DIRECT INFORMATION ON RESEARCH

LETTER FROM DR. BERGE MINASSIAN JULY 12, 2013 IN RESPONSE TO QUESTIONS FROM THE ITALIAN LAFORA ASSOCIATION

*We publish the prompt replies **in bold** translated from Italian by Dr. Berge Minassian*

Dear Berge, before the usual summer vacation I want to ask if there are any news' in your research on Lafora disease, in particular:

1) After the negative conclusion on the use of the mouse first molecule identified as an inhibitor of glycogen synthase, how's the experiment, after about 4 months, a dose greater than the first?

The experiment is going ahead and will be completed in two months

2) Have you found new molecules to be tested?

We are trying 6.

If you do not think you could extend the tests simultaneously on more research centers and not just on your own, we could save important time for us.

We have all the necessary services, patterns of genetically modified mice, labor. We have collaborators in Guelph University, Potsdam University of Berlin in Germany, Columbia University, New York, San Diego, Jefferson University in Philadelphia, Ohio State University, Columbus, Ohio, Massachusetts Institute of Technology in Boston, Hadassah University in Jerusalem Israel .

3) If you have identified molecules already present in some drugs on the market, why can we not begin to take them if they are already commercially available? If already existing on the market, they should not have unwanted side effects.

We have identified candidate molecules, but so far have not given any evidence, that make the difference on Lafora. We are actively testing each of these molecules. Once I see any evidence that they help, I will let all Lafora families know. It is possible that our care will be a cocktail of compounds collectively which will reduce glycogen synthesis sufficiently to make a major difference and stop the disease. If I find a small difference with any one molecule, I will let everyone know already to give it to patients even though it will have a small or partial effect. Also, it is not a trivial matter to tell patients whatever idea pops into our head to go try this or that because it might help. Even though certain compounds may be approved for clinical use, all compounds have side-effects and our patients are too fragile to risk unnecessary side-effects, including longer available side-effects as immune suppression, etc., which can be deadly.

4) Given the development of promising research "Amylase" on cells in culture, are tests already started on mice?

Right now we know that: The diphtheria (DT) vector Is able to translocate amylase enzyme across the membranes of cells into the inside of cells, and that having done so it regains activity! You see the amylase protein has to unfold to thread through the hole made by DT.

We are so happy that It seems to refold properly once inside and regain activity! Now, we are doing the experiment in cell lines that contain Lafora bodies, and we hope and pray that the refolded protein will erase the Lafora bodies. At that point, we will go to the animals.

5) What about the Negotiations with the Identified primary laboratory for the testing on using viral vectors? Has this work started?

Yes! We are collaborating with the world leaders in this field who have the best virus, AAV9. We sent them the amylase, they are putting in the viral vector and virus will grow enough and then will come to our lab with the virus to treat our mice! Yes!

We would also ask you the following things:
1 - Is there, in your opinion, some research path that has not been activated due to lack of funds?

No, I think all paths are covered

2 - Is there something in the works already started, that we could improve or do if there was a greater availability of funds?

The answer is always. Each route can be pushed more forward with more money. I realize that some families are giving their savings, etc. My heart is torn to pieces with this disease and of the sacrifices that people are making. All I can tell you is that with our entire team, day and night, we are working with full dedication and single minded purpose to find the treatment and cure.

3 - If so, what would need to be put in place for this improvement? Knowing this would help us to better program Association activities in support of your research work.

Dear friends, please allow me to focus as much as possible on the work. I leave it in the families hands to determine the fundraising methods. As you have seen I am an open book and tell you every last detail of what we are doing. I am forging ahead on all fronts without thinking of whether we will have sufficient funds or not. I know that somehow there will be and we must always advance.

Some questions that I address to you on behalf of the parents of sick children with Lafora, as you know time is running out and any information on the progress of research helps us to forge ahead and bite the bullet to face the inexorable advance of the disease. I'll send you our best wishes for your search with so much hope in our hearts.

Vincenzo.

Vincenzo, it is my personal mission in life to cure this disease, and all the kids are always in my consciousness. That's all I can say. Also I am a parent of older teenagers and I KNOW what our Lafora parents are going through. I send BIG hugs to all the families and thank you for always writing and asking and pushing us even more.

Berge