Molecular Medicine

Mollie Medcast
Episode 7 Transcript: Skeletal Muscle Atrophy, Angiogenesis, Sepsis

Hello everyone and welcome to another episode of "Mollie Medcast," the podcast for the biomedical journal, *Molecular Medicine*. This is Margot Gallowitsch-Puerta, I'm the Associate Editor here for the journal and in this episode's podcast: "Muscling In On Mechanism," "Angiogenesis In The AV Loop Model," and "AM/AMBP And ecNOS In Sepsis." I'll explain that when we get there, but first our mission statement.

Molecular Medicine's 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 diagnosis, treatment and prevention. We introduced our journal in 1994 so that scientists and researchers could communicate their recent discoveries to a multidisciplinary, international audience who is interested in understanding and curing disease. *Molecular Medicine* is published bimonthly by the Feinstein Institute for Medical Research located in Manhasset, New York.

Alright, so let's get started with the papers for this week's episode.
The first paper in our line-up for this week's episode of "Mollie Medcast" is:

Muscling In On Mechanism
Skeletal muscle atrophy can occur for many reasons, some of which include denervation, changes in hormone levels, it can occur as a result of some diseases such as sepsis and cancer or simply from ageing. Muscle wasting associated with long-term intensive care unit treatment has a negative effect on muscle function, which results in prolonged periods of rehabilitation and a decreased quality of life. More specifically, skeletal muscle atrophy is mediated by a shift in the normal balance between protein synthesis and protein breakdown. While the potential molecular switches controlling this balance have been identified, knowledge regarding these signaling pathways is limited. In this work entitled, "Transcription Factors in Muscle Atrophy Caused by Blocked Neuromuscular Transmission and Muscle Unloading in Rats" Dr. Jenny Nordquist from Uppsala University in Sweden and her colleagues investigate the mechanisms involved in muscle wasting using a rat model to mimic conditions in an intensive care unit. Animals were pharmacologically paralyzed and mechanically ventilated for one to two weeks thereby unloading the limb muscles. The researchers then analyzed transcription factor cellular localization and nuclear concentration in fast and slow twitch muscles. While their results show that ubiquitin ligases are up-regulated, differences exist between fast- and slow-twitch muscles, suggesting these muscles respond differently to muscle unloading signals. Future work using this model may allow for more detailed studies of muscle wasting, which may advance intensive care intervention for patients kept on a mechanical ventilator.

The next manuscript on deck here is called:

Angiogenesis In The AV Loop Model
The modulation of angigogenic processes in matrices is a hot area in tissue engineering.
And that's because cells which are transplanted in the body need to get enough oxygen and nutrients in order to survive. Suboptimal initial vascularization limits the survival of cells in the center of large cellularized implants. Angigogenic factors may be used to shorten the time period between implantation and vascularization of matrices. Basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF) are two of the

most extensively tested angioinductive growth factors in animal models. In this paper, Dr. Arkudas evaluated the angiogenic effects of vascular endothelial growth factor and Basic fibroblast growth factor immobilized in a fibrin-based drug delivery system in the arteriovenous, or AV, loop model. So what these authors did is they created a custom made cylindrical chamber a bit smaller than the width of a dime, and they constructed a loop between the left femoral artery and vein which they then placed in the chamber. They filled the chamber with a gel spiked with these growth factors, let some time go by and then analyzed the specimens. The title of the paper is: "Fibrin Gel-Immobilized VEGF and bFGF Efficiently Stimulate Angiogenesis in the AV Loop Model" Dr. Arkudas found that basic fibroblast growth factor and vascular endothelial growth factor both induced absolute and relative vascular density as well as blood vessel sprouting. Implanting these vascular carriers into growth factor-loaded matrix volumes may allow efficient generation of axially vascularized, tissue-engineered composites.

The final summary for this podcast episode of "Mollie Medcast" is:

AM/AMBP And ecNOS In Sepsis
Once you know what these things stand for, this will be a lot clearer. Sepsis, septic shock and multiple organ failure continue to be the most common causes of death in noncardiac intensive care units. Despite advances in the management of trauma victims, the incidence of sepsis and septic shock has actually increased significantly over the past two decades. Downregulation of vascular endothelial constitutive nitric oxide synthase (ecNOS) contributes to the vascular hyporesponsiveness in sepsis. Circulating levels of adrenomedullin abbreviated, AM, increase significantly in patients with septic shock, systemic inflammation response syndrome and after major surgery, but the AM binding protein (AMBP-1) was significantly reduced in sepsis. While co-administration of AM and the AMBP-1 maintains cardiovascular stability and reduces mortality in sepsis, it is unknown whether the combination AM/AMBP-1 prevents endothelial cell dysfunction. In this paper Dr. Zhou and her colleagues investigated this possibility in an animal model of sepsis and the title of the manuscricpt is "Adrenomedullin and Adrenomedullin Binding Protein-1 Protect Endothelium-Dependent Vascular Relaxation in Sepsis." Their results indicate that that AM/AMBP-1 preserves ecNOS and this mechanism may be responsible for the beneficial effect of AM/AMBP-1 in sepsis. These results suggest a possible novel treatment for patients.

That's it for this week's edition of "Mollie Medcast," thanks for joining me. For more information on any of the manuscripts discussed in this episode or to submit a manuscript of your own (which I'd love), please visit our website, ***www.molmed.org*** that's www.m-o-l-m-e-d.org. As always, thanks for downloading us. This is margot@molmed.org, thanks for listening!

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