Researchers develop new methods to assess organ failure caused by viruses

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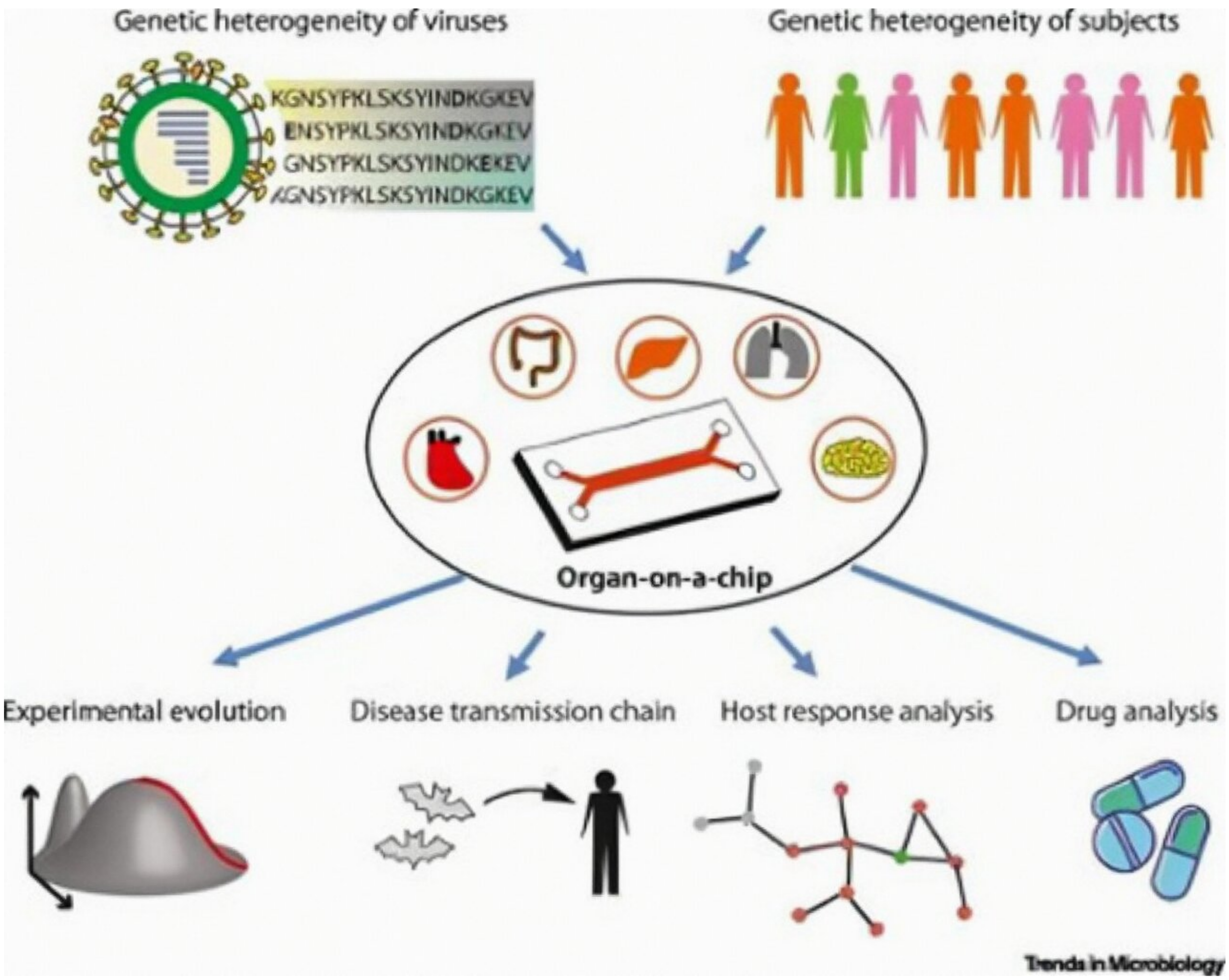

Credit: Leiden University

Dying from viral infection due to organ failure and blood loss is still little understood. Among other things, Huaqi Tang developed an organ-on-a-chip to figure it out. "These technologies can offer unprecedented opportunities to fight the viruses that threaten our society," said Tang.

