

**TARGETED DRUG DELIVERY FOR ANTHRACYCLINS USING PEPTIDOLIPOSOMAL CONSTRUCTS**

SAMI KAUKINEN<sup>1</sup>, SARI KUOSMANEN<sup>1</sup>, HELI VALTANEN<sup>1</sup>, YING ZHU<sup>1</sup>, ILKKA SIMPURA<sup>1</sup>, MERJA HAIKOLA<sup>1</sup>, MARJA TÄHTINEN<sup>1</sup>, MIKKO REINMAN<sup>1</sup>, OULA PENATE MEDINA<sup>1</sup> and KALEVI KAIREMO<sup>1,2</sup>

<sup>1</sup>Cancer Targeting Technologies Oy, Viikinkaari 4 C, 00790 Helsinki, Finland,

<sup>2</sup>Department of Oncology, Institute of Clinical Medicine, FIN-00014 University of Helsinki, Finland

Peptidoliposomal drug derivatives were constructed for targeted drug delivery and tested in tumor bearing animals. The targetor was a CTT peptide known to target matrix metalloproteinases-2/-9, essential components of tumor cell migration, neovascularization and tumor stromal destruction. The drug delivery system was tested in several tumor models, most often in nude mice bearing human ovarian cancer xenografts.

The affinity of radiolabelled (<sup>111</sup>In) peptides was determined in a competitive assay binding human breast ca cells and was approximately 20 nM. The biodistribution was detected by tissue sampling in mouse models, and higher uptakes than 15% ID/g tumor were observed with the naked peptide, 20% ID/g tumor with the peptidomicellar construction (17 nm particle), and 35% ID/g tumor with the peptidoliposome (100 nm particle). The bioactivity of these peptide/nanoparticle was always tested using peptideELISA. The drug concentrations in the nanoparticles were measured by HPLC, inclusive their metabolites.

In experimental therapy trials targeted drug delivery systems were compared with non-targeted drug and free drug in bioequivalent concentrations. The targeted liposomal doxorubicin increased survival these animals as compared to non-targeted system and free drug. The targetor principally increased survival of animals approximately 35% as compared to treatment with pegylated liposomes without targetor. The concentrations in tumor at 0-96 hours demonstrated approximately 40% increment in AUC (targeted drug vs. non-targeted drug). Similar results were obtained with other drugs.

We can conclude that targeted drug delivery improves survival at least in an experimental animal therapy, and that our CTT peptide acts as promising targetor.