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Podcast Transcript

Episode 66: HIV, Sepsis and PCOS

Hello *Mollie Medcast* listeners and welcome back. *Mollie Medcast* is the podcast for the biomedical journal, *Molecular Medicine*. My name is Margot Puerta, Managing Editor here at *Molecular Medicine* and your host for this podcast episode. In this week's podcast we're going to take a look at three research papers. The first two are from our January-February 2010 issue: "HIV Interrupted – Insight Into Pathways That Regulate Viral Integration" and "Biomarkers Point The Way To Better Sepsis Treatments." The third paper is from our March-April issue "No Sugar Coating: Insulin Signaling In Polycystic Ovary Syndrome".

As usual, we will start by taking a minute to remind you about what our goal here is at *Molecular Medicine*. 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're interested in submitting a manuscript to the journal, please visit our Web site for information, www.mol-med.org. Alright, so let's get started with this podcast and take a look at our first research paper.

HIV Interrupted – Insight Into Pathways That Regulate Viral Integration

The CDC estimates that every nine-and-a-half minutes someone in the US is infected with human immunodeficiency virus or HIV, the virus that causes AIDS [Acquired Immune Deficiency Syndrome].(1) The central event in the life cycle of this retrovirus is when HIV integrates into the host cell DNA. In order for this to occur, a combination of proteins are required, they are the viral integrase and the host LEDGF/p75. In their latest efforts, Dr. Aviad Levin and colleagues from Israel examined the early viral integration pathway and demonstrate that an inhibitor of viral integration, the Rev protein, associates with LEDGF/p75. Furthermore, they demonstrate a role for Rev in the dissociation of the integrase-LEDGF/p75 complex. The title of their paper is, "Integration of HIV-1 DNA Is Regulated by Interplay between Viral Rev and Cellular LEDGF/p75 Proteins." The authors propose a model whereby viral integration is regulated by the interplay between LEDGF/p75, Rev and integrase, with the LEDGF/p75-Rev and integrase-Rev complexes leading to inhibition of viral integration. This work could ultimately lead to new strategies for preventing and treating HIV infection. Supplementary data for this paper is available and can be viewed by visiting our Web site at www.molmed.org.

Okay, let's move on to our second paper for this episode:

Biomarkers Point The Way To Better Sepsis Treatments

During the course of polymicrobial sepsis, a range of pro- and antiinflammatory cytokines are produced by the host immune system. Successful recovery from sepsis involves striking a balance between these counteracting cytokines. Understanding gene expression of immune regulators such as cytokines is essential to developing better prognostic tools and therapeutic strategies for treating sepsis. The *preproptachykinin-A* gene, or *PPTA*, has previously been shown to induce expression of immunoregulatory proteins that protect against microbial sepsis. Dr. Akhil Hegde and colleagues from Singapore investigated circulating cytokine profiles in *PPTA* knockout (*PPTA*^{-/-}) mice. The title of their paper is, "Plasma Cytokine Profiles in *Preprotachykinin-A* Knockout Mice Subjected to Polymicrobial Sepsis." A range of both pro- and antiinflammatory cytokines was analyzed using multiplexed bead-suspension arrays. Deletion of the *PPTA* gene resulted in an increase of both pro- and antiinflammatory

cytokines in septic mice and improved survival. This study reveals that multiple factors controlled by *PPTA* are involved in the response to microbial sepsis, some of which may be detrimental to survival from sepsis. This work provides insight into the molecular mechanisms underlying the immune response to sepsis and identifies a technique for rapid and cost-effective biomarker identification, which has implications for improved clinical diagnostic tools for septic patients.

Lastly, let's take a look at one of the papers from our March-April 2010 issue:

No Sugar Coating: Insulin Signaling In Polycystic Ovary Syndrome

Polycystic Ovary Syndrome (or PCOS) is a steroid-related disorder that affects between 5 and 10% of reproductive aged women. PCOS affects endocrine metabolism and is linked with insulin resistance and compensatory hyperinsulinemia. However, little is known about the expression of insulin pathway molecules in endometrial tissue from women diagnosed with PCOS. Dr. Romina Fornes and colleagues from Chile examined the levels of several insulin signaling proteins in endometria from PCOS women with or without hyperinsulinemia. The title of their paper is, "Changes in the Expression of Insulin Signaling Pathway Molecules in Endometria from PCOS Women with or without Hyperinsulinemia." The authors found that the endometrium expresses insulin-sensitive glucose uptake machinery, and that some proteins which belong to the insulin signaling pathway show a significantly reduced expression in PCOS patients with hyperinsulinemia. This alteration suggests a disruption in the insulin signaling pathway which may account for impairment in glucose metabolism and homeostasis at the endometrial level.

That's it for this week's episode of *Mollie Medcast*. Join us next time when we measure MMPs & antioxidants in juvenile-induced arthritis noninvasively, look at MIF in Alzheimer's disease, and review a new view of carcinogenesis and an alternative approach to cancer therapy.

For questions or comments regarding this podcast, please feel free 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. You can also send me an e-mail if you have any scientific meetings that you'd like us to display on our Web site. Follow us on Twitter (@mol_med).

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1. <http://www.cdc.gov/hiv/topics/surveillance/basic.htm#hivest>