Public Abstract

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**CHARACTERIZATION OF PEPTIDES AND PHAGE THAT BIND
GALECTIN-3 SELECTED FROM BACTERIOPHAGE DISPLAY
LIBRARIES: A STUDY OF THE ROLE OF GALECTIN-3 IN
METASTASIS-ASSOCIATED CANCER CELL ADHESION**

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Intravascular cancer cell adhesion plays a significant role in the metastatic process. Studies indicate that galectin-3, a member of the galectin family of soluble animal lectins, is involved in carbohydrate-mediated metastatic cell heterotypic and homotypic adhesion via interactions with the tumor-specific Thomsen-Friedenreich glycoantigen (TFAg). We hypothesized that the specific molecular inhibition of the interaction between galectin-3 and its ligands would reduce carcinoma cell adhesion. To test this hypothesis, we identified peptide antagonists of galectin-3 using phage display technology. The peptides bound with high affinity to galectin-3 protein and to cell surface galectin-3. Further experiments indicated that the peptides bound the CRD of galectin-3. Moreover, the peptides did not bind the CRD of other galectins and plant lectins. Synthetic galectin-3 CRD-specific peptides blocked the interaction between galectin-3 and TFAg and significantly inhibited heterotypic adhesion of human MDA-MB-435 breast carcinoma cells to endothelial cells under flow conditions, as well as homotypic tumor cell aggregation. These results demonstrate that carbohydrate-mediated metastasis-associated tumor cell adhesion could be inhibited efficiently with short synthetic peptides.

We also investigated the possibility that galectin-3 specific phage would target to tumors highly expressing the protein in mice. The phage harboring galectin-3 binding peptides failed to exclusively target to human MDA-MB-435 breast tumor heterotransplanted in mice. However, the pharmacokinetic properties of random phage peptide display fd-tet libraries, *in vivo*, were fully investigated. This study will be extremely useful in the design of *in vivo* application strategies, especially in isolating tumor-avid molecules with a priori optimum *in vivo* properties