Viral hemorrhagic fevers (VHF) are diseases caused by viruses. Viral hemorrhagic fever affects many organs and damages the vascular system. Symptoms vary, but often, internal blood loss is involved due to leaking blood vessels. Hemorrhagic shock occurs when the body stops functioning due to this blood loss.

VHF can occur with many viral infections, including dengue, yellow fever and Ebola. The symptoms are also reminiscent of what happens in the most severe COVID cases. COVID is not a VHF virus, says Ph.D. student Huaqi Tang. However, Leiden researchers say their previous research results could apply to COVID research.

"An infection by SARS-CoV-2 can be mild, like that by VHF viruses, but can also cause severe vascular leakage in the lungs. This in turn leads to the acute respiratory distress known in the most severe cases of the disease. Colleagues at LUMC and my institute LACDR used the microvessel-on-a-chip model we developed to study the effect of COVID-19 plasma samples on vascular disruption."

Human-like environment on a small glass plate

Tang and his colleagues developed the ability to mimic the situation in our bodies with a few cells and artificial blood vessels on a small glass plate. The chip mimics what happens during hemorrhagic shock. It is composed of a human microvessel on a glass chip that interfaces a tissue model. "It works as a cheap, user-friendly and realistic system on which you can study how VHS viruses make vessels leak at the micro level. It is a human-like environment, which in time could also be useful for diagnostics and drug development."

The researchers also developed ways to analyze what happens in host cells. That is about being able to see exactly what substances the different parts produce. This is called metabolomics: mapping metabolism by analyzing which metabolic products are being produced. If you know all those products, you know the "metabolome" of the system.

Tang says, "With that, we can figure out which substances to look out for to reveal the fundamental mechanisms by which these viruses cause damage. The Ph.D. student worked on metabolomics in two ways. The first, somewhat broader analysis, shows the effect of the virus on host cells. In addition, I worked on single-cell metabolomics that coupled with an algorithm."

The best moment in his Ph.D. research partly came from weather conditions. Tang said, "I saw a rainbow in a clear blue sky after working in the laboratory for a whole day. I had successfully measured the effect of an experimental substance on blood vessel leakage caused by Ebola. I then got a very peaceful feeling, and life felt so promising. This quote from Indian writer and psychologist Amit Abraham came to my mind: 'I am looking forward to the day when I can become a virus and live my life peacefully.'"

Of course, there were also frustrations to overcome. Especially in the first year, says Tang. "I had to overcome culture shock and language barriers, and I had no experience with advanced organ chip technology. I doubted myself and thought about giving up, but my supervisor Dr. Alireza Mashaghi and colleagues in the group encouraged me to keep going. They helped me overcome these problems. Thanks to them, I had a great time and I hope to continue in this research field."

According to Tang, his Ph.D. research has contributed to the understanding of the effect of VHF viruses on host cells. "More importantly, the technologies we have developed are expected to open up unprecedented opportunities for virologists who are on the frontline in the fight against the viruses that threaten our society."

Tangs supervisor Alireza Mashaghi, principal investigator at the LACDR Division of Systems Pharmacology and Pharmacy, agrees with that.

"Our lab pioneered the use of organ-on-a-chip technology in studying viral diseases, opening new avenues for researchers in the field of virology. We are now taking another ground-breaking step by using bioprinting approaches to develop models of viral diseases. During his Ph.D., Huaqi took the first step in this direction using state-of-the-art bioprinters that have recently been installed in our lab. The results are very promising, and currently, new students and postdocs in our lab are following in the footsteps of Huaqi to bring this idea to fruition," Mashaghi said.

Provided by Leiden University