# Novel Treatment Strategy for Chronic Lymphocytic Leukemia: Malignant B1 Cell Depletion via Siglec-10 Stimulation

Jain, Jaison

Chronic Lymphocytic Leukemia (CLL), a cancer of B1 cells, is the most widespread leukemia in the world. Current chemotherapies fail to effectively target the malignant B1 cell subset in CLL, resulting in toxic, and often fatal, side-effects. Therefore, the purpose of the present study was to develop a B1-cell specific treatment with minimal toxicity. Siglec-10 (sialic-acid-binding Ig-like lectin 10) was seen as a promising area for investigation. First, Siglec-10 was knocked down in normal peripheral blood mononuclear cells via reverse transfection with siRNA, which resulted in elevated B1 cell proliferation, depressed B1 cell apoptosis, and a massive six-fold expansion of the B1 cell population, though other immune cells experienced no such phenotypic changes. Hence, Siglec-10 has a “tumor-suppressing” function in B1 cells, limiting proliferation and maintaining healthy levels of apoptosis. Understandably, therefore, underexpression of Siglec-10 was found to be linked to CLL malignancy, as determined by flow cytometry. Siglec-10 was then stimulated with its ligand (2,6 polyacrylic acid) in diseased samples as a potential therapy, yielding the expected opposite outcomes of gene knockdown--decreased proliferation, increased apoptosis, and depletion of malignant B1 cells, with no toxic effects on healthy lymphocytes. Thus, Siglec-10 stimulation comprises the first ever non-toxic therapy for CLL. This novel treatment strategy may also have therapeutic advantages in autoimmune diseases of B1 cells such as rheumatism and arthritis, potentially saving the lives of millions worldwide.

**Awards Won:**

Second Award of $2,000