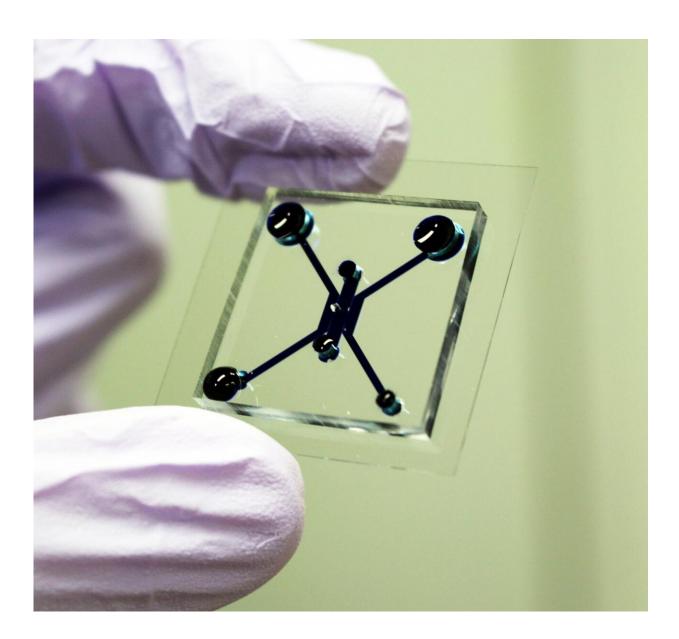


Using a chip to find better cancer fighting drugs

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The device allows researchers to mimic the environment inside the body to



screen for better cancer screening drugs. Credit: Kyoto University/Yokokawa Lab

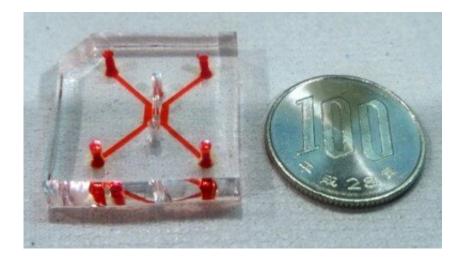
Kyoto University researchers have developed a new 'tumor-on-a-chip' device that can better mimic the environment inside the body, paving the way for improved screening of potential cancer fighting drugs.

The path to <u>drug</u> discovery is never easy. Scientists and clinicians can go through tens of thousands of potential compounds for years to find a handful of viable candidates, only for them to fail at the clinical level.

"Potential compounds are tested using animal models and cells cultured in a dish. However, those results frequently do not transfer over to human biology," explains first author Yuji Nashimoto formerly of the Graduate School of Engineering, and now at Tohoku University. "Furthermore, cells on a dish lack the three-dimensional structure and <u>blood vessels</u>, or vasculature, that keep it alive. So, we came up with a plan to construct a device that solves these issues."

The device, reported in the journal *Biomaterials*, is the size of a coin with a 1 mm well at the center. This well is flanked by a series of 100 μ m 'microposts.' The idea is that a three-dimensional culture of <u>tumor</u> <u>cells</u> is placed in the middle well, and then cells that construct blood vessels are placed along the microposts. Over a few days the vessels grow and attach to the culture.





The chip next to a standard Japanese 100 yen coin. Credit: Kyoto University/Yokokawa Lab

"This 'perfusable vasculature' allows us to administer nutrients and drugs into the system to mimic the environment in the body," continues Nashimoto. "This allows us to have a clearer picture of the effectiveness of cancer treating compounds."

This perfusion did significantly keep the tumor cells healthy by keeping <u>cell proliferation</u> up and cell death down. A drug assay was then performed with the team administrating an anti-tumor drug at low doses. Interestingly, the drug was more effective under static conditions compared to when nutrients were flowing through the tumor cells.

In contrast, the drug's effects became more potent when the flow was turned on and the dosage was increased. Ryuji Yokokawa, who lead the team, explains that the unexpected results prove that we need to consider the balance between proliferation of tumor <u>cells</u> and the efficacy of the drug under flow conditions.

"We hypothesize that at low doses the benefit of the nutrient flow



outweighs the effect of the anti-tumor drug. It proves the importance of blood flow in the vasculature when screening for drugs."

He concludes, "Due to its size and utility, we hope the new device can expedite the tests on the countless number of potential new drugs. While many questions remain, we are happy to have developed this device and have shown that three-dimensional perfused cell culture is vital for the next step in <u>drug discovery</u>."

More information: Yuji Nashimoto et al, Vascularized cancer on a chip: The effect of perfusion on growth and drug delivery of tumor spheroid, *Biomaterials* (2019). DOI: 10.1016/j.biomaterials.2019.119547

Provided by Kyoto University

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