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Integrin- and IGF1-Receptor-Mediated Liposomal siRNA Delivery to Alveolar Rhabdomyosarcoma Cells

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Rhabdomyosarcoma is the most common soft tissue sarcoma of childhood. Especially the alveolar rhabdomyosarcoma (ARMS) shows poor prognosis when metastases have developed.

The aim of this project is to downregulate the expression of several genes that are involved in the aggressive behaviour of ARMS by means of siRNA. Therefore, a liposomal delivery system, which is able to transport siRNA selectively to the ARMS cells, is being developed.

For enhancing the interaction of the delivery systems with the target cells and thus the effectivity, active targeting is intended. Therefore, the surfaces of the liposomes were modified with ligands binding to receptors expressed on the ARMS. Two different kinds of targeting devices were utilized: a RGD-peptide (arginine-glycine-aspartic acid tripeptide) recognizing integrins on ARMS as well as an antibody binding to the IGF1-receptor (insulin-like growth factor 1 receptor).

siRNA was encapsulated into the liposomes during liposome preparation by speedmixing (dual asymmetric centrifugation). This method is well suitable for efficient siRNA entrapment [1].

To modify liposomes for active targeting the ligands were coupled to the liposomal surface using the sterol-based post-insertion technique (SPIT) [2].

For optimization of the delivery systems, cellular interaction of fluorescently labeled liposomes with the ARMS cell line RH-30 and gene silencing of siRNA-loaded (anti-GFP siRNA) liposomes in stably GFP-transfected RH-30 cells were determined by flow cytometry.

RGD-peptide as well as anti-IGF1-receptor antibody modified liposomes showed significant interaction with RH-30 cells. Furthermore, specificity and extend of gene silencing was analyzed.
