Non-Confidential Disclosure

Immune Disease Institute	Office of Technology Development 3 Blackfan Circle, 3rd Floor Boston, Massachusetts 02115 www.idi.harvard.edu

IDI 05-004	HIGH AFFINITY I-DOMAIN AS ANTI-INFLAMMATORY OR IMMUNOSUPPRESSANT

Key Words: Protein Therapeutic, LFA-1, ICAM-1, Immunosuppressant, Anti-Inflammatory, Allograft Rejection, Psoriasis and Rheumatoid Arthritis

Application: I-Domain as an anti-inflammatory or immunosuppressant prophylactic or therapeutic to treat atherosclerosis, allograft rejection, psoriasis, and rheumatoid arthritis. Also could serve as a target to identify highly specific antibodies.

Inventor(s): Timothy A. Springer, Ph.D. and Moonsoo Jin, Ph.D.

Invention Summary:

Inhibition of LFA-1 binding to intercellular adhesion molecule-1 (ICAM-1) is a proven and powerful point of therapeutic intervention as evidenced by Genetech's Raptiva. Drs. Springer and Jin have developed this promising I-domain lead and additional candidates for the treatment of LFA-1 dependent ICAM-1 diseases. The I-domain is the ligand binding domain of LFA-1, and through directed mutagenesis, the engineered I-domain has a binding affinity drastically higher than wild-type. This I-domain mutant could be used as an anti-inflammatory or immunosuppressant to treat atherosclerosis, allograft rejection, psoriasis, and rheumatoid arthritis.

The I-domain has a molecular weight of 20 kDa and can be produced in a large-scale from bacteria. Therapeutics treating these disorders are Humira, Enbrel, Remicade, Kineret and Raptiva. We believe that the increase in the binding affinity to ICAM-1 and the lack of LFA-1 activation, which can be caused by approaches based on anti-LFA-1 antibody, e.g., Raptiva, will result in positive safety profiles as a result of fewer side effects.

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Supporting Publications: ***Current Topics in Medicinal Chemistry*** 2004, 4, 1485-1495.

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Availability: Exclusive worldwide license

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