Molecular Medicine

Podcast Transcript
Episode 63

Happy New Year 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. Since this is our first podcast of 2010 I thought it would be fitting to take a quick look back at the top five papers downloaded from our Web site in 2009.

Before we get to those top five papers, let me 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. We do this so that we may be able to design specific molecular tools for disease diagnosis, treatment and, ultimately, prevention. If you're interested in submitting a manuscript to the journal, please visit our Web site for information, www.molmed.org. Okay, so let's get started with this podcast and the countdown for the top five papers downloaded from our Web site in 2009!

#5: "Progesterone with Vitamin D Affords Better Neuroprotection against Excitotoxicity in Cultured Cortical Neurons than Progesterone Alone": this article is by Dr. Fahim Atif and colleagues from Emory University in Georgia.

#4: "The Selective α7 Agonist GTS-21 Attenuates Cytokine Production in Human Whole Blood and Human Monocytes Activated by Ligands for TLR2, [TLR]3, [TLR]4, [TLR]9, and RAGE": this research article is by Dr. Mauricio Rosas-Ballina and colleagues from the Feinstein Institute for Medical Research in New York.

#3: "Regulatory NK-Cell Functions in Inflammation and Autoimmunity": this review paper is by Dr. Anna Lünemann and colleagues from the Institute of Experimental Immunology in Switzerland.

#2: "Adipokines and Insulin Resistance": this review article is by Dr. Katja Rabe and colleagues from the University of Munich in Germany.

And the number one paper downloaded from our Web site in 2009 is…
"Requirement of STAT3 Activation for Differentiation of Mucosal Stratified Squamous Epithelium": this research article appears in Volume 9, Issue 3/4. It was written by Drs. Wu, Sun, and Steinberg. Congratulations Drs. Wu, Sun and Steinberg for having the number one paper downloaded from our Web site in 2009!

Now that we've been through the top five, let's take a closer look at these papers.

The #5: "Progesterone with Vitamin D Affords Better Neuroprotection against Excitotoxicity in Cultured Cortical Neurons than Progesterone Alone."
[This article is in Volume 15, Issue 9/10.]

Traumatic brain injury (or TBI) is a very complex systemic illness. It results in long-term neurodegenerative processes that last for months or even years after the initial injury. Researchers have been working for over 30 years to try to find a safe and effective agent to treat TBI. However, in the past two decades almost all phase II and

phase III clinical trials for moderate and severe TBI have failed. One reason for this may be the heterogeneity of TBI. Monotherapies, which target a single mechanism of action in the injury cascade, have limitations in their efficacy. A way to overcome this may be by combining agents into a cocktail that can simultaneously target different injury mechanisms and potentially stem the cascade of destructive events. This is what Dr. Fahim Atif and his colleagues from Emory University tested. The researchers wanted to determine whether the neuroprotective effects of two agents were greater than either one alone. The two agents used were progesterone and 1,25-dihydroxyvitamin D3 hormone, which we'll call VDH. Dr. Atif and his colleagues tested these agents in an exitotoxic assay for neuronal cell death. He found that pretreatment of primary rat neurons with either compound alone significantly increased neuroprotection, while the combination of progesterone and VDH provided a synergistic effect. While this technique allows rapid testing of experimental compounds and faster development of drug candidates for TBI treatment, the data also suggest that VDH should be further studied as a partner to progesterone for TBI therapy.

#4: "The Selective α7 Agonist GTS-21 Attenuates Cytokine Production in Human Whole Blood and Human Monocytes Activated by Ligands for TLR2, [TLR]3, [TLR]4, [TLR]9, and RAGE."
[This article is from Volume 15, Issue 7/8.]

