

Utilization of I-domain of LFA-1 to target drug and marker molecules to Leukocytes.

ABSTRACT

The long-term objective of this project is to utilize the I-domain protein for the α -subunit of LFA-1 to target drugs to lymphocytes by binding to ICAM receptors on the cell surface. The short-term goal is to provide proof-of-concept that I-domain conjugated to small molecules can still bind to and uptake by ICAM-1 on the surface of lymphocytes (i.e., Raji cells). To accomplish this goal, the I-domain protein was labeled with FITC at several lysine residues to produce the FITC-I-domain and CD spectroscopy showed that the FITC-I-domain has a secondary structure similar to that of the parent I-domain. The FITC-I-domain was taken up by Raji cells via receptor-mediated endocytosis and its uptake can be blocked by anti-I-domain mAb but not by its isotype control. Antibodies to ICAM-1 enhance the binding of I-domain to ICAM-1, suggesting it binds to ICAM-1 at different sites than the antibodies. The results indicate that fluorophore modification does not alter the binding and uptake properties of the I-domain protein. Thus, I-domain could be useful as a carrier of drug to target ICAM-1-expressing lymphocytes.

Keyword: ICAM-1; FITC-I-domain; Binding; Endocytosis; Raji cells.