

Technology Licensing Opportunity

Non-Confidential Summary



G31P –REDUCING I/R-INDUCED MORTALITY AND ORGAN INJURY ROI# 07-039

Technology:

An immunotherapeutic peptide which prevents the neutrophil sequestration that mediates local and remote organ injury induced by ischemia and reperfusion (I/R)

Market:

The incidence of ischemic injury is vast: myocardial infarction, stroke, and other thrombotic events affect more than 1.3 million individuals each year in the USA. Neutrophil responses play critical roles in host defense, but in an array of settings overly exuberant responses become a primary driver of host pathology. For example, neutrophil sequestration following intestinal ischemia-reperfusion (I/R) is known to play a critical role in mediating both local and remote organ dysfunction and may contribute to trauma-associated multiple organ failure. Therapies for such multiple organ failure have focused on blocking neutrophil recruitment. Positive experimental outcomes have been realized through antagonizing ELR-CXC chemokines, with superior protection observed when multiple chemokines are blocked suggesting that blockade of all ELR-CXC chemokines with an effective CXCR1/CXCR2 antagonist could be highly protective in I/R injury.

Innovations:

The inventors have generated a peptide, G31P, which is a CXCL8-based high affinity antagonist of the ELR-CXC chemokines. G31P antagonizes both CXCR1 and the CXCR2 and ameliorates neutrophilic inflammation in numerous disease models including intestinal I/R injury.

The rat superior mesenteric artery I/R model was used to examine the impact of G31P administration on intestinal I/R-induced local and remote organ injury. Epithelial cell apoptosis is prominent in intestinal I/R injury, and histologic data confirms that the intestinal epithelium suffers overwhelming damage in I/R injury animals. Importantly, subcutaneous injection of G31P significantly attenuates intestinal epithelial damage and blocks I/R-induced neutrophil sequestration in the gut and lung. Post-operative survival rates are also drastically improved in I/R injury animals that receive G31P injections. Evidence indicates that, unlike other CXCR1/CXCR2 under development, G31P blocks both these G protein-coupled receptors (GPCR), but also those for heterologous inflammatory GPCR ligands (e.g., C5a), thereby dramatically expanding its efficacy as an anti-inflammatory agent.

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Researcher profile:



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Professor, Division of Respiratory & Critical Care Medicine
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Research interests: allergy/asthma, regulation of immune responses, and therapeutic amelioration of neutrophilic inflammation, in both humans and veterinary species

Patent Status:

US Patent Applications No. 2011/0046069
WIPO: PCT/CA2009/000170

Development Stage:

Animal studies completed & working prototype

Select Publications:

Zhao X, Town JR, Li F, Zhang X, Cockcroft DW, Gordon JR. ELR-CXC chemokine receptor antagonism targets inflammatory responses at multiple levels. *J Immunol* 2009;182:3213–22.

Zhao X, Town JR, Yang A, Zhang X, Paur N, Sawicki G, Gordon JR. A novel ELR-CXC chemokine antagonist reduces intestinal ischemia reperfusion-induced mortality, and local and remote organ injury. *J Surg Res*. 2010 Aug;162(2):264-73. Epub 2009 Jun 6.

Zhao X, Town JR, Li F, Li W, Zhang X, Gordon JR. Blockade of neutrophil responses in aspiration pneumonia via ELR-CXC chemokine antagonism does not predispose to airway bacterial outgrowth. *Pulm Pharmacol Ther*. 2010 Feb;23(1):22-8

Gordon JR, Zhang X, Li F, Nayyar A, Town J, Zhao X. Amelioration of pathology by ELR-CXC chemokine antagonism in a swine model of airway endotoxin exposure. *J Agromedicine*. 2009;14(2):235-41

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