Inflammation, the body's reaction to infection, is linked with many disease forms. These can be as varied as atherosclerosis, Alzheimer's disease, cancer and sepsis. The vagus nerve is the tenth cranial nerve and stimulation of it activates the cholinergic antiinflammatory pathway. This occurs by downregulating proinflammatory cytokines such as tumor necrosis factor [TNF], and has shown therapeutic benefits in mouse models of sepsis. Dr. Rosas-Ballina and his colleagues at the Feinstein Institute present data in this current work, that cholinergic agonists selective to the alpha-7 subunit of the nicotinic acetylcholine receptor could reduce the levels of TNF. They show this ex vivo in endotoxin treated whole blood. One such agonist, called GTS-21, effectively reduced TNF production in stimulated human monocytes, demonstrating that this compound targets inflammation. GTS-21 also reduced TNF levels in whole blood collected from severe septic patients. These findings contribute to our understanding of inflammation and could lead to improved solutions for the wide range of patients that suffer from inflammation-associated pathologies.

#3: "Regulatory NK-Cell Functions in Inflammation and Autoimmunity."
[This is a review article from Volume 15, Issue 9/10.]

Natural killer (NK) cells are multicompetent lymphocytes with the ability to regulate innate and adaptive immune responses through their interactions with antigen-presenting cells as well as T and B cells. In this review, Dr. Anna Lunemann and her colleagues from the Institute of Experimental Immunology in Zürich provide insight into the regulation of NK cell–mediated innate and adaptive immune responses, as these pertain to autoimmunity and inflammation. The authors highlight the ability of NK cells to limit adaptive immune responses. They also discuss a significant role for these cells in the development and regulation of autoimmune states in both experimental models and patients. Future studies focused on the regulatory role of NK cells may provide promising prospects for NK cell–directed therapies.

#2: "Adipokines and Insulin Resistance."
[This review article is from Volume 14, Issue 11/12.]

Obesity affects more than 1 billion adults worldwide and is associated with a multitude of health problems in adult and pediatric populations. Some of these include type 2 diabetes, fatty liver disease, atherosclerosis, airway diseases, degenerative disorders and even some types of cancer. Understanding the pathogenesis of obesity and its metabolic sequelae has advanced rapidly over the past decade. Due to the sharp rise in obesity, adipose tissue – traditionally considered to be an energy storage depot – has gained tremendous scientific interest. Dr. Katja Rabe and her colleagues from the University of Münich in Germany summarize data on the effect of adipose tissue-derived hormones on insulin resistance. A better understanding of the pathophysiological roles of adipokines in

obesity-induced diseases may result in new pharmacotherapeutic approaches.

And, finally, the number one paper downloaded from our Web site in 2009:
"Requirement of STAT3 Activation for Differentiation of Mucosal Stratified Squamous Epithelium."

Laryngeal papillomas are benign squamous epithelial tumors caused by infection of the low-risk Human Papillomavirus (HPV) type 6 or 11. Removal of these tumors requires surgery, sometimes as often as every few weeks, and currently, there is no cure. STAT3, a member of the signal transducers and activators of transcription [STAT] family, has been shown to play a key role in promoting proliferation, differentiation, or cell cycle progression, depending on cell type. Since papillomas show abnormalities in terminal differentiation, Dr. Wu and colleagues examined the potential role of STAT3 in regulating epithelial differentiation. They measured differentiation by western blot analysis of keratin 13. In models of STAT3 activation, keratin 13 expression was increased, while expression of a dominant negative STAT3 inhibited keratin 13.
The authors concluded that activation of STAT3 was required for the differentiation of normal human stratified squamous epithelium and that this data could be useful for developing a therapeutic strategy for Human Papillomavirus patients.

That's it for this week's episode of The Mollie Medcast. Join us next time when we look at lupus, malaria and acute lung injury.

And, here's a quick stump for our Centricity Series. The idea behind Centricity Series is to bring together clinicians and scientists so that we can facilitate interaction and knowledge sharing. Our next installment, "Living with Lupus: A Window into Autoimmunity," will take place at the Feinstein Institute on January 20th. CME credits will be available and all are invited. Registration forms can be downloaded from our homepage [www.molmed.org].

This podcast is available on molmed.org and is up in iTunes. *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
Margot Puerta, Managing Editor, *Molecular Medicine*
Robert L Pinsonneault, Associate Editor, *Molecular Medicine*

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

Music: Opuzz.com
Photos: iStock