Molecular Medicine

Mollie Medcast
Episode 10 Transcript: Sepsis, Cardiac Proinflammatory Stress

Hello and welcome back to "Mollie Medcast," the podcast for the biomedical journal, *Molecular Medicine*. This is Margot Gallowitsch-Puerta the host for your podcast episode. I'm the Associate Editor here at *Molecular Medicine* coming to you from the north shore of Long Island, New York.

In this week's podcast: "Fractalkine Pumps Up Phagocytosis," "Lovastatin Effects On Macrophages," and "Getting To The Heart Of An Inflammatory Response."

But before we get started with that let me just take a minute to tell you about how we got started. We've seen great advances in the biomedical sciences over the last several decades and this has been due to the integration of fields like molecular and structural biology, biochemistry and immunology. Integrating these fields has done two things. It has given us a new perspectives to think about and given us powerful new tools which we're now using in medical research. *Molecular Medicine's* 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 diagnosis, treatment and prevention. We introduced our journal in 1994 so that scientists and researchers could communicate their recent discoveries to a multidisciplinary, international audience who is interested in understanding and curing disease.

Molecular Medicine is published bimonthly by the Feinstein Institute for Medical Research which is located in Manhasset, New York.

Alright, so let's get started with the papers for this week's podcast episode.

Injury or infection initiates inflammatory responses that are beneficial to the host and contribute to healing. However, when this inflammatory response goes unchecked, systemic inflammation may lead to multiple organ failure, shock and ultimately death. The papers in this week's podcast report mechanisms involved in various immune responses, which may allow researchers to discover novel treatments for these complex diseases.

Fractalkine Pumps Up Phagocytosis
Sepsis is a systemic inflammatory response to infection, which may lead to multiple organ failure and is associated with increased rates of apoptosis. Clearance of apoptotic cells is crucial to maintaining cellular function under normal and pathological conditions. Administration of exosomes, derived from immature dendritic cells, promotes phagocytosis of apoptotic cells and improves survival in an animal model of sepsis by providing milk fat globule epidermal growth factor-factor VIII (MFG-E8). In this paper, entitled, "Fractalkine-induced MFG-E8 Leads to Enhanced Apoptotic Cell Clearance by Macrophages," Dr. Miksa and his colleagues investigate whether the CX3CL1-chemokine fractalkine plays a role in apoptotic cell clearance. Their results show that CX3CL1 induces MFG-E8 in vitro and in vivo and enhances clearance of apoptotic cells in an MFG-E8 dependent manner. These findings suggest a possible novel treatment for patients with sepsis.

Lovastatin Effects On Macrophages
Sepsis is a systemic response to infection and a major health problem with approximately 750,000 cases per year in the United States. Adequate therapies do not exist and patient care is mainly supportive. Statins, which

are widely used for the treatment of hypercholesterolemia, also show antiinflammatory effects, however, their mechanisms are not well understood. Lipopolysaccharide (LPS) induces an inflammatory response and interacts with CD14, a major LPS binding site on macrophages. Here Drs. Frey and De Maio investigate the effect of statins on CD14 expression. The paper title is, "Increased Expression of CD14 in Macrophages After Inhibition of the Cholesterol Biosynthetic Pathway by Lovastatin." Their results suggest that statin treatment may modulate macrophage function and have an impact on inflammation and the outcome of sepsis.

The last paper for this week's line-up is:

Getting To The Heart Of An Inflammatory Response
Acute activation of a proinflammatory cytokine stress response initially provides the heart with adaptive and protective mechanisms. However, prolonged cytokine activity can lead to overt cardiac decompensation, edema and failure. While several mechanisms of cardiac induction of proinflammatory cytokines have been investigated, the effects of sympathetic overactivity on the proinflammatory stress response are less clear. Beta-adrenoceptor activation contributes to proinflammatory stress responses and in this work, Dr. Rohrback and her colleagues analyze myocardial cytokine expression under various conditions of ß -adrenoceptor activation. In this paper, "Activation of AP-1 contributes to the ß-adrenoceptor-mediated myocardial induction of interleukin-6," the authors show that ß -adrenoceptor-mediated activation of cAMP-responsive element and activating protein-1 directly contribute to interleukin 6 induction in healthy and failing myocardium. These results advance our understanding of sympathetic activity during cardiac proinflammatory stress.

That's it for this week's episode of "Mollie Medcast." You can find these papers and many more of them on our website, ***www.molmed.org*** that's www.m-o-l-m-e-d.org.

I'll be giving away an iPod Shuffle to one of our frappr map members. To be eligible for the contest just visit our podcast page, www.molmed.org/podcast.html and put your pin on our *Molecular Medicine* frappr map. At the end of this month one winner will be randomly selected from our frappr map members and will receive a free shuffle. All you have to do is sign up!

For questions or comments regarding this podcast, please send me an email at margot@molmed.org, m-a-r-g-o-t @molmed.org. From Long Island, New York, this is margot@molmed.org, thanks for listening!

Written and Produced by Margot Gallowitsch-Puerta
Associate Editor, *Molecular Medicine*
Music: Opuzz.com
Photos: iStock

###