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Modulation of Hematopoiesis and Inflammatory Cell Production by ST6Gal-1

Ref# RP09-011

Keywords: Bone marrow disorders, leukemia, asthma, G-CSF, liver restricted promoter P1, ST6Gal-1.

Summary: Hematopoiesis is the mechanism that produces circulating blood cells and certain other cells that participate in immune responses in various tissues. Inflammation is part of a complex of biological responses to harmful stimuli, such as pathogens, damaged cells, irritants, or tissue malfunction. Inflammation is normally a protective attempt to remove injurious stimuli and to initiate the healing process. However, dysregulated inflammation or failure to resolve inflammation is deleterious. Many disease conditions that affect vast numbers of people involve aberrant activity of such cells, including various cancers, autoimmune disorders, organ and tissue transplantation rejections, and multiple conditions that involve undesirable inflammation as a component of disease etiology.

Technology: Researchers at Roswell Park Cancer Institute (RPCI) have developed a method for reducing inflammation by administering a composition of recombinant α2,6-sialyltransferase (ST6Gal-1). ST6Gal-1 is a sialyltransferase enzyme that constructs the sialyl α2,6 to Gal β1, 4GlcNAc glycan structure common on many cell surface and glycoproteins. Much of ST6Gal-1 remains within the cell that synthesizes it (cell restricted), but there is a significant pool of circulatory or systemic ST6Gal-1.

Circulatory ST6Gal-1 originates predominantly from the liver and specific inactivation of the liver-restricted promoter (P1) of the ST6Gal-1 gene resulted in depressed systemic ST6Gal-1 levels. Current data point to a role for systemic ST6Gal-1 in modulating hematological/progenitor cell homeostasis, myelopoiesis, and inflammation. In the presence of high systemic ST6Gal-1, hematopoiesis and inflammatory cell production and release into circulation are attenuated. Upon depletion of systematic ST6Gal-1, these hematologic processes are enhanced.

Systemic ST6Gal-1 levels can easily be altered by infusion of recombinant ST6Gal-1 or inhibitors to ST6Gal-1, and provide a novel axis to modulate hematopoietic homeostatic balance as well as control production of inflammatory cells and their release into circulation.

Collaborative Research Opportunity:

Roswell Park Cancer Institute is seeking parties interested in collaborative research to further evaluate or commercialize the use of recombinant ST6Gal-1 for modulation of hematopoiesis and inflammatory cell production.

Potential Commercial Applications:

- Potential therapy for bone marrow disorders.
- Potential therapy for hyper-eosinophilic related diseases (asthma or idiopathic hyper-eosinophilic disorders) or for chronic inflammatory conditions.
- Potential treatment in myeloid leukemic conditions.

Competitive Advantages:

- Shorten duration of chemotherapy induced neutropenia.

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- Can augment or supplant existing growth factor (G-CSF) based strategies
- Can alter the efficacy and kinetics of stem cell repopulation in bone marrow transplantations.

Development Status: PCT filed in the US, Canada, and Europe. (December 2013).