Immunoliposomes containing simvastatin, targeted towards EGFR, as potential therapeutic for a treatment of EGFR-dependent breast cancer tumors.

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Abstract (300 word limit)

Introduction: Epidermal growth factor receptor (EGFR) was shown to be highly expressed in many types of human cancer, among others, in breast cancers. EGFR overexpression correlates with advanced stage of the disease and with poor response to chemotherapy. One of the promising strategy for the treatment of EGFR-dependent tumours is to inhibit signal transduction from EGFR via disruption of cholesterol rich membrane rafts. We assume that targeted delivery of simvastatin, a popular cholesterol-depleting drug widely prescribed in the treatment of cardiovascular diseases, will specifically disorganize membrane rafts and therefore disturb the EGFR dependent signalling pathways that usually promote cell proliferation and metastases. Statins were shown to exert antitumor effects in high doses, but those may lead to serious side effects. Therefore, the main purpose of this work is to obtain targeted, long circulating liposomes with simvastatin and to test their anticancer activity both in vitro and in vivo. **Methodology:** Liposomes were prepared via lipid film hydration method and modified by attachment of antibodies specific to EGFR. Stability, selectivity and toxicity of targeted liposomes were analyzed both in vitro and in vivo. The level of activation of selected kinases involved in transduction of signals stimulated via EGF in cells treated by immunoliposomal statin was examined. Moreover, changes in plasma membrane order of cells exposed to liposomal simvastatin were examined using FLIM method. **Findings:** Designed immunoliposomes were stable over 6 months, selective towards EGFR overexpressing cells and showed antitumor efficacy both in vitro and in vivo. Inhibition of signaling pathway involving Akt in cells treated with immunoliposomal simvastatin and disruption in plasma membrane order were observed. **Conclusions:** Presented immunoliposomal formulation of simvastatin seems reasonable solution of a specific delivery of high doses of this drug into tumor cells and a candidate of further evaluation for efficacy either in monotherapy or in combination in anticancer therapies in the future.

Image

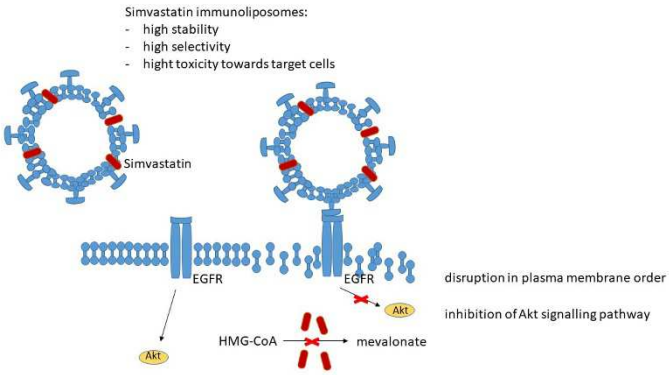


Figure 1: Effect of simvastatin immunoliposomes on cancer cells.

Recent Publications (minimum 5)

1. Matusewicz L, Meissner J, Toporkiewicz M, Sikorski AF (2015) The effect of statins on cancer cells-review. Tumour Biol. 36: 4889-904.
2. Babina IS, Donatello S, Nabi IR, Hopkins AM (2011) Lipid Rafts as Master Regulators of Breast Cancer Cell Function. Available at: http://epubs.rcsi.ie/surgart.
3. Luput L, Licarete E, Drotar DM, Nagy AL, Sesarman A, Patras L, Rauca VF, Porfire A, Muntean D, Achim M, Tomuta I, Vlase L, Catoi C, Dragos N, Banciu M (2018) In Vivo Double Targeting of C26 Colon Carcinoma Cells and MicroenvironmentalProtumor Processes Using Liposomal Simvastatin. J Cancer. 9: 440-449.
4. Alupei MC, Licarete E, Patras L, Banciu M (2015) Liposomalsimvastatininhibitstumorgrowthviatargetingtumor-associated macrophages-mediated oxidative stress. Cancer Lett. 356: 946-52.
5. Coimbra M, Banciu M, Fens MH, de Smet L, Cabaj M, Metselaar JM, Storm G, Schiffelers RM. Liposomal pravastatin inhibits tumor growth by targeting cancer-related inflammation (2010) J Control Release. 148:303-10.
6. Kutty RV, Feng SS (2013)Cetuximab conjugated vitamin E TPGS micelles for targeted delivery of docetaxel for treatment of triple negative breast cancers. Biomaterials. 34: 10160-71.
7. Ahern TP, Lash TL, Damkier P, Christiansen PM, Cronin-Fenton DP (2014) Statins and breast cancerprognosis: evidence and opportunities. Lancet Oncol. 15: e461-8.



Biography (150 word limit)

LucynaMatusewicz is aPhD student at University of Wroclaw.Lucyna graduated with MSc in biotechnology in 2012. After graduation she started her PhD project and for almost 6 years she focuses mainly on drug delivery systems in anticancer therapy.

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Notes/Comment