Ron Davis discusses his recent NIH Grant

https://www.youtube.com/watch?v=eQR4zpiyE6I

Dr Ron Davis: Hello. I'd like to talk about our new grant from NIH, that was issued from Allergy and Infectious Disease, that's looking at T cell activation in ME/CFS patients.

This is an exciting time, because it's a large RO1 grant that lasts for five years.

What's also exciting about it is that we have a lot of people involved in this at Stanford. Namely, Mark Davis is a co-PI on this grant. He will help tremendously in all the immunology components of this puzzle.

We also have Lars Steinmetz, who is a full professor in genetics, and his lab has developed a lot of new technology with single cells, including the single cell receptor sequencing and the single cell gene expression. We will use those in this project.

We also have Jose Montoya. We've been trying to collaborate with Jose for a number of years, and now finally we've got together a proposal that will allow us to do that. He will provide ME/CFS patient samples.

But we also have other people, that are unpaid, in this proposal. Namely, we have to do HLA sequencing and we are going to do a KIR sequencing. KIR is a locus that makes a protein that is a receptor on NK cells. And we know the NK cells are heavily involved in this disease. There's been very little in the way of KIR sequencing, but we have a group that can do that sequencing, along with the HLA. So, we have Chunlin Wang and Michael Mindrinos and Marcelo Viña, are all experts in HLA and KIR sequencing. That group has developed a high-throughput method of very high accuracy sequencing, that's now being used commercially, and is being used in transplants at Stanford. So, it's highly accurate, and that's great news, and we'll be able to do a good job with that sequencing.

We also have Robert Phair, who's an expert in pathway analysis, and he will be working with us to understand what might be activating this locus.

In addition to these projects, we will be looking at the possibility of infectious diseases. Now, we have already done a number of studies on infectious diseases. We have looked for particles that are in the blood, and we don't find any pathogens other than organisms that are expected to be there, that apparently don't cause any problem. We've also done cell-free DNA by amplifying specific sequences that we have a very high sensitive method from all of the DNA viruses, and we don't find anything unusual in that analysis. So, the next step is to do a random cell-free DNA sequencing looking for pathogens.

Now, the reason we're gonna look for pathogens is that that could be what's activating the T cells. So, preliminary data with Mark Davis's lab have shown that there is T cell activation. We talked about it last year at our symposium. Now we're going to take on a big project looking at that, now that we have the funding.

So, that activation could come from a pathogen. It could also come from autoimmunity. And we could like to try to distinguish those two. And that's why we need the sequencing. And, we will try to determine exactly what the T cells are recognizing. And, it's also possible – and that's where Robert Fehr also comes in – that there's some form of just general activation of the immune system, and it's not very specific in terms of what they recognize. That is also a potential possibility.

So, I hope that this project will really give us some new light in the importance of immunology in this disease. And we're hopefully right at the heart of what may be going on in patients with ME/CFS.

Thank you.