Molecular Medicine

Podcast Transcript
Episode 32

Hello and welcome back to the *Mollie Medcast*, the podcast for the biomedical journal, *Molecular Medicine*. My name is Margot Puerta. I'm the Managing Editor here at *Molecular Medicine* and your host for this podcast episode. In this week's podcast, "Bipolar Disease: A Vicious Cycle," "Burning Up Over Cytokines," and "Choline Antiinflammatory Efficacy."

Let's take a minute to review what our *Molecular Medicine's* goal is. Our mission is to publish novel work that's concerned with understanding the pathogenesis of disease at the molecular level, so that we may design specific molecular tools for disease diagnosis, disease treatment and ultimately disease prevention. If you're interested in submitting a manuscript to our journal, please visit the website for information, www.molmed.org.
The first paper that I'd like to review in this podcast deals with bipolar disease:

Bipolar Disease: A Vicious Cycle
Approximately one percent of people have biopolar disorder and while the disorder occurs equally in men and women, the severe rapid cycling form is more prevalent in females.[1] The rapid cycling syndrome, which is characterized by at least four episodes of depression or mania per year, is present in about 10-30% of the bipolar population. The molecular mechanisms underlying this bipolar disorder remain unknown and in this paper, Dr. Martin Begemann and his colleagues in Germany hypothesized that the cycling alterations in brain function might also be reflected in systemic changes with a molecular genetic basis. Molecular signatures of manic and depressed states in peripheral blood, while not disease-inducing, may shed light on similar cyclic alterations in the brain. The authors examined peripheral gene expression in a female subject during recurrent stages of the disease. They found several dysregulated gene transcripts and these included genes involved in the synthesis and metabolism of prostaglandin D2. Prostaglandins, which are associated with inflammation, are also known to induce hibernation in certain animals. Based on this finding the authors conducted a clinical experiment, treating the patient with a cyclooxygenase inhibitor celecoxib (off-label). In contrast to prior pharmacological attempts to treat this patient for over 17 years, targeting prostaglandin synthesis resulted in a reduced clinical severity rating of both depressed and manic phases. While additional studies will have to be completed, this encouraging result is compatible with a mediator role of prostaglandins in this psychiatric disease.

Burning Up Over Cytokines
The severe hypermetabolic response following burn injury correlates with age. It may also be a major contributor to higher morbidity and mortality rates observed in adult burn patients compared with children. Dr. Celeste Finnerty and her colleagues hypothesized that the factor linking age and morbidity was the inflammatory response. To examine this hypothesis the authors compared plasma cytokine profiles following a severe burn in adults and children. Their findings show that cytokine profiles in pediatric patients differ compared with those in adult patients. These results may provide insight with respect to the higher morbidity rate in adults, and suggest children and adults may benefit from different post-burn therapeutic interventions.

Choline Antiinflammatory Efficacy
Excessive proinflammatory cytokine production and release into circulation by immune cells is associated with

septic shock, sepsis and other disorders. The exacerbated release of proinflammatory cytokines and lethality during endotoxemia and sepsis can be controlled by the efferent vagus nerve-based "cholinergic antiinflammatory pathway." The α7 subunit-containing nicotinic acetylcholine receptor [α7nAChR] is an essential component of this pathway. Choline, which is an essential nutrient, is a selective natural α7nAChR agonist. Dr. William Parrish and his colleageus at the Feinstein Institute in New York studied the antiinflammatory potential of choline in models of endotoxemia and sepsis. Their data characterize the antiinflammatory efficacy of choline. They also demonstrate that the modulation of the proinflammatory cytokine tumor necrosis factor release by choline requires α7nAChR-mediated signaling. These results suggest that choline may have therapeutic potential in the treatment of sepsis and other inflammatory disorders.

That's it for this week's episode of the *Mollie Medcast*. You can find all these papers and many more of them on our website, www.molmed.org that's www.m-o-l-m-e-d.org. If you have any questions or comments send me an email at: margot@molmed.org. Check out our podcast webpage molmed.org/podcast. You can play around with our frappr map and see where other *Molecular Medicine* readers are coming from. I've got my pin up there on the map, and if you're not shy you can put a picture up with your own pin.

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1. Mayo Clinic, http://www.mayoclinic.com/health/bipolar-disorder/DS00356/DSECTION=risk-factors, August 5, 2008