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Podcast Transcript Episode 36

Hello *Mollie Medcast* listeners and welcome back. *Mollie Medcast* is 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. This week we'll be looking at papers involving insulin which seems appropriate since it's just after Halloween and before Thanksgiving. The two primary research papers we'll go over are: "Hyperglycemia Impedes Therapeutic Angiogenesis" and "Hemorrhage And Skeletal Muscle Insulin Resistance"; and then one of our Review and Assess papers from the November-December issue, "Adipokines And Insulin Resistance."

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 disease diagnosis, treatment, and prevention. If you're interested in submitting a manuscript to the journal, check out our website for information, www.molmed.org.

Hyperglycemia Impedes Therapeutic Angiogenesis

Diabetes occurs when the body can't make or use the hormone insulin properly, and it's estimated that almost 24 million people in the US have diabetes.¹ Diabetic patients have impaired angiogenesis which often leads to problems with wound healing and organ transplantation. Being able to harness angiogenesis or arteriogenesis therapeutically may represent a beneficial strategy for patients with diabetes, but also for patients with peripheral or coronary artery disease who are ineligible for surgical revascularization. Trials involving therapeutic angiogenesis have garnered negative responses due in part to the direct effect of hyperglycemia on neovascularization. To further investigate this, Dr. Giovana Di Marco and her colleagues in France tested the activity of proangiogenic molecules under hyperglycemic conditions. They used the chicken chorioallantoic membrane model. Transfected cells expressing either ACE, ET-1, or VEGF were placed onto either hyperglycemic or control embryos. Then, three days later, Dr. Di Marco looked at the proangiogenic effects using angiography and histological analyses. Of the three molecules tested, results showed the negative effects of diabetes on capillary density could be overcome only by vascular endothelial growth factor (VEGF) overexpression. This suggests the proangiogenic factors may play a role in patients with diabetes and that future trials involving therapeutic angiogenesis should be monitored for hyperglycemic interference.

Hemorrhage And Skeletal Muscle Insulin Resistance

Activation of the insulin receptor by insulin is important for the proper regulation of cellular metabolism. Several injuries like surgical trauma, hemorrhage, thermal injury, and sepsis can lead to acute insulin resistance. And, interestingly, the mortality of critically ill patients can be reduced by intensive insulin therapy. The efficacy of intensive insulin therapy in these injuries suggests that understanding acute insulin resistance mechanisms may be important for developing new therapeutic strategies. Dr. LaWanda Thompson and colleagues used a surgical trauma and hemorrhage model to determine the development, timing, and muscle selectivity of hemorrhage-induced skeletal muscle insulin resistance. The data indicate that defects in insulin signaling occurred rapidly and were reversible. Additionally, insulin signaling was more severe in some skeletal muscles but did not occur in cardiac muscle. The mechanisms leading to recovering insulin responsiveness may be key in reducing morbidity

and mortality in the intensive care environment.

Adipokines And Insulin Resistance

Obesity is associated with an array of health problems in adult and pediatric populations. Understanding the pathogenesis of obesity and its metabolic sequelae has advanced rapidly over the past decades. Adipose tissue represents an active endocrine organ that, in addition to regulating fat mass and nutrient homeostasis, releases a large number of bioactive mediators – adipokines – that signal to organs of metabolic importance, including the brain, liver, skeletal muscle, and the immune system, thereby modulating hemostasis, blood pressure, lipid and glucose metabolism, inflammation, and atherosclerosis. In this review, Dr. [Katja] Rabe and colleagues summarize the current data on the effect of adipose tissue-derived hormones on insulin resistance.

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 that's www.m-o-l-m-e-d.org. If you have any questions or comments regarding this podcast, please feel free to send me an email at: margot@molmed.org. That's m-a-r-g-o-t@molmed.org. This podcast is available on our website [www.molmed.org] and is up in iTunes. Just type "Mollie Medcast" in the search bar. *Molecular Medicine* is published bimonthly by The Feinstein Institute for Medical Research.

From Long Island, New York, this is margot@molmed.org, thanks for listening!

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Photos: iStock or BigStock

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1. American Diabetes Association. <http://www.diabetes.org/about-diabetes.jsp>. October 6 2008