

A CCR2 antagonist with immunosuppressive and anticancer properties

Information Summary

Reference code:	ROI 08079
Technology Overview:	A biopharmaceutical that inhibits activated lymphomyeloid or tumor cell
Application:	Transplantation, autoimmune diseases, cancer
Validation	In vitro mechanistic studies; In vivo efficacy.
Inventors:	Dr. Jacques Galipeau; Mouth Rafei
Contact:	Astrid Reimann Ph.D. MBA Tel: 514-398 5887 Astrid.reimann@mcgill.ca

Technology Description

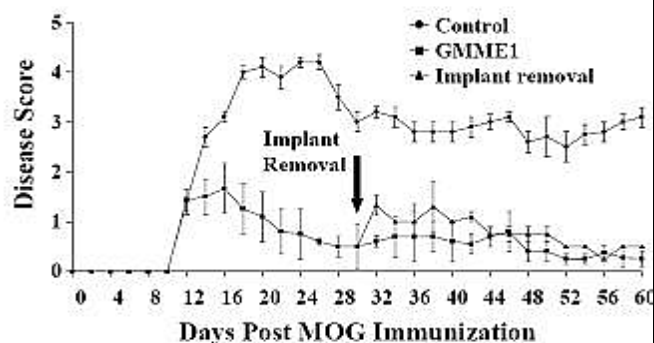
CCR2 antagonists have been identified as potential agents for autoimmune diseases, inflammation, and cancer. While many small molecule CCR2 antagonists have been disclosed, they manifest cross reactivity with other G protein linked receptors or exhibit limited bioavailability and stability. GMME1 is a new fusion protein and an antagonist of the CCR2 receptor. GMME1 secreted by implanted Mesenchymal stromal cells (MSC), exhibits efficacy at steady state plasma concentrations of 2 pM, GMME1 has now been prepared on a laboratory scale.

Validation

The inventors have shown that GMME1 expressed by MSC (i) induces apoptosis of CCR2-expressing cells, (ii) blocks Th1/Th17 responses in mouse splenocytes, (iii) inhibits inflammation in an experimental autoimmune encephalomyelitis (EAE) mouse model (**figure**); and (iv) sustains the engraftment of xenogenic cells in immunocompetent mice. Thus, the recombinant protein GMME1 could find utility in killing CCR2 expressing solid tumor cells, counteracting the pathogenesis of rheumatoid arthritis and multiple sclerosis and suppressing the immune response in transplantation. GMME1 secreted by MSC induces an

immunosuppressive effect on activated lymphomyeloid cells in autoimmune diseases.

Secreted GMME1 leads to persistent remission of EAE



MOG challenged mice having a floppy tail were administered parenterally with GMME1-expressing mesenchymal stromal cells and control. GMME1 treated EAE mice recovered 10 days after treatment onset while the control group reached the highest disease score. Removal of the GMME1 expressing implant did not lead to relapse.

Medical/Market Need and Opportunity

The global anti-cancer market was estimated at \$47 billion in Y2006 and is projected at over \$65 billion by 2012, including supportive care. Solid tumors, such as breast, prostate, lung, account for 67% of all malignant types. Biological products in autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis generated \$4 billion and the same products are anticipated to achieve \$6 billion in 2009. Additional potential therapeutic fields might be psoriasis, uveitis, and Crohn's disease. Asthma and COPD have also been linked to CCR2 and might be addressed by the GMME1 antagonist. The market share of biopharmaceuticals in therapeutic indications such as cancer and autoimmune diseases is increasing exponentially.

1. Provisional Patent Application (priority date July 8, 2008)
2. 1 paper submitted, 1 under editing



Dr. Jacques Galipeau

MD, University of Montreal, 1988

Specialty (internal medicine) McGill-affiliated Jewish General Hospital

Subspecialty (hematology, oncology) Tufts-affiliated New England Medical Center, Boston

Scientific fellowship (gene therapy) St-Jude Children's Research Hospital, Memphis, Tennessee

Clinician/Scientist, Lady Davis Institute for Medical Research

Associate Professor of Medicine and Oncology, McGill University, 1997

In 1997 Dr Galipeau initiated and developed a research program in cell and gene therapy of severe illnesses such as cancer, anemia, heart disease and hemophilia. His research is funded by multiple peer-reviewed public and philanthropic societies. Dr.

Galipeau plays a major leadership role in the Canadian Stem Cell Network as therapeutics theme leader and is an active member of the Montreal Center for Therapeutics in Cancer and the Jewish General Hospital Cancer research program. He has also been on staff as a clinical hematologist at the Jewish General Hospital since 1997. He is a tenured Associate Professor Medicine and Oncology at McGill University. Since 2001 he is Medical Director of the Cell and Gene Therapy Program at the Montreal Center for Experimental Therapeutics in Cancer.

Dr Jacques Galipeau

M.D., Université de Montréal (1988)

Spécialisation (médecine interne) affilié à McGill et à l'Hôpital général juif

Sous-spécialité (hématologie, oncologie) Tufts-affiliated New England Medical Center de Boston

Bourse de recherche scientifique (thérapie génétique) St-Jude Children's Research Hospital, Memphis, Tennessee

Clinicien-chercheur à l'Institut de recherche médicale Lady Davis

Professeur agrégé au Département de médecine et d'oncologie de l'Université McGill (1997)

En 1997, Dr Galipeau a mis en place et élaboré un programme de recherche sur la thérapie cellulaire et génique de maladies graves telles que le cancer, l'anémie, la maladie cardiaque (cardiopathie) et l'hémophilie. Cette étude de recherche est subventionnée par plusieurs sociétés publiques et philanthropiques révisées par les pairs. Dr Galipeau joue un rôle important dans le Réseau des cellules souches du Canada en tant que leader du volet thérapeutique et est membre actif du Centre de thérapies du cancer de Montréal et du programme de recherche sur le cancer de l'Hôpital général juif. Il évolue aussi comme membre du personnel de l'Hôpital général en tant qu'hématologue clinicien depuis 1997 et est professeur titulaire agrégé au Département de médecine et d'oncologie de l'Université McGill. Depuis 2001, il œuvre à titre de directeur médical du Programme de thérapie cellulaire et génique du Centre de thérapie expérimentale du cancer de Montréal (CTECM).