G31P – AN EFFECTIVE TREATMENT FOR ASPIRATION PNEUMONIA
ROI# 07-040

Technology:
A peptide which ameliorates neutrophilic inflammation in numerous animal models including aspiration pneumonia

Market:
The accidental aspiration of bacteria-laden, acidified gastric content is associated clinically with serious illness, including acute lung inflammation (ALI) and/or acute respiratory distress syndrome (ARDS), often with lethal outcomes. The incidence of pulmonary aspiration is approximately 1 in 3000 during general anaesthesia surgeries. ALI/ARDS associated with aspiration pneumonia carries a mortality rate of 10-30%. Neutrophil responses play critical roles in host defense, but in an array of settings overly exuberant neutrophil responses become a primary driver of host pathology such as the inflammatory cascade in aspiration pneumonia.

CXC chemokines that display the amino sub-terminal ELR-CXC motif (e.g., CXCL8 [interleukin-8]) are redundantly expressed neutrophil agonists that bind to two G-coupled protein receptors, the CXCR1 and CXCR2. It has been shown in multiple models and species that neutralization of CXCL8 reduces host pathology. However, the redundant expression of the ELR-CXC chemokines is problematic for therapeutic approaches that target any one of these chemokines or receptors. Thus, development of an effective combined CXCR1/CXCR2 antagonist has been a pharmaceutical industry focus for some time.

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. Neutrophils are the primary driver of the inflammatory cascade in aspiration pneumonia and G31P dramatically dampens bacterial pneumonia pathology (e.g., hemorrhagic consolidation, neutrophilic infiltration; see figure) without predisposing to local bacterial outgrowth. 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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Research interests: allergy/asthma, regulation of immune responses, and therapeutic amelioration of neutrophilic inflammation, in both humans and veterinary species

Patent Status:
US: 61/027,959
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Development Stage:
Animal studies completed & working prototype

Select Publications:


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