Molecular Medicine



***Mollie Medcast***
Episode 4 Transcript: Skin Papilloma, Psychotic and Affective Disorders, Squamous Cell Carcinoma, Craniosynostosis

Hello and Welcome! This is Margot Gallowitsch-Puerta, bringing you the "Mollie Medcast," the podcast for the biomedical journal, *Molecular Medicine*. In this week's podcast: "Garlic – It's Not Just For Vampires," "Genetic Variation in Psychotic and Affective Disorders," "A Potential Biomarker For Oral Cancers," and last but not least, "Bone Up On Craniosynostosis."

Before we get started with that, I'd just want to review our mission. The mission of *Molecular Medicine* 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 the journal in 1994 to serve as a forum through which scientists and researchers could communicate recent discoveries to a multi-disciplinary and international audience that was interested in understanding and curing disease. *Molecular Medicine* is published bimonthly by the Feinstein Institute for Medical Research located in Manhasset, New York.

Now, let's get on to our manuscripts for this episode.

**Garlic – It's Not Just For Vampires**
This manuscript has two things that I like very much, garlic and liposmes, which are clever little vesicles used to deliver drugs. (Thank you, Sir Alec Bangham) So, garlic has a long history of potential health benefits. Garlic was part of the Egyptian diet and it actually was given to workers who were building the pyramids because they thought it would give them strength and the ability to work longer and harder. Greek athletes ate garlic before competing in the earliest Olympic games. And Hippocrates, the Father of Medicine, prescribed if for a variety of conditions.[1] The chemotherapeutic and antitumor activity that's associated with garlic has been attributed to the presence of various organosulfide-based compounds including diallyl sulfide. So this is an active component of garlic, it possesses strong anti-neoplastic properties against various forms of cancer. Topical application is the most promising approach for local treatment of skin tumors. However, we need more efficient methods because when you apply something topically the molecules diffuse across the skin surface. Topical liposome-based formulations have shown promise in this area and in the present study Dr. Khan and his colleagues evaluated the effects of liposomised-diallyl sulfide against dimethyl benz (a) anthracene (DMBA)-induced skin papilloma. And the title of this manuscript is, "Potential of Diallyl Sulfide Bearing pH Sensitive Liposomes in Chemoprevention of DMBA Induced Skin Papilloma." Their results showed that liposomiseddiallyl sulfide could effectively delay the onset of tumorogenesis and reduce the cumulative numbers and size of tumor papillomas in treated mice. The promising chemo-preventive nature of liposomal diallyl sulfide may form the basis for establishing effective means of controlling various forms of cancer including skin papilloma.

So let's switch gears a little bit and move on to our next paper.

**Genetic Variation in Psychotic and Affective Disorders**
It's by Dr. Funke from the Harvard Partners Center for Genetics and Genomics out of Cambridge, MA. The manuscript title is, "Analysis of TBX1 Variation in Patients with Psychotic and Affective Disorders." A significant portion of patients that have the 22q11 deletion syndrome (22q11DS) develop psychiatric disorders

including schizophrenia and other psychotic and affective symptoms. The gene or genes responsible for this syndrome may also play a significant role in the etiology of nonsyndromic psychiatric disease. The primary candidate 22q11 deletion syndrome gene is called TBX1, it's involved in epithelial and mesenchymal interactions, a mechanism which is crucial for the development of a wide variety of organs including the forebrain, heart, face and limbs. So TBX1 may therefore play a role in brain development and thus in the 22q11 deletion syndrome-associated as well as nonsyndromic psychiatric disease. Dr. Funke and her colleagues tested whether variation in the TBX1 gene could be associated with psychotic and affective disorders that are relevant to the 22q11 deletion syndrome in Caucasian patients. Her results show that allele and haplotype frequencies were not significantly different between affected cases and controls. So it's unlikely that the TBX1 gene plays a major role in the genetic etiology of nonsyndromic schizophrenia and other psychiatric disorders observed in 22q11 deletion syndrome. However, the 22q11 deletion syndrome may still represent a genetic subclass of schizophrenia, which is very similar but genetically distinct from the nonsyndromic form. In this case, TBX1 may still contribute to the risk of developing psychiatric disease in patients with 22q11 deletion syndrome.

