Science to patients (Wetenschap voor Patiënten)
Chat: **Q&A**

During a chatwing-session on May 22, 2015 Prof. Alan Light answered the following questions.

Q: For quite some time I´m already suffering from myoclone epilepsy. Some time ago I had an inflammation at my temporomandibular joint for which I took the controller Diclofenac. All of a sudden my epileptic seizures stopped. We tried another controller, but without the desired effect and undesired side-effects. Is this explicable?
A: This may be related to another project we are working on that is looking at the mechanisms of muscle cramp, believe it or not. It may be related to Pannexin1 activation.

Q: How does one know if it's the antibodies or the virus itself that's eliminated when blood tests just search for antibodies?
A: Typically, the virus is not present (or at least only present in small amounts) when the autoantibodies are damaging the body. This is one of the reasons that the cause of the autoantibodies is so difficult to discover. So basically, we can't know this.

Q: Adrenergic receptors: are there many of them? What is their general function?
A: There are 6 adrenergic receptors (5 of which are found in humans). In general, they regulate your blood flow and keep your heart beating as it should. They also help your gut digest food, and affect your mood by actions in the brain.

Q: In your webinar you talked about the difference in pain and fatigue in healthy people and ME/CFS,FM depression. Do you also know about people with EDS (Ehler-Dahlos syndrome)?
A: We haven't looked at EDS. Now I know what it is.

Q: have you heard of stealth viruses?
A: Stealth viruses---does this mean the same as viruses like HIV that attack the immune system--retroviruses?

Q: Beta2 adrenergic receptor is changed with people with POTS. Does that mean it causes POTS?
A: Yes, it very likely could cause all of the symptoms of POTS. We have treated some patients with beta2 antagonists effectively. (At least Dr. Bateman has). I should say that there could be other receptors that could also mediate this, so this may not be true for all POTS patients.

Q: What are toll-like receptors?
A: Toll-like receptors are on immune cells and cause them to be activated by specific pathogens.
Q: Where are they found? (Toll-like receptors)
A: They are found primarily in circulating and non-circulating white blood cells, most of which are involved in immune function

Q: You are saying they give protection. In what way?
A: Yes, they are sensitive to disease causing pathogens like bacteria, microbes, and viruses. They cause the cells they are on to activate and make substances that will kill these organisms.

Q: IL 10 (Interleukine- 10) are proteins which are messenger particles. What messages do they give, and what message in particular does IL 10 give?
A: IL10 generally causes the reduction in activation of immune cells. It helps turn off the immune system after whatever has caused inflammation is gone. This is the normal function. It should not be made in large amounts when there is no pathogenic process going on.

Q: TRVP1 not only senses but also seems to regulate the body's temperature. Or only the sensation of heat and cold?
A: TRPV1's role in controlling body temperature is controversial. It definitely allows you to detect heat and cold, and can send that signal to the brain, but whether it actually is the mechanisms for maintaining the temperature is the controversy. I think it is one of the players--others do not.

Q: Now all the dysfunctions and alterations that you mentioned in the one-but-last webinar: can they be caused by one common factor? Like a virus, or a retrovirus?
A: The answer could be "yes" the virus activates the immune system to make several autoantibodies, or if the factor causes other long-term changes in fatigue pathway proteins, like ASIC receptors, TRPV1, lactate production etc. We think that it is more likely that a double "hit" is required than a single factor.

Q: Can all auto-immune diseases be distinguished from each other by their gene-expression? Is that difficult or costly to do?
A: Unfortunately, the answer is "no". It is very difficult to determine if a disease is caused by autoantibodies, because you have to know what that autoantibody is before you can detect it, even though you can see the gene dysregulations.

Q: About PEM: could the changes in gene-expression with ME make up for the lower uptake of oxygen ME-patients experience?
A: Actually, some of the changes we see might actually be causing the decreased O_2. Others do seem to be attempts to restore the normal function.

Q: And can the altered gene-expression with ME-patients be linked to many or all the symptoms as described in the ICC? In other words: are they valuable diagnostic tools?
A: Yes, the altered gene-expression relates to nearly all of the symptoms of ME. Yes, they could be diagnostic tools. We tried to make this kind of test, but RNA is too unstable, and the exercise protocol is too expensive to produce a marketable diagnostic.

Q: Do you know if there is any good research done about the role of the thymus in ME/CFS? I read a lot about the important role of the thymus for (building) the immune system.
A: Yes, there has been excellent work on the thymus in ME. It seems not to be a primary cause in most patients, but may play a role in at least some.

Q: In your webinar of this week you say: Usually we see 1 or 2 (3 total) out of the 46 we've now looked at are the same in all fatiguing patients. This is telling us that that is just fatigue and is not ME/cfs. It's all the rest of these genes that are altered and that includes at least 13 others that tell us a person has ME/cvs. Is there a study or is this published somewhere?

A: We are working on publication of this. We have only submitted one manuscript so far on this, and it is still under review (not yet rejected, as we like to say).
Q: And is it after publication possible to get these genes tested?
A: We only know that the expression of these genes is a marker. It may be that the DNA of these genes is not different. This gets back to the problems with using RNA instead of DNA. We are using a new method that, someday, might solve this problem. It is called RNAseq. If it could become inexpensive enough it could be used.

Q: About Post exertional malaise, does that oney occur in ME or also in other diseases. Like MS, Lyme disease, etc
A: PEM is not unique to ME. However, it is much less severe in MS. We haven't looked at Lyme patients, PEM can occur in mononucleosus, caused by Epstein Bar, and post EB ME is fairly common (when the virus is essentially non-active). Normal people if they are not fit, can experience a relatively short period of PEM if they really over exercise to an extreme degree. This lasts no more than 3 days, and the sickness response is much milder than in most cases of ME.
Q: And what about PoTS/Orthostatic intolerance?
A: POTS and Orthostatic intolerance commonly occurs with relatively little PEM. Only some of the POTS patients have ME.

Q: Can you explain how it's possible that before i got ME I had very often herpoes blisters on my mouth. And sinds I have ME never again.
A: You are lucky! Many ME patients get those blisters very often, and also get almost every disease they are exposed to. It could be your immune system has created a very good attack on the herpes virus in your mouth cells (these viruses are found in nearly every one, but only get activated in some people.

Q: If I have a fever, I never experience transpiration, memory problems or concentration disorders. The difference is very substantial. I do experience this many times for many years now. Do you have any explanation for this ?
A: Very likely that being sick is improving your brain blood flow.