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CAN ORGANOIDS, DERIVED FROM STEM CELLS, BE USED IN DISEASE TREATMENTS?

Relevant for: Science & Technology | Topic: Biotechnology, Genetics & Health related developments

Across-section of a brain organoid, with each colour marking a different type of brain cell. | Photo Credit: AFP

The story so far: On Monday, October 21, at Neuroscience 2019, the Society for Neuroscience's 49th annual meeting, held in Chicago, U.S., two neuroscientists warned the gathering that fellow scientists are "perilously close" to crossing the ethical red line of growing mini-brains or organoids in the laboratory that can perceive or feel things. In some cases, scientists have already transplanted such lab-grown brain organoid to adult animals. The transplanted organoid had integrated with the animal brain, grown new neuronal connections and responded to light. Similarly, lung organoid transplanted into mice was able to form branching airways and early alveolar structures. These are seen as a step towards potential "humanisation" of host animals.

Organoids are a group of cells grown in laboratories into three-dimensional, miniature structures that mimic the cell arrangement of a fully-grown organ. They are tiny (typically the size of a pea) organ-like structures that do not achieve all the functional maturity of human organs but often resemble the early stages of a developing tissue. Most organoids contain only a subset of all the cells seen in a real organ, but lack blood vessels to make them fully functional. In the case of brain organoids, scientists have been able to develop neurons and even make specific brain regions such as the cerebral cortex that closely resemble the human brain. The largest brain organoids that have been grown in the laboratory are about 4 mm in diameter.

Organoids are grown in the lab using stem cells that can become any of the specialised cells seen in the human body, or stem cells taken from the organ or adults cells that have been induced to behave like stem cells, scientifically called induced pluripotent stem cells (iPSC). Stem cells are provided with nutrients and other specific molecules to grow and become cells resembling a specific organ. The growing cells are capable of self-organising into cellular structures of a specific organ and can partly replicate complex functions of mature organs — physiological processes to regeneration and being in a diseased state.

Organoids of the brain, small intestine, kidney, heart, stomach, eyes, liver, pancreas, prostate, salivary glands, and inner ear to name a few have already been developed in the laboratory.

Since the use of embryonic stem cells to grow organs of interest has been mired in controversy leading to a ban on such research, researchers have turned to generating organoids using stem cells. Researchers have been successful in generating organoids of increasing "complexity and diversity". Since the organoids closely resemble mature tissues, it opens up new vistas. These include studying the complex arrangements of cells in three-dimension and their function in detail, and understanding how cells assemble into organs.

Organoids can be used to study the safety and efficacy of new drugs and also test the response of tissues to existing medicines. Organoids will bring precision medicine closer to reality by developing patient-specific treatment strategies by studying which drugs the patient is most sensitive to. Since the use of animals during drug development studies is becoming increasingly difficult, the focus has been on refining, reducing and replacing them. While scientists have been increasingly using human cell lines and other methods, such alternatives have some inherent

limitations — they cannot mimic the whole organ system. Organoids are a far superior alternative to cell lines.

Organoids offer new opportunities to studying proteins and genes that are critical for the development of an organ. This helps in knowing how a mutation in a specific gene causes a disease or disorder. In a study in Europe using intestinal organoids from six patients with an intestine disorder, it became possible to identify the mutation in a gene that prevented the formation of a healthy intestine. Researchers have used brain organoids to study how the Zika virus affects brain development in the embryo.

Scientists are already using stem cells taken from tumours to grow organoids that are poised to develop cancer. The ability to grow organoids using cancer stem cells allows researchers to study the genes, proteins and signalling pathways that cancer cells use to develop and grow. They are also using healthy organoids to identify and verify the gene mutations that cause cancer.

In an opinion piece in *Nature*, scientists argued that the largest brain that has been grown in the laboratory is only 4 mm in diameter and contains only 2-3 million cells. In comparison, an adult human brain measures 1,350 cubic centimetres, and has 86 billion neurons and another 86 billion non-neuronal cells and a similar number of non-neuronal cells. The authors argue that organoids do not have sensory inputs and sensory connections from the brain are limited. Isolated regions of the brain cannot communicate with other brain regions or generate motor signals. They wrote: “Thus, the possibility of consciousness or other higher-order perceptive properties [such as the ability to feel distress] emerging seems extremely remote.”

The 2019 Nobel Prize for Chemistry was awarded to John B. Goodenough, M. Stanley Whittingham and Akira Yoshino for working towards the development of practical lithium-ion batteries.

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