Molecular Medicine

Podcast Transcript
Episode 85

Hello *Mollie Medcast* listeners and welcome back to the podcast! *Mollie Medcast* is the podcast for the biomedical journal, *Molecular Medicine*. My name is Margot Puerta, Managing Editor here at *Molecular Medicine* and I'll be your host for this podcast episode. In this week's podcast we'll take a look at two primary research papers and one review paper from our November-December 2010 issue. The primary research papers are: "PPAR□ In Sepsis" and "Dietary Restriction In Acetaminophen Hepatotoxicity," and the review, "Chiro-Inositol Glycans in Insulin Signaling and Insulin Resistance Chiro-Inositol Glycans-Insulin Action And Resistance".

We'll start by taking a moment to review our goal here at *Molecular Medicine*. Since 1994 our mission has been 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're interested in submitting a manuscript to the journal, please visit our website for information, www.molmed.org. Ok, now onto the podcast.

The first paper in this podcast episode is:
PPARγ In Sepsis
Sepsis, an overwhelming inflammatory response to infection or injury, may lead to shock, multiple organ failure and death. Peroxisome proliferator-activated receptor-γ (abbreviated PPARγ) is a transcription factor which regulates inflammation. Post-translational modifications to PPARγ regulate its function, potentially affecting inflammation. In this work, Dr. Jennifer Kaplan and colleagues at Cincinnati Children's Hospital Medical Center in Ohio investigated the kinetics of altered PPARγ expression and activation in a model of polymicrobial sepsis. The title of the paper is, "Phosphorylation of ERK1/2 Is Associated with the Downregulation of PPARγ during Polymicrobial Sepsis." Data demonstrate that PPARγ is reduced in immunomodulatory and parenchymal cells during polymicrobial sepsis. Restoration of PPARγ correlates with an increase in levels of the antiinflammatory adipokine, adiponectin. These results provide a mechanism through which a decrease in PPARγ in sepsis may be partially explained and support the notion that additional studies investigating the molecular link between adipokines and the inflammatory response in sepsis are warranted.

Next up is:
Dietary Restriction In Acetaminophen Hepatotoxicity
Drug-induced liver injury is a major clinical concern and a leading cause of acute liver failure. Acetaminophen is a widely used analgesic which is safe at therapeutic doses. However, acetaminophen hepatotoxicity following overdose contributes to a significant proportion of cases of acute liver failure worldwide. While biochemical events leading to acetaminophen hepatotoxicity are well-defined, little is known about the cellular mechanism linking metabolic activation to clinical outcome. In this study, Dr. Daniel James Antoine and colleagues in the United Kingdom investigated the effect of dietary restriction on cellular mechanisms during acetaminophen hepatotoxicity. The title of their paper is, "Diet Restriction Inhibits Apoptosis, HMGB1 Oxidation and Promotes Inflammatory Cell Recruitment during Acetaminophen Hepatotoxicity." Their findings indicate the inhibition of caspase driven apoptosis and HMGB1 oxidation by ATP depletion from fasting, promotes an inflammatory response during drug-induced hepatotoxicity. This work may aid the development of intervention therapies for

cases of acetaminophen overdose and could improve the clinical management of drug-induced liver injury.

The last paper in this episode is a review paper:
D-Chiro-Inositol Glycans in Insulin Signaling and Insulin Resistance
Classical actions of insulin involve increased glucose uptake from the bloodstream and its metabolism in peripheral tissues. However, non-oxidative and oxidative glucose disposal remain incompletely explained by current models for insulin activation. In this work, Dr. Larner and colleagues from Virginia review the possible role of second messengers in responses and resistance to insulin. The authors postulate that inositol glycans, particularly of the D-chiroinositol class, are insulin mimetic and may serve as insulin second messengers.
http://www.ncbi.nlm.nih.gov/pubmed/20811656

And that's it for this week's episode of *Mollie Medcast*. For questions or comments regarding this podcast, please feel free to send me an e-mail at: margot@molmed.org. You can also keep up with the journal by following us on Facebook at www.facebook.com/molmed and Twitter (@mol[underscore]med).

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

Produced by Margot Puerta
Managing Editor, *Molecular Medicine*

Written by Kavin G Shah, Saurav Guha
Volunteer Associate Editors, *Molecular Medicine*

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

Music: Opuzz.com
Photos: iStock or BigStock