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Podcast Transcript
Episode 33

Hello and welcome to *The Mollie Medcast* the podcast for the biomedical journal, *Molecular Medicine*. My name is Margot Puerta Managing Editor here at *Molecular Medicine* and your host for this podcast episode. This week we'll be looking at: "Genetic Predictors of Anti-TNF Response", "Gelsolin In Pancreatic Cancer", and "Chronic Fatigue Syndrome", getting tired already.

Before I get too tired, let me take a minute to remind you about what our goal here at *Molecular Medicine* is. *Molecular Medicine's* mission is to publish novel work that's concerned with understanding the pathogenesis of disease at the molecular level. We do this so that we may design specific molecular tools for disease diagnosis, treatment and ultimately, prevention. To submit a manuscript to the journal, check out the author center at our website www.molmed.org.

Genetic Predictors Of Anti-TNF Response

Rheumatoid arthritis is prevalent in over one million Americans.¹ Tumor necrosis factor, or TNF, is a key regulator of the inflammatory cascade in rheumatoid arthritis as well as in several other inflammatory diseases. TNF antagonists have been approved by the FDA to treat arthritis and their therapeutic utility is well established. You may know some of them. They go by the names Remicade, Enbrel and Humira and their job is to block TNF from binding to its cell surface receptors. By blocking TNF binding, the drugs are limiting the cell signaling pathways. The effectiveness of these drugs has been shown, however, efficacy in patients is unpredictable and approximately one-third of patients exhibit minimal or no response. Therefore, the prediction response to anti-TNF treatment for rheumatoid arthritis is a pressing clinical problem. In this research, Dr. Liu and colleagues conducted a genome wide association study on 89 rheumatoid arthritis patients prospectively followed after beginning anti-TNF therapy as part of the Autoimmune Biomarkers Collaborative Network or ABCoN. Several single nucleotide polymorphisms, or SNPs, show significant association with the change in disease activity score observed in rheumatoid arthritis patients over a 14-week period of treatment. While additional data sets are necessary to replicate and further support this data, these results suggest that SNP analysis may be useful to predict response to anti-TNF therapy. You can imagine how useful it would be to identify patients who might successfully respond to therapy, avoiding giving a non-responsive patient an ineffective drug.

If you or someone you know is affected by rheumatoid arthritis or lupus and you want to find out more about research, 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 and over 8 with Lupus. So if you're interested in finding out more about this or any of our other studies really, you can call the following number: 516-562-4874, and ask for Ruth. That number again in case you need it is 516-562-4874. And if you want to look at the Mol Med website [www.molmed.org], you'll be able to find the transcript for this episode, and the phone number and website for contact information.

Gelsolin In Pancreatic Cancer

Pancreatic cancer is a really powerful cancer. And, unfortunately, the overall five-year survival rate is only 3-5% and the median survival rate after diagnosis is less than six months. So, even though pancreatic cancer is such

a virulent malignancy, and has such a poor prognosis, relatively little is known about it and the mechanisms that cause it, especially when we compare it with what we know about other cancers. But, what we do know is that pancreatic tumor cells usually display a disturbed cytoskeleton. Gelsolin, which was originally isolated from rabbits², generally helps to keep the cytoskeleton intact by regulating actin. This makes it a key suspect when things go wrong in diseases such as pancreatic cancer. In order to better understand gelsolin's role in pancreatic cancer, Dr. Ni and colleagues from China and the Netherlands, compared proteomes from pancreatic cancer samples with control samples. The gelsolin protein, which is capable of severing and capping actin filament cytoskeletal structural proteins, was diminished in the cancerous samples. Interestingly, the gelsolin mRNA was not downregulated in cancerous samples. This suggests that posttranscriptional mechanisms may mediate low gelsolin protein levels. Further investigation into gelsolin degradation in cancer progression may have clinical significance in diagnosis, treatment and prognosis of pancreatic as well as other cancers.

Tired Of Chronic Fatigue Syndrome

Chronic fatigue syndrome (CFS) is a clinically defined condition characterized by long-lasting disabling fatigue. The symptoms can be different in different patients, but can also change over time in the same patient.³ Some symptoms include difficulties with concentration and memory, muscle aches, headaches, and problems sleeping. Some of these seem pretty common and if you've had a bad week, you might feel all of these! And that's part of the problem in diagnosing chronic fatigue syndrome. We still don't know exactly what causes chronic fatigue syndrome or why it happens. And because of that, biomarkers for pathological fatigue assessment don't exist. In order to try to find biomarkers for fatigue assessment, Dr. Saiki and colleagues in Japan looked at the gene expression profiles in chronic fatigue syndrome subjects and compared them with control subjects. They were able to identify nine genes that were differentially regulated in chronic fatigue syndrome. What's really interesting is that they then tested this expression profile in a new set of chronic fatigue syndrome and non-chronic fatigue syndrome subjects with long lasting fatigue. Dr. Saiki was able to correctly classify over 90% of the patients as either chronic fatigue syndrome patients or non-chronic fatigue syndrome patients. These encouraging results suggest that this gene cluster could be used in detecting pathological responses in chronic fatigue syndrome patients and for differential diagnosis of this syndrome.

That's it for this week's episode of "Mollie Medcast." Tune in next time when we see what chronic lymphocytic leukemia B cells have on their surface and look at some transcriptional profiles in recurrent respiratory papillomatosis. You can find all these papers and many more of them on our website, www.molmed.org that's www.molmed.org.

Check out our updated podcast page molmed.org/podcast. There are some new links up there that let you subscribe to *The Mollie Medcast* right from that page. And, if you scroll down you can check out our frappr map. If you don't know what it looks like, it's a map of the world and by visiting our site you can stick your pin in the map at your location. A bunch of listeners have posted their pictures up too. And it's so interesting to see where other Molecular Medicine readers are coming from, but it's also great to see the community of scientists trying to understand and prevent disease spread out across the globe.

This podcast is available on molmed.org, the iTunes music store, and several other podcast aggregators. To find us in iTunes, go to the search bar and put in "Mollie Medcast".

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

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