

## TARGETING OF LIPOSOMES TO ANGIOGENIC ENDOTHELIAL CELLS

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Given the dependency of tumours on angiogenic blood vessels, inhibiting the formation of new capillaries or disrupting the newly formed vessels has attracted a great deal of attention. In addition, angiogenesis is also part of the inflammatory response offering the potential possibility of inflammation modulation by inhibiting this process. One of the most attractive target cell type to achieve inhibition of angiogenesis is the endothelial cell which plays a pivotal role in the angiogenic cascade. For successful application of a treatment strategy based on targeting angiogenic blood vessels, angiogenic EC need to be very specifically discriminated from the normal quiescent endothelium. Several proteins are (strongly) over-expressed on angiogenic EC as compared to the quiescent endothelium, and could potentially serve as targets for site-specific drug delivery. One of the best-defined over-expressed angiogenic target protein and corresponding ligand is the alpha v beta 3-integrin/RGD-motif system. The alpha v beta 3-integrin mediates EC adhesion to the extracellular matrix by recognizing a conserved arginine-glycine-aspartic acid (RGD) sequence, which is present in several matrix proteins. Synthetic cyclic RGD-peptides show a high affinity for the alpha v beta 3-integrin. Unfortunately, RGD-peptides appear to have a short circulation half-life ( $t_{1/2} < 10$  min) and, as a result, are expected to have limited interaction with the target site. In addition, the use of peptides as drug carriers provides limited drug transport capacity.

To improve circulatory half-life and drug transport capability while preserving the target affinity of the RGD-motif, RGD-peptides can be coupled to the distal end of long-circulating PEG-ylated liposomes (RGD-PEG-L). Moreover, the liposome may function as a platform allowing multivalent interactions with the target molecules to take place. In this contribution in vitro and in vivo results obtained with RGD-PEG-L will be presented pointing to exciting prospects of this targeted system for tumor eradication or inflammation modulation.

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