Molecular Medicine

Podcast Transcript
Episode 80

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 our go over the rest of the papers from our September-October 2010 issue: "Regulating HMGB1 Release", "Scavenging Peroxynitrate In Diabetic Angiopathy," and "Mediators of Bilirubin-Mediated Toxicity".

We'll start by taking a minute 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. Alright, let's move on to the papers in this podcast.

First up is:
Regulating HMGB1 Release
High mobility group box-1 (also referred to as HMGB1) is a ubiquitous nonhistone nuclear protein as well as an extracellular molecule regulating innate and adaptive immunity. Extracellular HMGB1 plays an important pathogenic role in infectious and sterile inflammation. Several HMGB1 specific antagonists have provided beneficial results in multiple preclinical models of inflammatory disease. However, since no HMGB1 blocking therapies have been approved for clinical use, Hanna Scheirbeck and colleagues from the Karolinska Insitute in Sweden studied the effects on HMGB1 release by well established antirheumatic compounds. The title of the paper is, "Immunomodulatory Drugs Regulate HMGB1 Release from Activated Human Monocytes." Results demonstrate that treatment with dexamethasone, chloroquine or gold sodium thiomalate have the ability to inhibit HMGB1 release, and that further study in this area is warranted.

Our next paper is:
Scavenging Peroxynitrate In Diabetic Angiopathy
Chronic vascular complications of diabetes, including microvascular (nephropathy) and macrovascular (atherosclerosis) diseases, are major causes of morbidity and premature mortality. Evidence shows that inflammation and oxidative stress play important roles in this pathophysiology. While peroxynitrite is a key mediator of diabetic complications, the effect of peroxynitrite on nitration of two key enzymes with roles in inflammation and oxidative stress remains unknown. These two key enzymes are: cyclooxygenase-2 (or COX-2) and inducible nitric oxide synthase (abbreviated iNOS). Yanning Li and colleagues in China examined this issue and the title of the paper is, "Peroxynitrite-Induced Nitration of Cyclooxygenase-2 and Inducible Nitric Oxide Synthase Promotes Their Binding in Diabetic Angiopathy." The authors concluded that in vivo binding of COX-2 and iNOS exists in diabetic angiopathy, and peroxynitrite-induced nitration of COX-2 and iNOS can promote binding, which contributes to diabetic angiopathy. Therefore, scavenging peroxynitrite in order to attenuate binding of COX-2 and iNOS may represent a more effective intervention for this disease.

Last paper for this episode is:

Mediators of Bilirubin-Mediated Toxicity

Hyperbilirubinemia, or increased levels of bilirubin in the blood, may lead to neurotoxicity and neuronal death. Although the mechanisms of nerve cell damage by unconjugated bilirubin or UCB appear to involve a disruption of redox status and excitotoxicity, the contribution of nitric oxide and N-methyl-D-aspartate, or NMDA, glutamate receptors is unclear. Mario Brito and colleagues at the University of Lisbon in Portugal therefore investigated the role of nitric oxide and NMDA glutamate receptors in UCB neurotoxicity. The title of the paper is, "N-Methyl-D-Aspartate Receptor and Neuronal Nitric Oxide Synthase Activation Mediate Bilirubin-Induced Neurotoxicity." Results reinforce the involvement of oxidative stress and data highlight important steps in neuronal oxidative damage by UCB. Inhibitors and receptor antagonists may represent therapeutic tools to reduce risk associated with oxidative stress and neurotoxicity in unconjugated hyperbilirubinemia.

And that's it for this week's episode of *Mollie Medcast*. Join us next time when we look at sepsis, telomere dysfunction and metabolic syndrome. 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 keep up with the journal by following us on Facebook at www.facebook.com/molmed and Twitter (@mol[underscore]med).

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