

InvenioIP - Technology Details

Institution: University of Maryland, Baltimore

Docket: BH-2007-086

Title: A Novel Role for RNase-L in Host Defense Against Bacterial Pathogens

Summary: UMB researchers have identified a novel target for broad spectrum antibacterial treatment, the endoribonuclease RNase-L. This enzyme has been previously shown as a mediator of the immune response to viruses and tumors, but is now shown to have an equally important role in the immune response to bacterial pathogens. In mice exposed to anthrax or E. coli bacteria, the UMB researchers found that mice without RNase-L were unable to clear the bacteria from their tissues and were much less likely to survive the infection. The known biological activities of RNase-L require its activation by a small molecule, 2-5A, which itself is not a viable drug candidate. Suitable small molecule activators of RNase-L have been identified and are in development at UMB as a new class of antibacterial agents.

Applications: The CDC states that 2 million patients acquire a bacterial infection in the hospital each year and 90,000 of those patients die from the infection. More than 70% of hospital-acquired bacterial infections are resistant to standard antibiotic treatments. This results in longer hospital stays and the use of more expensive drugs in an effort to treat such antibiotic-resistant infections. Developing new classes of antibacterial agents such as the present UMB technology is critical for countering bacterial infections that have become resistant to older antibiotics. Further, new antibacterial treatments are required to combat the emergence of new pathogens and the potential use of biological weapons.

Advantages:

- Broad spectrum antimicrobial activity anticipated.
- Treatment may be given prior to or without identifying the causative agent, particularly relevant when people may be exposed to biologic weaponry or new pathogen variants.
- Antibiotics provide clear endpoints for clinical success
- Development further streamlined by use of (i) small molecule; (ii) commercially available compound or analogs

State of Development: Promising therapeutic strategy as demonstrated in knock-out mice. Studies are underway to optimize lead compounds for antibacterial activity and in vivo dosing parameters.

R and D Required: Further pre-clinical optimization prior to initiating clinical development.

Licensing Potential: UMB seeks partners for licensing, clinical development, and/or sponsored research to advance this technology into the healthcare field.

Patent Status: U.S. Patent Application pending, "Methods of Treating a Microbial Infection by Modulating RNase-L Expression and/or Activity".

**Related
Publications:**

- [An essential role for the antiviral endoribonuclease, RNase-L, in antibacterial immunity.](#) Li X-L, Ezelle HJ, Kang T-J, Zhang L, Shirey KA, Harro J, Hasday JD, Mohapatra SK, Crasta OR, Vogel SN, Cross AS, and Hassel BA. Proc Natl Acad Sci U.S.A. 2008 Dec 15 [highlighted in Nature Reviews Microbiology, Feb 2009].
- [Post-transcriptional regulation of RNase-L expression is mediated by the 3'-untranslated region of its mRNA.](#) Li XL, Andersen JB, Ezelle HJ, Wilson GM, Hassel BA. J Biol Chem. 2007 Mar 16;282(11):7950-60.
- [RNase-L regulates the stability of mitochondrial DNA-encoded mRNAs in mouse embryo fibroblasts.](#) Chandrasekaran K, Mehrabian Z, Li XL, Hassel B. Biochem Biophys Res Commun. 2004 Dec 3;325(1):18-23.
- [RNase-L-dependent destabilization of interferon-induced mRNAs. A role for the 2-5A system in attenuation of the interferon response.](#) Li XL, Blackford JA, Judge CS, Liu M, Xiao W, Kalvakolanu DV, Hassel BA. J Biol Chem. 2000 Mar 24;275(12):8880-8.

Files:  [Li et al., 2008, Proc. Natl Acad Sci.](#)

Technology Bret Hassel

Inventors: Alan Cross
Xiao-Ling Li
Tae Jin Kang

Contact Info: Technology Licensing Officer
cvip@umaryland.edu
620 West Lexington St.
Baltimore, MD, 21201
410-706-1187