**Potential Biomarker For Oral Cancers**

So the next manuscript we're going to discuss is by Dr. Sartini and his colleagues from Italy. It's entitled, "Nicotinamide N-Methyltransferase Upregulation Inversely Correlates with Lymph Node Metastasis in Oral Squamous Cell Carcinoma." Squamous cell carcinoma is the most common type of cancer in the oral cavity, and it represents about 90% of all the oral cancers. It affects approximately 30,000 Americans every year. Some of the risk factors, which you may imagine are smoking and alcohol consumption.[2] Treatment methods for this type carcinoma usually include surgery or radiation, and it can be with or without chemotherapy. Though despite advances in surgical techniques and these therapies, the mortality rate of this carcinoma has shown little improvement over the past three decades. The overall survival rate of these patients is less than 50% and it seems that the ability to diagnose this disease may be responsible for this poor prognosis. So it would be beneficial to be able to detect this disease earlier and possibly alter the prognosis. An abnormal expression of nicotinamide N-methyltransferase abbreviated NNMT, an enzyme involved in the biotransformation and detoxification of many xenobiotics, has been reported in various cancers. Upregulation of NNMT is inversely related to tumor size, and it may play a role in the initial step of malignant conversion. Dr. Sartini and his colleagues looked at tumor and non-tumor tissues. They found a correlation between the NNMT enzyme gene upregulation and favorable prognosis in oral squamous cell carcinoma patients. While the function of NNMT in cancer cell metabolism is still unclear, Dr. Sartini's data suggest that NNMT may serve as a therapeutic target and potential biomarker for oral squamous cell carcinoma, which may lead to earlier detection of this disease.

Alright, so here we are with the last manuscript for this podcast epidsode.

**Bone Up On Craniosynostosis**

This is an interesting disease. A baby's skull has five thin bony plates that are held together by a fiber-like material called sutures. And these sutures allow a baby's skull to expand as the brain grows. Over time, the sutures will harden and fuse the skull bones together.[3] So when child has craniosynostosis, that means that one or more of these sutures close too soon. This causes the child's head to become abnormally shaped.Craniosynostosis is a common malformation and early corrective surgery is necessary to allow proper brain and skull growth. However, as a result of continuous bone healing defects, several surgeries are usually necessary during childhood and puberty. Apert syndrome is a severe form of craniosynostosis and it's caused by mutations in the fibroblast growth factor 2 receptor. The periosteum, is a dense fibrous membrane covering bone surfaces may play a role in cranial bone regeneration and the contribution of the periosteum to Apert syndrome and its cranial pathophysiology is unknown. So here, Drs. Fanganiello, Sertié and their colleagues observed that Apert syndrome periosteal cells are more committed towards the osteblast lineage. Additionally, they did a global gene expression analysis on Apert syndrome patients periosteal cells and this showed that several genes involved in cellular proliferation and extracellular matrix formation are differentially expressed when compared with control subjects.

So while we still need additional studies are needed these results suggest that the periosteum maybe involved in the pathophysiology of craniosynostosis.

That's it for this episode of the "Mollie Medcast." For more information on any of the manuscripts discussed in this episode or to submit a manuscript of your own, please visit our website, ***www.molmed.org*** that's www.molmed.org. This podcast is available on molmed.org and is up on iTunes. For questions or comments regarding this podcast, please send me an email at: margot@molmed.org. For those of you listening to this podcast in iTunes on your laptop or if you happen to be fortunate enough to have an iPod that includes a photo view, you may have noticed that this podcast is the first one in this series to include images. So for example, the first paper we discussed regarding garlic has an image of garlic followed by the chemical structure of diallyl sulfide and a data slide from the paper. So if you have a chance to check it out, I'd appreciate some feedback.
As always, thanks for downloading us. This is margot@molmed.org, thanks for listening!

Written and Produced by Margot Gallowitsch-Puerta
Associate Editor, *Molecular Medicine*
Music by Opuzz.com
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Work cited in this podcast:

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3 WebMD Medical Reference from Healthwise. Accessed August 6, 2007. http://www.webmd.com/brain/tc/Craniosynostosis-Topic-Overview

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