

Molecular Medicine

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Podcast Transcript Episode 69

Hello *Mollie Medcast* listeners and welcome back! *Mollie Medcast* is the podcast for the biomedical journal, *Molecular Medicine*. My name is Margot Puerta, Managing Editor of *Molecular Medicine* and your host for this podcast episode. In this week's podcast we'll be moving into our papers from our May-June 2010 issue. First up is our cover story, "Play To Win: Antithrombotic Effects Of ACE2 Activators", then we have, "Proteolytic Dysfunction in Cystic Fibrosis" and, finally, "Factor VIIa Aids Wound Healing."

We'll start by taking a minute to remind you about what our goal here is at *Molecular Medicine*. 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, please visit our Web site for information, www.molmed.org. Now, on to the papers.

First up is our cover story from the May-June issue:

Playing To Win: The Antithrombotic Effects Of ACE2 Activators

Thrombogenic events, such as ischemic stroke, pulmonary embolism, deep venous thrombosis, mesenteric ischemia and acute coronary syndrome, are major complications of certain pathological conditions, such as hypertension, atherosclerosis and diabetes mellitus. Despite many therapeutic advances and increasingly effective drug treatments, thrombogenic events remain the major cause of morbidity and mortality worldwide. Recent data suggest activation of the ACE2/Ang-(1-7)/Mas axis produces antithrombotic activity. In this work, Dr. Fraga-Silva and colleagues evaluated the role of ACE2 in thrombus formation in normotension and hypertension *in vivo*. They also tested a novel ACE2 activator called XNT on thrombus formation. The title of their paper is, "ACE2 Activation Promotes Anti-Thrombotic Activity." Results demonstrate the pharmacological activation of ACE2 by ACE2 activator XNT attenuated platelet attachment to vessels and thrombus formation. These results suggest that XNT could be a potential lead compound for the treatment of thrombogenic diseases.

Next up is:

Proteolytic Dysfunction In Cystic Fibrosis

Cystic fibrosis, or CF, is a lethal genetic disorder characterized by airway remodeling and inflammation, leading to premature death. Recent evidence suggests the importance of protease activity in CF pathogenesis. One protease, matrix metalloprotease 9 (or MMP-9 for short) demonstrates increased activity in CF patients undergoing acute pulmonary exacerbation. This may be due to increased MMP-9 activation as well as degradation of MMP-9's natural inhibitor, tissue inhibitor of metalloprotease-1 (or TIMP[-1]). To examine if this relationship exists in nonexacerbating CF patients, Dr. Patricia Jackson and her colleagues examined protease activity in nonexacerbating CF patients and controls. The title of their paper is, "Human Neutrophil Elastase-Mediated Cleavage Sites of MMP-9 and TIMP-1: Implications to Cystic Fibrosis Proteolytic Dysfunction." Results demonstrate increased MMP-9 activity is stable in CF lung disease, and the presence of specific protease products in CF sputum highlights that human neutrophil elastase-mediated activity plays a role in this dysregulation. This data may have implications for disease-specific therapeutics.

And last up for this episode:

Factor VIIa Aids Wound Healing

Injury to the skin initiates a dynamic process of wound healing characterized by an inflammatory phase, a proliferative phase, and a final remodeling process that removes the cells no longer required. Skin keratinocytes express Tissue Factor, a protein associated with skin wound healing, but little is known about Factor [F] VII, a Tissue Factor ligand. In this work, Dr. Xu and colleagues employed a dermal punch model to demonstrate that low-expressing FVII mice exhibited impaired skin wound healing. This manifested as defective re-epithelialization and reduced inflammatory cell infiltration at wound sites associated with diminished expression of the transcription factor, early growth response-1 [Egr-1]. The title of the paper is, “A Factor VII Deficiency Impairs Cutaneous Wound Healing in Mice.” In this work, the authors demonstrate an *in vivo* relationship between FVIIa, early growth response-1, and the inflammatory response in keratinocyte function during the wound healing process. Greater insight into the mechanism of wound healing holds implications that stretch from the surgical site to the battlefield.

And that's it for this week's episode of *Mollie Medcast*. 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 Twitter (@mol_med). This podcast is available on molmed.org and is up in iTunes, just type “Mollie Medcast” in the search bar. If you've enjoyed this podcast, visit us in iTunes and post a review!

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

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