

EDITORS-IN-CHIEF

Kevin J Tracey, MD
*The Feinstein Institute for Medical Research
Manhasset, NY, USA*

Anthony Cerami, PhD
*Kenneth S Warren Laboratories
Tarrytown, NY, USA*

EDITORIAL STAFF

*The Feinstein Institute for Medical Research
Manhasset, NY, USA*

Christopher J Czura
Executive Editor

Margot Gallowitsch-Puerta
Managing Editor

Veronica J Davis
Communications Editor

Robert L Pinsonneault
Associate Editor

Podcast Transcript
Episode 70

Hello *Mollie Medcast* listeners and welcome back! *Mollie Medcast* is the podcast for the biomedical journal, *Molecular Medicine*. My name is Margot Puerta, I'm the Managing Editor here at *Molecular Medicine* and your host for this podcast episode. In this week's podcast we're going to go over some more papers from our May-June 2010 issue. We have a gene theme this week with "A Molecular Fingerprint Of Lung Injury," "Gene Therapy For Fabry Disease," and our review paper, "Endocytosis And Gene Delivery."

Let's start by reviewing our goal here at *Molecular Medicine*. Established in 1994, our mission is to publish novel work that's concerned with understanding the pathogenesis of disease at the molecular level, which may lead to the design of specific molecular tools for disease diagnosis, treatment and prevention. If you are interested in submitting a manuscript to the journal, please visit our Web site for information, www.molmed.org. So let's move on to our gene-themed podcast.

The first paper in this podcast episode is:

A Molecular Fingerprint Of Lung Injury

Sepsis can be caused by an imbalance in the body's immune response to overwhelming bacterial infection. It affects more than 750,000 people per year and that's just in the US.¹ Mouse preprotachykinin-A, which we'll call PPTA for short, encodes mainly for the neuropeptide substance P. Deletion of PPTA can protect against lung injury and mortality in sepsis. In this paper, Dr. Akhil Hegde and colleagues from New Zealand and Singapore explore differential gene expression in PPTA-deficient lung tissue eight hours after inducing microbial sepsis. The title of their paper is, "Substance P in Polymicrobial Sepsis: Molecular Fingerprint of Lung Injury in Preprotachykinin-A-/- Mice." After sepsis induction, the authors found that the PPTA knockouts (so, those with the genetic deletion of substance P) showed significantly different inflammation and immunomodulation gene expression profiles, compared to the wild-types. Interestingly, the interleukin-1 receptor antagonist gene was elevated in PPTA knockout septic mice. The authors postulate that the observed, elevated levels of inflammatory gene expression in the early stages of sepsis in PPTA knockout mice could point to treatment options that limit excessive immunosuppression.

Since sepsis is such a huge clinical and global problem, the Feinstein Institute (the publishers of *Molecular Medicine*) will be hosting a symposium at the end of September to discuss it. The Merinoff Symposium will feature worldwide thought leaders in sepsis, healthcare, federal government, industry partners and public health agencies. It's going to take place this fall September 30th and October 1st here at the Feinstein. There are three major goals of the symposium: first, the establishment of an agreed upon laymen definition of sepsis; second, the establishment of an agreed upon molecular definition of sepsis; and lastly, we're going to pull together a call to action for philanthropists, governments, and industry. This is to recognize that sepsis kills more Americans each year than prostate cancer, breast cancer and HIV/AIDS combined, yet few resources are deployed to combat it. We also aim to get public health agencies to recognize that current reporting schemes do not adequately capture the number of sepsis diagnoses and deaths each year. If you'd like to review the agenda and speaker list, please visit the Merinoff Web site, it's www.merinoffsymposia.com (m-e-r-i-n-o-f-f-s-y-m-p-o-s-i-a.com).

Next up is:

Gene Therapy For Fabry Disease

Fabry disease is a lysosomal storage disorder, and it's caused by a deficiency of α -galactosidase A activity (α -gal A). This leads to a buildup of globotriaosylceramide, or Gb3, resulting in cardiac, renal and cerebrovascular disease. Fabry disease is the second most prevalent lysosomal storage disorder and it's a model for the development of therapy for single gene defects. Now, while enzyme replacement therapy is available, it requires frequent lifelong infusions and only seems to slow progression of the disorder. Because gene therapy is a promising approach for Fabry disease, Dr. Higuchi and colleagues from Canada and Japan sought to optimize a construct for α -gal A delivery. The title of their paper is, "Alpha-galactosidase A-Tat fusion enhances storage reduction in hearts and kidneys of Fabry mice." In it, the authors demonstrate that administration of a lentivector containing α -gal A fused to a region of Tat more efficiently reduces Gb3 accumulation in Fabry hearts and kidneys than the vector with α -gal A alone. If you are unfamiliar with Tat, it's a protein transduction domain from HIV that allows proteins to penetrate the cell membrane. These data may advance gene therapy for Fabry disease, and suggest that α -gal A linked to Tat may make existing enzyme replacement therapy more effective.

And, lastly, our review article:

Endocytosis And Gene Therapy

Gene therapy is presently being investigated for its therapeutic potential in treating a number of maladies. Gene therapy relies upon a variety of viral and nonviral vectors which are delivered to target body cells and are subsequently endocytosed and disassembled. The mechanisms by which vectors such as adenoviruses, adeno-associated viruses, retroviruses and liposomes enter the cell are being increasingly focused upon as the effort to increase the efficiency of gene therapy continues. In this review, Dr. Ziello and colleagues focus on the mechanisms of endocytosis and how they relate to the trafficking of viral and nonviral vectors in gene therapy.

And that's it for this week's episode of *Mollie Medcast*. For questions or comments regarding this podcast, please to send me an e-mail at: margot@molmed.org, that's m-a-r-g-o-t(at)m-o-l-m-e-d.org. We are currently conducting a social technology survey. Visit our Web site to take the survey and receive a free subscription to our journal for the year 2011, and the chance to win an iPod Touch!

This podcast is available on the Web site and is up in iTunes, just type "Mollie Medcast" in the search bar. If you've enjoyed this podcast, leave us a review, or rate it in iTunes. During the month of March we received over 4,600 podcast downloads! *Molecular Medicine* is published bimonthly by The Feinstein Institute for Medical Research.

From New York, this is margot@molmed.org, thanks for listening!

Produced by Margot Puerta
Managing Editor, *Molecular Medicine*

Written by Robert L Pinsonneault
Associate Editor, *Molecular Medicine*

Edited by Veronica J Davis
Communications Editor, *Molecular Medicine*

Music: Opuzz.com
Photos: iStock or BigStock