Gut-on-a-chip for more realistic biological models

As one of **Micronit Microtechnologies**' customers, Wageningen University & Research uses the Netherlands-based company's platform for its gut-on-a-chip research. Senior scientist Hans Bouwmeester talks *Medical Device Developments* through the benefits of in-vitro models compared with traditional methods in assessing intestinal conditions.

Could you tell us about Wageningen University & Research and how gut-on-a-chip fits into your research scope?

Hans Bouwmeester: We are interested in new models for assessing food safety, so we research the uptake of compounds and ingredients via the intestine, and potential toxicity. We are also looking to supplant the reliance on animal models for current risk assessment using in-vitro models.

We believe that gut-on-a-chip models are an innovation that can result in powerful in-vitro models suitable for replacing some of these animal experiments.

Gut-on-a-chip better mimics the environment in the intestine. It provides a more realistic biology and, thus, the outcome has the scope to be more realistic when it comes to human risk assessment.

Could you shed some light on your latest gut-on-a-chip projects?

There are several projects, which are primarily centred on two main topics. One is intestinal functions, and the residues of pesticides and food contaminants taken up. It's always a question of how much is taken up. What's the bioavailability of compounds? This calls for a combination of biological models and state-of-the-art detection.

We try to couple these models with sensitive detection methods to assess the uptake or metabolism of compounds over the intestinal epithelium. So bioavailability and metabolism – that's one area in which we use these models.

The other topic relates to the effects of the compound on the functioning of the intestinal epithelium. This means studying local toxicity and bioavailability. In future projects – which have recently been granted – we will continue to increase the complexity of the biology on these models in order to grow a gut microbiome in anaerobic conditions on the cells.

If you can create this complex biology in the laboratory, you can start studying mechanistically, investigating immune-related effects, for example. This may lead to good models for diseases like chronically inflamed intestines and Crohn's disease-like phenomena.

What are the benefits of the gut-on-a-chip method and platform compared with traditional methods?

It depends on which research question you are dealing with. For some of the basic-uptake or bioavailability questions, you might want to use traditional models because they are simpler, more established and more recognised.

Gut-on-a-chip could result in more realistic models that allow researchers to better understand diseases of the gut.

However, I am strongly of the opinion that if you have more mechanistic questions – which are starting to become increasingly important in toxicology – they can be better understood using these models. The great challenge, of course, with all in-vitro models is how predictive and valid they are in terms of human end-points. That's a topic to further explore, I think.

How do you see the future of gut-on-a-chip? Does it rest on standardisation?

Standardisation might be needed to make it available to groups not only in academia, but also in industry. By doing so, we will create a database of knowledge and results that can be used by industry and also by regulatory authorities for use in safety evaluations and health claims, for example.

If the equipment is readily available and not too costly, I think we will see growing numbers of people start to use these chips.

I also think we need to have strong in-silico modelling. This should go hand in hand with the improvement of experimental models. The development of in-vitro models – including organ-on-a-chip – needs to go together with in-silico pharmacokinetic models. ■

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