Letter from Saskia
July 10th 2020

Dear all,

The TPI Helpathon was a great inspiration for me.
As a scientist that actively makes use of animal experimentation to answer research questions in liver physiology, it is usually difficult to engage with people that seem to be opposed to using animals in research at all. Those two viewpoints are so far apart, that it is hard to find a middle ground to discuss. To aim for abandoning all animal research by 2025 is in my opinion an illusion, and would greatly harm therapeutic innovations for human health.

It is therefore that I was very happy to put my research forward to discuss the viewpoint and difficulties of many researchers; that there are no off-the-shelve alternatives available to replace the animal experiments, and it takes (part of) a career to set this up, if at all yet possible. To illustrate this further, I also want to share with you a quote from the Editor's comments to a manuscript I currently have submitted to Gastroenterology, the highest ranked journal in my field:

'Comments from the Editors:
The dependency on mouse liver organoids is an important limitation of the study. Several reviewers commented on the need for isoform specific modeling in the mouse liver. We suggest that some of the same kind of studies could be done with AAV based overexpression of FXR isoforms in the FXR null mouse.'

In the end, we did no extra mouse experiments to tackle this (it is also not yet accepted for publication), but relied on very different mouse experiments than requested, which we already had done a long time ago. Also because we believe that the suggested experiments by the editor were not adding much. But you will get the point I want to make; if I want to publish in the highest ranking journal, which gives me visibility, greater possibilities for new funding etc., then I have to jump the hoop. Thus, in the greater science community, alternative models are also not widely accepted. I want to stress that journal editors, but also EMA/FDA, are also stakeholders if you want to accomplish in your goal to greatly diminish/eliminate animal experimentation in the foreseeable future.

This does of course not dismiss me from the felt responsibility to try to reduce in animal experimentation. I have set out the following:

1. With help of the TPI Helpathon discussions, I am now actively pursuing to test the Cellulose Nanofibril Hydrogel, which was brought in by Melanie Krueger. If it works also for the experimental read-outs we are interested in, I will show the results also within my department and propose to change to using this hydrogel instead of the Matrigel. As a department, we use approximately 230 ml Matrigel per year, for which approximately 560 mice have been used. I hope to have the results by the end of September.

As a department, we also use 400 litre of fetal calf serum to culture cell lines per year. We have set up a small committee of technicians that will actively test alternatives on the market to try to reduce this. Shortly, we will start testing the most promising ones for some of our most frequent read-outs/assays. I can give an update by the end of the year.

2. In addition, I have an appointment with Sue to see/get a demo from her set up for the organ on chip. Subsequently, I have planned to invite someone from one of the companies listed in the hand-over document to our department meeting and explore whether we can test the set-up to include liver, intestinal and blood compartments (as a start), to see if the FXR isoform selective actions can be studied in this set-up. I will have to run this research parallel to the Vici research (also to satisfy reviewers/editors), and will therefore have to see how I can cost this (Q3/4).

3. I completely share your views that there would be no need for a NASH therapy if we would be able to make a healthy life style cheaper and would be able to persuade that exercise and healthy food are essential for a healthy life. By initiating the NASH working group in the Netherlands, including clinicians, dieticians, surgeons, patient associations and scientists, to create more awareness and collaborative research on NASH, is my way of trying to influence this.

4. Also as just installed governing board member of the European Association for study of the Liver (EASL), I will actively stimulate the use and development of human in vitro organ on chip models by organizing sessions on this topic during the flagship meeting ILC.

In the ideal world, you would like me to be much more of an 'influencer', and I will do my best, but I wanted to give you a realistic prospect of what I can do in the near future.

I very much hope you will keep up the good work to provide and contribute to a platform where scientists, policy makers and organisations like Proefdiervrij can be actively engaged in promoting innovation and development of alternative model systems replacing animal experimentation. This discussion is crucial to get all stakeholders aligned and reform the scientific community in this respect!

Thank you all for a very inspiring Helpathon!

Best,
Saskia

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