Molecular Medicine

Mollie Medcast
Episode 3 Transcript: Hepatocellular Carcinoma, CD36, CADASIL

Welcome back to the "Mollie Medcast," the podcast for the biomedical journal, *Molecular Medicine*. Thanks for downloading us. This is Margot Gallowitsch-Puerta, Associate Editor, and I'm coming to you from the north shore of Long Island, New York. This week in the *Molecular Medicine* podcast: "Researchers Use Phage Display Library For Target Practice ", "CD36 And Disease", "Racking Up Knowledge of Arthritis Signaling Pathways" and "Steps Towards Understanding CADASIL."

Before we get on with that, let me remind you about what our goal here at *Molecular Medicine* is. Our mission is to publish novel work 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. Our journal was introduced in 1994 to serve as a forum through which scientists and researchers could communicate recent discoveries to a multi-disciplinary, international audience interested in understanding and curing disease. *Molecular Medicine* is published bimonthly by the Feinstein Institute for Medical Research which is located in Manhasset, New York.

If you're interested in submitting a manuscript to the journal, please visit our website for information, ***www.molmed.org***.

Alright, let's get to this weeks manuscripts…

Researchers Use Phage Display Library For Target Practice
Hepatocellular carcinoma is a form of cancer, which originates in the liver cells. It is a challenging malignancy, which unfortunately results in high patient mortality rates. Current therapies do exist, however, they have drawbacks such as cytotoxicity and this has prompted researchers to seek more effective methods of treatment. Phage display technology is a powerful tool in this field and may impact clinical issues including functional diagnosis and targeted drug delivery. Identification of high affinity ligand biomarkers that could specifically discriminate between normal and cancerous cells as well as differentiate between specific types of cancer cells are keys to the development of early detection methods and preoperative treatment strategies. Biopanning, or panning phage-displayed peptide libraries on intact cells in culture and on the tissues of living animals, has proven successful for isolating peptides, which show high cell-specificity and tissue-specificity. In this manuscript entitled, "Screening and Identification of a Targeting Peptide to Hepatocarcinoma from a Phage Display Peptide Library" Dr. Zhang and colleagues used a hepatocellular carcinoma cell line and a normal hepatocyte cell line to carry out subtractive screening with a phage display-7 peptide library. Their results showed that phage, as well as a synthetic peptide they identified called HCBP1, bound to cell surfaces of hepatoma cell lines and biopsy specimens, but not to normal hepatocytes or non-tumor liver tissues. While further studies are needed to focus on the binding specificity of HCBP1 in human hepatoma tissues and their future applications, these results indicate that the peptide HCBP1 may be a potential candidate for targeted drug delivery in hepatocarcinoma.

CD36 And Disease
Cell differentiation molecule 36 or CD36, is a transmembrane glycoprotein located on chromosome 7q11.2 encoded by 15 exons. The defective CD36 gene may be a candidate for several diseases some of which include

atherosclerosis, arterial hypertension, diabetes, cardiomyopathy, Alzheimer's disease, and malaria. Contradictory data regarding CD36 indicates the necessity for further investigation into its role. In this re- view, "Molecular Basis of Human CD36 Gene Mutations" Dr. Rac and her colleagues from Poland summarize the current knowledge regarding CD36 and the consequences of CD36 genetic mutations in various diseases.

Racking Up Knowledge of Arthritis Signaling Pathways
Rheumatoid arthritis or RA, is a chronic disorder that causes progressive joint destruction. Our next manuscript deals with this topic and is entitled, "The GTPase Rac Regulates the Proliferation and Invasion of Fibroblast-Like Synoviocytes from Rheumatoid Arthritis Patients". Fibroblast-like synoviocytes isolated from RA patient joints display proliferative and invasive properties reminiscent of malignant tumor cells. Rac small GTPases play an important role in tumor cell proliferation and invasion. Dr. Chan from the Feinstein Institute for Medical Research investigated the potential role of Rac proteins in the proliferative and invasive behavior of rheumatoid arthritis fibroblast-like synoviocytes. Results demonstrate for the first time that Rac proteins play an important role in the aggressive behavior of fibroblast-like synoviocytes isolated from RA patients. This work also raises the possibility that Rac proteins contribute to synovial hyperplasia, cartilage invasion and destruction, suggesting that signaling elements in Rac-regulated pathways may include novel drug targets for therapeutic intervention in rheumatoid arthritis.

In case anyone listening is interested, the North Shore-LIJ Health System on Long Island (http://www.northshorelij.com) has over 1000 clinical research studies going on right now in a variety of diseases. Over 15 of these studies deal with Rheumatology. So if you are interested in finding out more about this, you can call 516-562-4874 for information and ask for Ruth. That number again in case you need it is 516-562-4874.

Steps Towards Understanding CADASIL
So the next disease we're going to discuss is a vascular degenerative disease. It's called CADASIL and that stands for cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy. So it's no wonder they call it CADASIL for short! People who suffer from CADASIL may experience migraines, speech problems, depression and dementia. CADASIL is caused by mutations in the NOTCH3 gene and over 140 different mutations have been identified in the gene that encodes the Notch 3 protein. The majority of mutations are missense point mutations, which lead to protein misfolding. Additionally, an uneven number of cysteine residues appear in the extracellular domain of the Notch3 receptor. Accumulation of these receptors on small and middle-sized arteries, along with degeneration of vascular smooth muscle cells, characterize this disease. In this study, Dr. Ihalainen from the University of Helsinki and colleagues characterized the protein expression pattern in cultured human vascular smooth muscle cells from CADASIL patients. The manuscript is entitled, "Proteome Analysis of Cultivated Vascular Smooth Muscle Cells from a CADASIL Patient." In it, the authors identified 11 differentially expressed proteins, which are involved in protein degradation and folding, contraction of the vascular smooth muscle cells and cellular stress. Their results indicate that Notch3 misfolding may lead to endoplasmic reticulum stress and an in increase in reactive oxygen species and cell proliferation inhibition. Additional data suggests the possibility that the angiotension II regulatory feedback loop is activated. This may enhance the cells ability to respond to angiotension II stimulation. An understanding of these interactions enhances current knowledge of this hereditary disease and may also lead to improved treatment measures.

That's it for this week. You can find these papers and many more on our website: ***www.molmed.org*** that's w..w..w…dot m o l m e d… dot… o r g.

This podcast, I'm happy to say, is now up in iTunes which means you can subscribe to it by clicking on the little subscribe button and that will allow you to get new podcasts whenever we post one. Also, you can find the podcast on our website. There is a podcast icon in the upper right-hand corner. Click on it and you'll be able to find our back episodes and transcripts of all the podcasts.

Also, we have a “pre-submission enquiry service.” So if you’re thinking about submitting a paper to the journal but you’re not sure if it falls with in the scope of what we normally publish send me an email with a summary of your novel work and its significance and I’ll respond. My email address is: m-a-r-g-o-t@molmed.org
That’s it for this week. From Long Island, New York this is margot@molmed.org thanks for listening!

Written and Produced by Margot Gallowitsch-Puerta,
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