

**IN VIVO IMAGING USING LIPOSOMAL PHAGE DISPLAY PEPTIDE
DERIVATES TARGETING INTEGRINS IN ACTIVATED
LEUKOCYTES**

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A bioactive peptide obtained recently by phage display is a specific ligand to the leukocyte β_2 integrins, $\alpha_M\beta_2$ integrin (CD11/CD18). This LLG peptide is a nonapeptide which is dependent on two disulfide bridges that constrain the peptide structure. This peptide is known to inhibit the β_2 integrin-mediated leukocyte cell adhesion and binds to the cation-sensitive I-domain of the integrin α subunit. Biodistribution of the phage display peptide LLG (14 amino acids) and its conjugates in the targeting moiety were studied in various animal models. Additionally peptidoliposomal derivatives were constructed for targeted drug delivery.

The affinity of radiolabeled (¹¹¹In) peptides was determined in a competitive assay was found to be of high nanomolar range. The biodistribution, detected both by external imaging and tissue sampling, did not reveal any specific accumulation sites and the peptide was rapidly excreted via kidneys. In several animal inflammatory/ infectious disease models excellent targeting signals based on biodistribution analysis were observed. We used *E. coli* LPS and thioglycolate inflammation models in mice (several locations), *S. aureus* infections in rats (thigh muscle) and *E. coli* infections in rabbits (thigh muscle). Special attention was paid to different isomeric conformations (disulfide bridge orientation) and their effect to biodistribution.

The possibilities to use LLG as a therapeutic agent had been studied, absolute tumor-to-blood ratio at 24 hrs using labeled peptide as leukemic tumor targeting agent was 4.7. Pegylation of LLG increased circulation time. The LLG can also function as a therapeutic agent on surface of liposome, resulting in a even longer circulation half-life. Using liposome we can modify drastically the pharmacokinetics and dynamics of the peptide. Our animal models (mice, rats, rabbits) demonstrated excellent in vivo targeting of infectious and inflammatory tissue.