

# Highlights of Dr. Daniel Peterson's presentation to medical practitioners

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Dr. Peterson began his presentation by describing ME/CFS as a complex scientific journey in research.

Viral infections, endotoxemia, altered intestinal microflora, GI mucosal barrier dysfunction, cytokines and inflammation including low NK cell function, increased activation markers, oxidative stress, and mitochondrial dysfunction are a few of the possible markers found in patients with ME.

There are no diagnostic tests available, however, there are definitive bio-markers for ME.

Finding a diagnostic test is critical for the validity of the condition and to stimulate more treatment research.

## RECENT RESEARCH

Currently there is much exciting research being published including the Schutzer et al. study that compared cerebrospinal fluid proteomes to differentiate ME and Post Treatment Lyme Syndrome (PTLS).

Patient sets were 43 ME subjects that met the Fukuda Criteria, 25 subjects who met the CDC criteria for Lyme disease and had completed a minimum of three weeks of IV antibiotic therapy at least four months earlier, and 11 healthy controls.

Using mass spectroscopy and liquid chromatography, the research team generated a comprehensive list of 30 000 peptides in the sample pooled from the subjects in each disease group. The results were as follows:

- 738 proteins were found only in the ME subjects
- 692 proteins were only found in PTLS samples
- 724 proteins were only found in the normal controls.

Conclusions drawn from this study are that there are distinct sets of proteins that can distinguish ME patients from PTLS patients and normal controls.

PTLS patients also have a distinct profile.

Proteins relevant to specific neurological functions were lower in ME patients indicating that the brain is not functioning properly and proteins specific to immune function were markedly elevated.

Another study presented was the LEUKOTROPIC (living in white blood cells) HERPES VIRUS IN PATIENTS WITH POST INFECTIOUS FATIGUE, Knox et al., March 2011.

The goal of this study was identification of chronic active herpes virus infections in individuals in order to prevent the misdiagnosis of "ME/CFS" and thereby justify new intervention strategies, such as antiviral therapy.

All subjects met the CDC criteria for ME and had systemic signs and symptoms of an active, ongoing infection. They also met the Canadian Consensus Criteria (CCC), Carruthers et al., 2003, which Dr. Peterson stated should be referred to as the "World Definition" for ME.

Below are the results of patients positive for the following:

- HHV-6 (human herpes virus 6) - 54/194 27.8%
- HCMV (human cytomegalovirus) - 71/249 28.5%
- EBV (Epstein Barr virus) - 79/153 51.6%

An association has been found between several critical human molecules such as the thyroid peroxidase protein and leukotropic human herpes viruses.

This suggests a mechanism for the commonly reported finding of increased prevalence of autoantibodies in people with ME and strengthens evidence that autoimmunity can be triggered by infection.

Furthermore, there is speculation that the immunosuppressive potential of HHV-6 may synergistically enhance the reactivation and replication of both CMV and EBV.

Dr. Peterson added that beta herpes viruses are treatable.

#### ELEVATED LEVELS OF HHV-6 ANTIBODIES IN INDIVIDUALS WITH PSYCHIATRIC DISORDERS

HHV-6 antibodies in individuals with psychiatric disorders were discussed, Yolken and Dickerson, March 2011.

This research showed that individuals with established schizophrenia had elevated levels of antibodies to HHV-6, which suggests schizophrenia can be treated with antivirals.

CMX001-CIDOFOVIR PIM CONJUGATE is an antiviral drug in phase 3 trials. By linking a lipid to the phosphonate group of cidofovir, a drug has been formed which is able to cross the intestinal wall and penetrate target cells before being cleaved to free the antiviral, cidofovir.

Improved potency has been demonstrated in preclinical studies. In cell culture assays, CMX001 is significantly more active than cidofovir against double-stranded DNA viruses including:

- orthopox viruses (variola, monkeypox, vaccinia, cowpox and ectromelia)
- herpes viruses (CMV, herpes simplex virus (HSV)-1, and 2, HHV6, -8, varicella zoster virus (VZV), Epstein Barr virus (EBV)
- multiple adenoviruses.

Dr. Peterson suggested that CMX001 is an almost perfect drug as it only needs to be administered orally 2 times a week. This makes it much more accessible than the current intravenous options for the human herpes viruses.

#### APOPTOTIC SERUM DNA TESTING

Apoptosis is a natural process of self-destruction (programmed cell death) in certain cells that is determined by the genes and can be initiated by a stimulus or by removal of a repressor agent. In March, 2011, Chronix Biomedical filed a provisional US patent application jointly with Hemispherx Biopharma, Inc on a blood test for ME.

Chronix is developing disease-specific biomarkers based on DNA fragments that are released into the bloodstream by damaged and apoptotic cells.

The Chronix Biomedical blood test for ME is limited to investigational use because it has not been evaluated by any regulatory agents yet.

It is expected that this test will be 100% accurate and that it will be inexpensive.

#### XMRV

XMRV is proving to be highly controversial and is providing much healthy debate and research.

Xenotropic viruses originate in mice but can only infect cells from another species. Most retroviruses, especially members of the gamma retrovirus genus, can induce tumors as a consequence of integrating their viral genome into the host cell chromosome and activating proto-oncogenes (a normal gene that has the potential to become an oncogene).

To date, there have been at least 21 studies of XMRV research in ME. Two studies, Lombardi et al, October 2009 and Lo et al, September 2010, have supported XMRV in ME. Nineteen studies have not found a link to XMRV. These include Erlwein et al., January 2011, Groom et al., February 2010, Hong et al., September 2010, Heinrich et al., October 2010.

There are suggestions that some test kits were contaminated.

#### NEW RESEARCH DIRECTIONS FOR ME

Currently there are two large studies for ME. The first is at Columbia University, headed by Dr. Ian Lipkin.

Dr. Lipkin is internationally recognized for his work with SARS. He is responsible for discovering SARS and is credited with saving millions of lives, especially in China.

The ME world is truly fortunate that Dr. Lipkin has agreed to do two studies on ME. Through viral assays for known and unknown pathogens, Dr. Lipkin will be looking for all human viral pathogens.

As well, there is a study of 240 post SARS patients from Toronto, Canada. These patients are being tracked and approximately 6 to 8% developed identical symptoms to ME.

Dr. Peterson is involved with the second large study which is being conducted at Bond University, Gold Coast, Australia.

This research study is looking at Natural Killer (NK) cell phenotype and functional study. Currently, the team is applying for permission to do spinal fluid tap for a viral assay on ME to determine the cause of NK cell dysfunction.

At this time, Dr. Peterson recommends measuring of NK function for diagnosis of ME as it is the most reliable marker for ME.

## THE FUTURE

Significant strides are being made in research due to registries and biobanking. Nosology is the branch of medicine dealing with the classification of diseases, which traditionally was built using signs and symptoms.

Now, nosology can be based on gene expression and is improved with clinical markers, lab markers and biotech markers. Because all disease could be redefined from a molecular perspective, patient outcomes will improve.

Translational medicine allows researchers and clinicians to work together. Future direction of the translational model will ensure there is large scale clinical data gathering through multiple international sites involving patient and provider.

It will allow biospecimen collection with connection to a clinical database with RNA expression, DNA sequencing as well as other molecular testing. There will be focus on chronic and syndromic diseases such as ME.

The future looks promising.

## REFERENCES

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