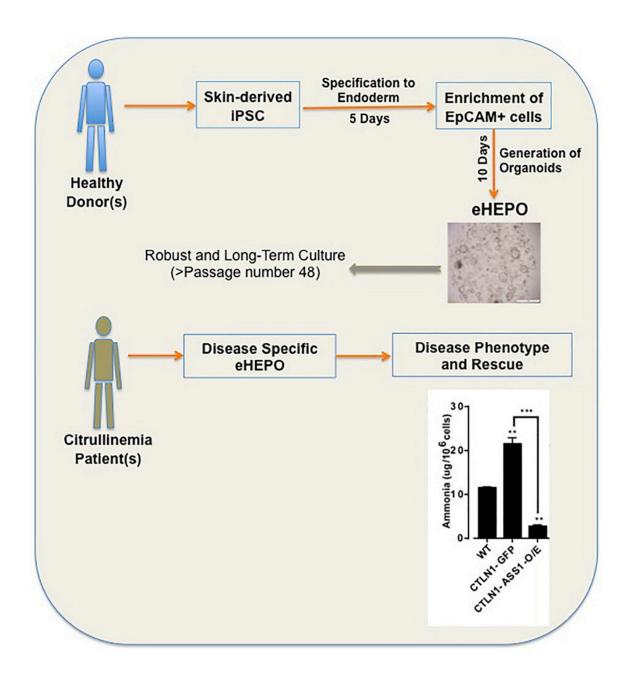


Organoids: The future of disease modelling?

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Graphical abstract. Credit: DOI: 10.1016/j.stemcr.2019.08.007



Organoid technologies have become a powerful emerging tool to model liver diseases, for drug screening, and for personalized treatments. Assoc. Prof. Tamer Önder of Koç University and his team generated and characterized the hepatic organoid culture system using human induced pluripotent stem cell (iPS) as an intermediate.

Developing a treatment for certain diseases is extremely difficult due to several reasons, leaving the medical world helpless. However, with organoids, it is now possible to do some of the things that were once deemed "impracticable" and Assoc. Dr. Tamer Önder of Koç University School of Medicine and his colleagues are among scientists putting an effort into this research area.

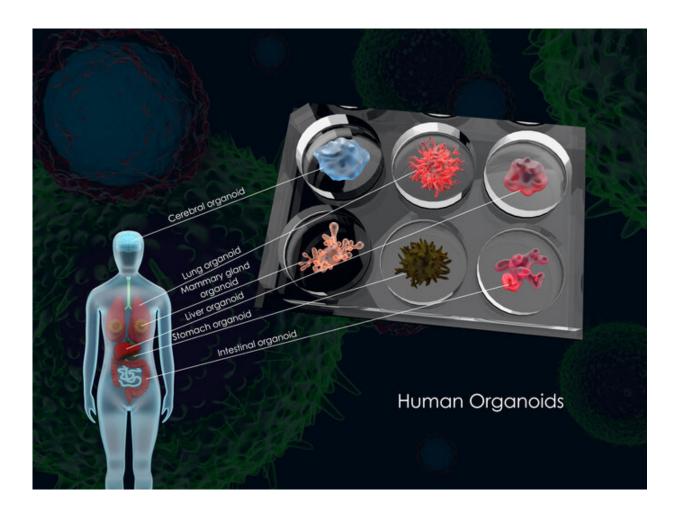
There are about 20–25 genetic-based diseases that affect <u>liver</u> metabolism, which can be fatal or cause permanent damage. When such a disease is seen in a new-born, it is not possible to work on the diseased organ—as there is no way of obtaining liver tissue from a baby. Furthermore, if the disease is a rare type, the challenge is double as there is limited knowledge about it. Consequently, if one wishes to develop drugs against such diseases or understand the metabolic basis of liver <u>disease</u>, one needs to have cells that one can work with in the lab.

Assoc. Dr. Tamer Önder and his colleagues are pegging away at overcoming this challenge. A study they are carrying out in a joint effort with İzmir Biomedicine and Genome Center (İBG), as part of the TÜBİTAK 1003 Project, aims to model diseases that affect the liver or are very rare. According to the article published in *Stem Cell Reports*, the team takes a skin cell sample and transforms it into a <u>pluripotent stem cell</u> (iPS) using the Cellular Reprogramming Method.

Initially, they grew the iPS cells up to a certain stage, transforming them



into hepatocyte progenitor cells, and then placed them in a medium where they can grow in three dimensions. In the next stage, these labmade human liver cells were labeled with a green fluorescent protein and then transplanted intravenously to mice with damaged livers. Cells seemed to adhere to the damaged areas of mice livers and started growing there.



Credit: Koc University

In these experiments, the team saw that the enzyme ASS1 had no



function in diseased cells, and they were able to place the enzyme back into the cell using viral vectors. Thus, they managed to insert a normal copy of this gene into organoids. This way, they were able to see that the ammonia levels decreased once the <u>cells</u> received a normal copy of their faulty genes causing the release of excess ammonia as the urea balance was impaired. In other words, they were able to heal the cell with gene therapy.

They placed this treated <u>organoid</u> in the diseased livers in mice. The next step ahead is to observe the treated organoid doing its job in the liver it is transplanted into, ensuring successful completion of the urea cycle.

More information: Soheil Akbari et al, Robust, Long-Term Culture of Endoderm-Derived Hepatic Organoids for Disease Modeling, *Stem Cell Reports* (2019). DOI: 10.1016/j.stemcr.2019.08.007

Provided by Koc University

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