

# Molecular Medicine

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## *Mollie Medcast*

Episode 25

Hello everyone and welcome back to “Mollie Medcast,” the podcast for the biomedical journal, *Molecular Medicine*. My name is Margot Puerta. I’m the Associate Editor here at *Molecular Medicine* and your host for this podcast episode. In this week’s podcast: “Smoking Out Oxidants,” sepsis gets “Stuck In The Filter,” “Library Screening For IFN- $\alpha$ ” and “Chewing The Fat,” a review paper dealing with obesity.

Let me take a minute to remind you about what our goal here at *Molecular Medicine* is. 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 used for diagnosis, treatment and prevention. If you are interested in submitting a manuscript to the journal, please visit our website for information, [www.molmed.org](http://www.molmed.org). Alright, so let’s get started with the papers in this podcast. The first paper in this “Mollie Medcast” episode is:

### **Smoking Out Oxidants**

Inflammation occurs in a number of life-threatening diseases and is associated with an increase in oxidant stress. Oxidants can activate monocytes through the Toll-Like Receptor 2, or TLR 2, however, the functional downstream consequence on immune system bacterial surveillance is unknown. Dr. Mark Paul-Clark and his colleagues from the Imperial College London investigated the effects of oxidants on activation of human cells derived from smokers and from nonsmokers. Their manuscript is entitled, “Gram-Positive and Gram-Negative Bacteria Synergize with Oxidants to Release CXCL8 from Innate Immune Cells.” Paul-Clark and his colleagues found that blood from smokers was more sensitive to bacterial stimulation than blood from non-smokers. This suggests that oxidant stress associated with smoking provides an initiating inflammatory signal, potentially via the TLR2 or associated transduction pathways, which sensitizes cells to pathogenic stimuli. Such a synergistic relationship between oxidants and pathogen-induced cell activation provides insight to inflammation-associated oxidant stress.

### **Sepsis Gets Stuck In The Filter**

Cytokines play a pivotal role in the complex pathophysiology of severe sepsis and septic shock. Cytokine-targeting treatment modalities for these conditions have been devised and tested, however, few have exhibited beneficial therapeutic effects. Blood purification, originally developed for the treatment of renal failure, has been applied to critical illnesses. In this manuscript, entitled, ‘Continuous Hemodiafiltration with PMMA Hemofilter in the Treatment of Patients with Septic Shock,’ Dr. Taka-aki Nakada and colleagues from Japan used polymethylmethacrylate-continuous hemodiafiltration, which is abbreviated PMMA-CHDF, and they removed cytokines from patients with septic shock. By using this method they improved hypercytokinemia and dysoxia in patients with septic shock. Their findings suggest that cytokine-oriented treatment using PMMA-CHDF may be an effective strategy for treatment of septic shock.

### **Library Screening For IFN- $\alpha$**

Systemic Lupus Erythematosus, abbreviated SLE, is an autoimmune disease, which affects mainly women during their childbearing years. Lupus is characterized by anti-nuclear autoantibodies and inflammatory lesions, which target several tissues in the body. There remains an urgent need for novel, safe, and effective therapies. Inhibition of type I interferons, such as IFN- $\alpha$ , may provide a therapeutic benefit for Lupus and other autoimmune diseases. Dr. Chen and colleagues from Maryland screened a small compound library to identify modu-

lators of IFN- $\alpha$  biological effects. A high throughput genomic-based screen was applied to prioritize small molecule inhibitors targeting various intracellular signaling pathways. This work describes a novel strategy to identify small molecule inhibitors for the treatment of autoimmune disorders.

And last up, our “Review and Assess” article for this week’s podcast:

### **Chewing The Fat**

Over the past few decades more than half of Americans were among the billion people worldwide who had become overweight or obese. Inflammation has been recognized as a major driver in the pathogenesis of common diseases, such as diabetes and cancer, in which obesity is a major risk factor. While it’s not suggested that obesity’s initial cause is inflammation, obesity does frequently lead to inflammation that appears to arise first in certain fat deposits. In this review article, Dr. Carl Nathan reviews evidence that reactive oxygen and nitrogen intermediates help drive chronic inflammation in the obese. His article is entitled, “Epidemic Inflammation: Pondering Obesity.”

That’s it for this week’s episode of “Mollie Medcast”. You can find all these papers and many more of them on our website, [www.molmed.org](http://www.molmed.org) that’s [www.m-o-l-m-e-d.org](http://www.m-o-l-m-e-d.org). For questions or comments regarding this podcast, please send me an email at: [margot@molmed.org](mailto:margot@molmed.org).

If you’re taking a coffee break and have a moment, check out our podcast webpage [www.molmed.org/podcast](http://www.molmed.org/podcast). You can play around with our frappr map and see where other *Molecular Medicine* readers are coming from. Help us expand our community by adding your own pin to the map. If you’re not shy you can even include your picture.

This podcast is available on [molmed.org](http://molmed.org) and is up in iTunes. *Molecular Medicine* is published bimonthly by The Feinstein Institute for Medical Research.

From Long Island, New York, this is [margot@molmed.org](mailto:margot@molmed.org), thanks for listening!

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