

TLR7/8 Antagonists: Anti-bacterial and Anti-inflammatory Agents

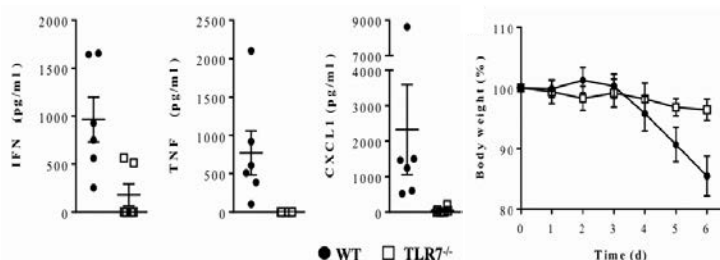
Summary

Toll like receptors (TLR) are the 'intruder detectors' of the body. TLR7 and 8 are expressed within leukocytes and specifically recognize RNA. Most often, TLR7/8 are described as well-characterized sensors of viral RNA, yet their important role in bacterial infections is now being revealed.

Dr. Gantier has discovered that bacteria in the gastrointestinal (GI) tract can be detected by intracellular TLR7 sensors. TLR7 bacterial detection plays a fundamental role in the inflammation process in the GI tract. The specific inhibition of TLR7 by antagonists was found to protect mice from aberrant inflammation and, in some cases, bacterial colonisation.

Inhibition of TLR7/8 bacterial sensing in the GI tract could be used to treat infection or alleviate inflammation associated with common GI conditions, such as inflammatory bowel disease and colitis. There is also potential application for multidrug resistance treatment (e.g. ESKAPE pathogens) and bioterrorism preparedness.

Key Data



Circulating pro-inflammatory serum cytokines (IFN, TNF and CXCL1) are strongly decreased in *Salmonella* infected TLR7 deficient mice. In TLR deficient mice acute *Salmonella* infection does not affect body weight, whereas in wild type mice >10% body weight is lost.

Advantages and research strengths

- World leading nucleic acid and innate immune system expertise
- *In vivo* and *in vitro* infection and inflammation models established

IP position

PCT patent filed in Feb 2015.

Market

Host (i.e. human) targeted treatments, mediated by controlled augmentation of the innate immune system, are an important alternative to antibiotics. Antibacterial resistant infections to common human pathogens are responsible for tens of thousands of deaths in the US and EU. Because host targeted treatments are not directed at the pathogen, normal mechanisms of drug resistance are avoided. Targeting TLR7/8 is a ground breaking means to potentially overcome antibacterial resistance, with significant implications for global healthcare.

Aberrant inflammation of the GI tract can manifest as conditions such as ulcerative colitis (UC) and inflammatory bowel disease (IBD). UC and IBD are major unmet needs in healthcare with combined global market size >US\$6B. TLR7/8 are critical mediators of GI inflammation and promising therapy targets.

Opportunity

Hudson welcomes opportunities for co-investment or collaboration to further develop this project.

For further information

Rob Merriel
BD Executive
rob.merriel@hudson.org.au
+61 418 186 265

Nadine Brew
BD Coordinator
nadine.brew@hudson.org.au
+61 423 351 757

Dr Michael Gantier
Research Head, Nucleic Acids and Innate Immunity
+61 3 8572 2709