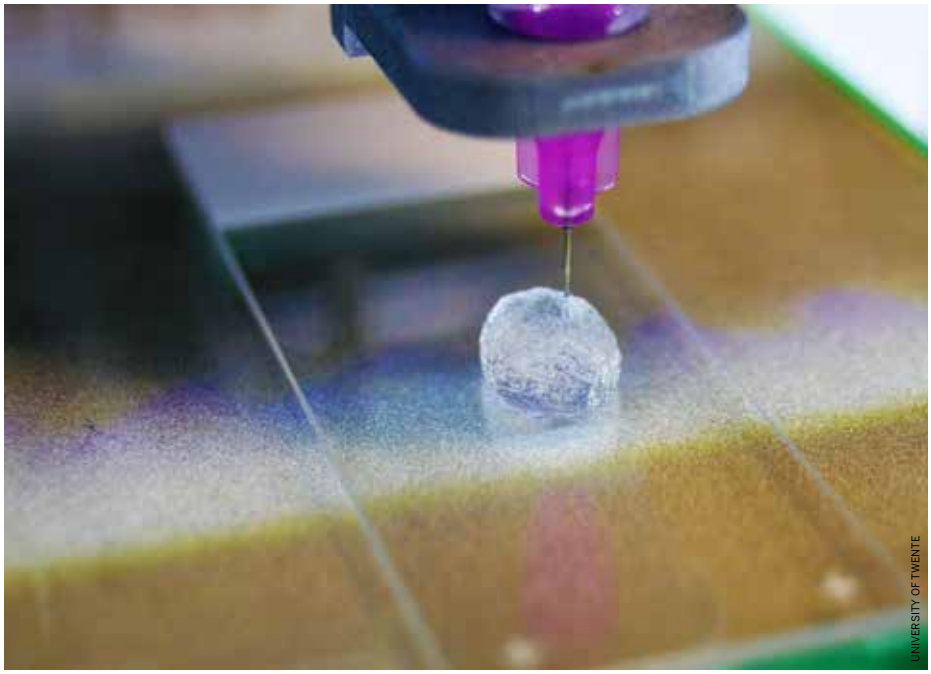

3D-bioprinted mini-brains

Glioblastoma is an aggressive brain tumour that currently has no effective treatment. Marcel Heinrich developed 3D-bioprinted mini-brains that can be used to evaluate novel therapeutics.

'When testing new drugs, the transition from 2D cultures to animal studies is challenging', says Marcel Heinrich, PhD student at the University of Twente. 'There is a big gap in between. These mini-brains can serve as a bridge.' 3D mini-organs in themselves are not new, but when bioprinted, they yield better results, according to Heinrich. In 3D bioprinting, living cells are used to print living structures layer by layer. 'Regular 3D culture techniques, such as using a hydrogel as a scaffold, does not give sufficient control of the architecture of the fabricated organ', says Heinrich. 'Control, however, is very important in situations in which the required biological structure is complex, like in a brain tumor surrounded by glial and stromal cells. When 3D bioprinting, you can print the cells exactly where you want them to be.'

Heinrich printed a brain tumour called glioblastoma multiforme. Patients with this type of cancer usually live no longer than two years after diagnosis. 'The only treatment is cutting out the malignant cells', explains Heinrich. 'But you cannot remove the whole tumor, as you will be cutting into healthy brain tissue. There is a need for drugs to specifically target the diseased brain part. I think my model can be used to test those drugs.'

'Evaluating new drugs in our mini-brains can be an interesting tool'

For his PhD research, Heinrich focused on two 3D-bioprinted brain tumour models. 'In the first, we studied the interactions of glioblastoma cells with macrophages. These macrophages are known to be sort of brain-washed by the tumor cells to become tumour-promoting cells. In our model we saw exactly this. We also checked patient data regarding biomarkers that were upregulated in the tumor. We saw very similar expression levels in our model.'

Heinrich also used the mini-brains to test drugs that are already used in clinics or in preclinical and clinical trials. These drugs work by inhibiting macrophage activity and eventually tumor growth. 'That was indeed what we saw happening in our models. So hereby we demonstrated that evaluating new drugs in our mini-brains can indeed be an interesting tool.'

Sustainable models

Heinrichs next goal is to use the same principle for pancreatic and breast cancers. He also aims to use a more complex second version of the glioblastoma mini-brains to study more intricate interactions. 'For example, the role of supporting brain cells such as microglia and astrocytes. It is not yet fully understood how these cells interact with tumour cells and how they eventually promote tumor growth and invasion.'

Can these mini-brains eventually replace animal studies altogether? 'No, at least not yet. I do envision the use of this technique to cut back the use of animal models. Say you have ten new drugs. Instead of taking all of them to animal studies right away, you can first test and screen them in a 2D culture and then in a 3D mini-organ. After that you may only have one or two really good candidates left for animal studies. That saves a lot of time and many animal lives.' ●

Marcel Heinrich is participating in the PhD Student Competition at the FIGON Dutch Medicines Days