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Drug chimerism as a fusion of two anticancer chemotherapeutics into one entity: Discovery of potent molecular chimera CM358 for treatment of metastatic melanoma

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Resistance to drugs that cancer cells develop and the inherent capability of these cells to survive the drug treatment, produces a great motivation to look for new techniques of chemotherapeutic cure and search for novel anti-proliferative agents. In the present report, we demonstrate a facile synthetic strategy towards the discovery of new anti-cancer substances. This strategy is based on simple covalent coupling between known anti-cancer drugs, which results in novel 'chimeric' small molecules. One of the novel compounds presented here, CM358, is a result of amide bond formation between known Topo II inhibitor amonafide (AM) and DNA mustard alkylator chlorambucil (CLB). It demonstrates a significant cytotoxic predominance over the equimolar mixture of AM and CLB in various cancer cell lines and in xenograft model of human metastatic melanoma. Modeling studies and FACS analysis of CM358 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 the position of Vice-president, Molecular Diversity 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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