skin cancer frequently associated with metastasis and poor survival prognosis. Systemic therapy for MMel is still too early in development to demonstrate efficacy, and chemotherapy still remains the major adjuvant treatment against MMel. Obviously, new targeted drug delivery approaches are needed to overcome toxicological problems and improve efficacy. Integrins are a family of at least 24 distinct cell surface receptors commonly over-expressed on many types of cancer cells. They are essential for tumor progression, and therefore attractive targets for selective therapeutic intervention and drug delivery. Importantly, integrins are generally recognized by the "RGD tripeptidic sequence" and therefore many peptides bearing this recognition motif have been found to be effective ligands for the selective delivery of chemotherapeutics. However, their therapeutic and targeted effectiveness was not adequately demonstrated in clinical trials and even paradoxically can enhance, rather than suppress, tumor progression. We developed new non-RGD cyclic peptide ALOS-4 which binds to a non-RGD site on integrin $\alpha_v\beta_3$. Our preliminary *in-vivo* studies demonstrate that ALOS4 markedly blocks murine B16F10 melanoma tumor growth and lung metastasis, dramatically increases animal survival rates and prevents cancer-related weight loss. In addition, *ex vivo* fluorescence imaging studies on human metastatic melanoma (WM-266-4) animal model showed the accumulation of the ALOS4-FITC only in the tumor tissue and not in the spleen or liver. The ALOS4-Drug conjugates as well as their potency in treatment of human metastatic melanoma will also be presented.

Biography

Gary Gellerman has completed his PhD from Tel Aviv University in 1994 and joined Compugen Ltd. In 2000, he accepted VP, Molecular Diversity position in Compugen where he was responsible for developing drug discovery platform. In 2005, he moved to Ariel University, currently holding Deanship of Faculty of Natural Sciences. He has published more than 50 articles in reputed journals.

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