Les courriels du Professeur Frederick Kaplan de Philadelphie à Jean-Luc Le Nan du 12 au 15 mai 2012 à la suite de la publication du livre « Mon petit homme de Pierre ».

Dear Jean-Luc,

As always, thank you so much for this extremely kind and thoughtful letter. Someday I would love to return to Roscoff. I have such fond memories of my visit there and a very good warm feeling of real welcome and great hospitality.

I remember so well the wonderful gala seafood celebration that you had at the hotel, more than a year before the gene was discovered, but somehow, it seemed imminent, and the good spirits and camaraderie among the families and scientists carried the day and made it happen. It is a good lesson of life because often the greatest satisfactions of life come from the journey, not just the destination. Everything seemed right in Roscoff – the emotions, the desire, the commitment, the support – it was a wonderful occasion that we could all celebrate. Pierre-Yves was there, and could see the wonderful things his family was doing to bring the FOP community together, heal old wounds, and have hope for the next generation. I was rarely so moved in my entire career as when I visited you and your family at Roscoff. It was a highlight of my professional life.

During the past several years, we have been focusing a lot of our effort on how we may make a difference with this new knowledge of not only the FOP gene alone, but how the FOP gene orchestrates such catastrophic bone formation.

You are absolutely correct that gene therapy to silence the mutant copy of the gene and leave the normal copy alone may be the ultimate treatment someday, but it is not the immediate "first stop" on our therapeutic journey.

The likely "first stops" will be small molecules in the Dorsomorphin class of compounds that we wrote about in our annual report that target the mutant receptor (ACVR1/ALK2) and other small molecules in the RAR-gamma class of compounds that target the "bridge" in heterotopic ossification between the inflammation of a flare-up and the eventual formation of bone. This latter class of compounds is also discussed in this year's annual report, but was discussed even in more detail in last year's annual report and is highlighted in an editorial that I wrote (that is attached). We have been working hard to move forward with one of these compounds in clinical trials, hopefully in the next few years, but we will have to see whether the dosage that is feasible and the attendant side-effects will warrant such a study. There are some very powerful compounds in this RAR-gamma agonist class that offer great hope, along with some of the more specific Dorsomorphin-like compounds being developed.

There are other possibilities as well that target the mutant receptor and that are very new and exciting, and we are working with pharmaceutical companies to develop them as well. It is so exciting to have a real mouse model of FOP that can be used to test drugs.

So, in summary, gene therapy is a long way off, but other small molecule inhibitors of the overactive pathway are much more realistic and feasible for the short term, and hopefully will be the next stop along this incredible journey that ultimately will bring great tribute to the memory of Pierre-Yves as it already has done.

With much love to the entire family from me here in Philadelphia,

Fred

Les courriels du Professeur Frederick Kaplan de Philadelphie à Jean-Luc Le Nan du 12 au 15 mai 2012 à la suite de la publication du livre « Mon petit homme de Pierre ».

Dear Fred,

"My little stone man" is in bookstores April 14. The book received a very good success reported in the press, radio and television.

I sent you an autographed copy, a month ago, have you received?

Many questions hang on your work: this book gives hope to other orphan diseases and joined David Ben Gurion as everything is finally possible. Just believe it ...

I learned a new French association, with the parents of little Alexander wanted to help you; I'm very happy. Compared to 1995, things, though still difficult, can only improve.

I hope that your deliberations will bring you satisfaction and may one day improve the condition of patients with FOP.

I hope we can meet again one day. The FOP is always present in my mind ;you're always in my mind and in my heart.

Please, thank you for telling me as soon as you receive the book, thank you to tell me once you have new information on treatment.

Much love from family Le Nan,

Jean-Luc

Dear Jean-Luc.

Thank you so much. The book arived safely and in good condition, and it is a great honor to receive such a beatiful autographed copy.

Il will cherish it forever.

I have been meaning to write and thank you, but have been pre-occupied these past weeks with my own health follow-ups. The lesion (benign) in my brain has enlarged slightly, and I have seen my doctors here. They advise me to just keep an eye on it and do not advise surgery, medications, or radiation, so I am cautious. Hopefully, it will stop growing and possibly involute. I hope so. I am feeling pretty good, although do have problems at times with balance. Life certainly presents its challenges!

I was delighted to hear that the book is doing well. It is beautifully written, and the story is told from the heart. I am so grateful that you did this in Pierre-Yves memory and to set the record straight on this incredible journey. Your family and organization did so much to help us in finding the gene. It was wonderful. It was wonderful too having such a great association with Martine LeMerrer. She is a great lady and did so much to help me understand what a really bad man L***** was. Anyway, it helped us all to move on and find the right gene that will certainly lead the way to better treatments for the next generation of children God willing.

We just finished the annual report for this year. It has a little different beginning tom make it interesting. The science part comes after the long introduction.

We are always busy here, have recently renovated the lab, and when we get all the pictures back-up, the poster of Pierre-Yves will be there with all of the others.

I too look forward to seeing you in the future. Your family and your inspiration are eternal.

Please give my love to Marie-Helene and the children.

And thank you again for such a magnificent an heartwarming tribute in your comments in the book.

With many thanks and warmest personal regards,

Fred

Les courriels du Professeur Frederick Kaplan de Philadelphie à Jean-Luc Le Nan du 12 au 15 mai 2012 à la suite de la publication du livre « Mon petit homme de Pierre ».

Dear Fred,

I am sorry to hear about your health problems. I sincerely hope that your condition will improve rapidly. We think about you in these moments to be difficult and unpleasant.

Regarding the treatment against FOP, can you tell me if you target only the gene therapy? Or do you favor a therapy that can control the outbreaks of the disease?

Personally, I always said that healing the sick belong to another generation. We had to stay lucid and accept all the difficulties of a complete recovery.

By cons, in the understanding of gene and ossification of the phenomenon, it may be possible to better control the FOP. This will take time. But the creation of the disease in the animal model will allow investigations that would not have been possible otherwise. In our generation, in the next generation, priority will be to block the disease process and to allow surgical procedures that would make the positions of comfort to the sick.

If gene therapy occurs before, great!

I believe it is possible today, with luck, in full consciousness, with strength and courage. I know you have all the qualities required, and even more.

The world of the FOP is in dire need of you; but you must also be careful with your health. Nobody can give you as much as you could give to relieve our children. I admire you, I want to help you; but how do you help in this case?

What reassures me is that you must have great doctors at your side.

If you have to rest, my house is modestly ready to welcome you to breathe the fresh Breton air.

Thank you for answering my questions about possible treatment that is not that of gene therapy. In the book signings, I have often asked the question.

Take care of yourself!

Much love from family Le Nan,

Jean-Luc

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Source: Jean-Luc Le Nan. Avec l'aimable autorisation l'auteur