
HUB ORGANOIDS
A patient in the lab

HUB Organoids

Hubrecht Organoid Technology (HUB)

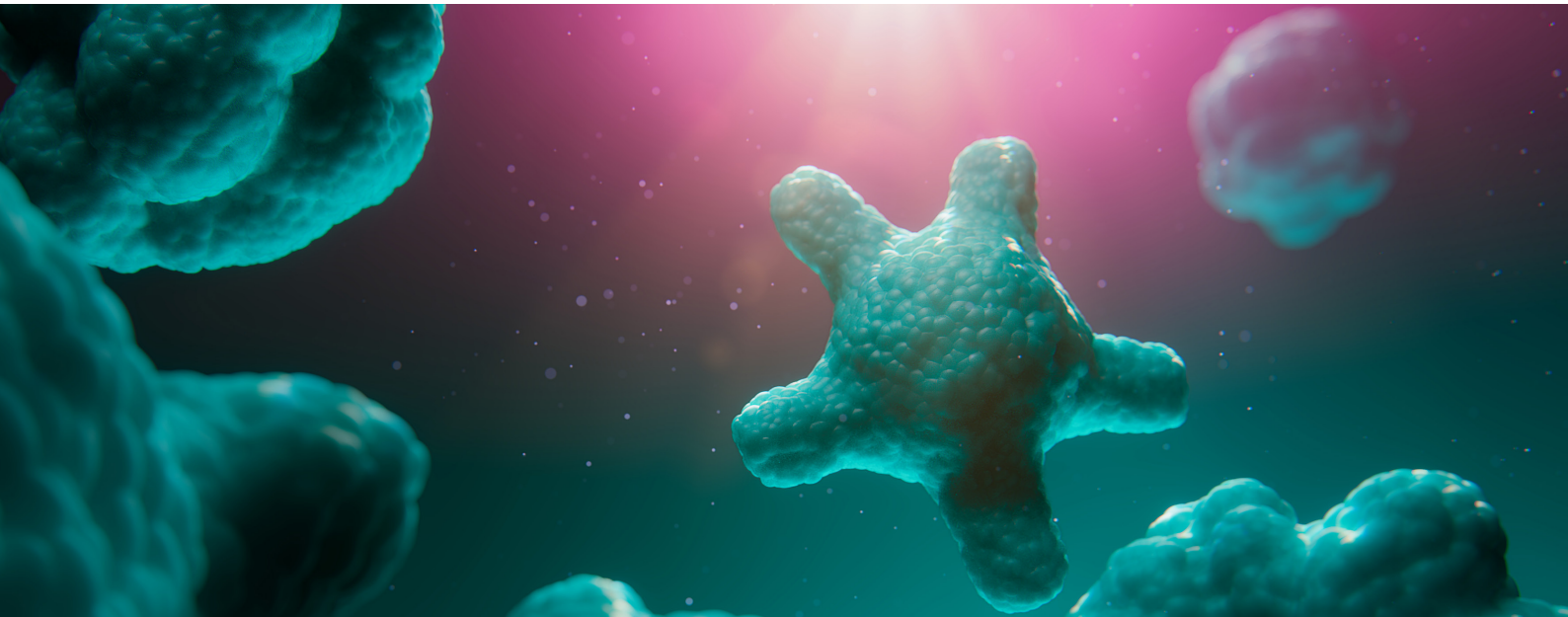
HUB was founded by the Hubrecht Institute, the University Medical Center Utrecht, and the Royal Netherlands Academy of Arts and Sciences (KNAW). HUB's technology constitutes a paradigm-shifting platform for drug discovery and development, (pre)clinical patient stratification, predictive diagnostics, personalized medicine, clinical trials, regenerative medicine, and companion diagnostics.

HUB exploits the pioneering work of Prof. Dr. Hans Clevers, who discovered the HUB Organoid Technology methods how to grow 'mini-organs' – organoids – from epithelial tissue derived adult stem cells.

HUB is the global leader in Organoid Technology with over 150 patents and many more patent applications that provide broad coverage for its Organoid Technology across twenty different jurisdictions worldwide. HUB offers licenses to its proprietary Organoid Technology and provides (pre)clinical and clinical trial services, research and development collaborations, predictive diagnostics, and access to its 'living organoid biobanks'.

History of Adult Stem Cell Culture

Previous attempts to grow epithelial stem cells *in vitro* resulted in very rare, genetically unstable cultures which have lost most molecular and clinical characteristics, as well as normal differentiation potential. In 2007, groundbreaking work by the Clevers` lab showed that, in adult intestinal tissue, Lrg5+ epithelial cells are the stem cells of the tissue. Subsequent work by the Clevers` group led to the first 'mini-organs' of the gut – organoids - a historical event that triggered a whole new era in *in vitro* patient like models and redefined the term organoid as we know it today.



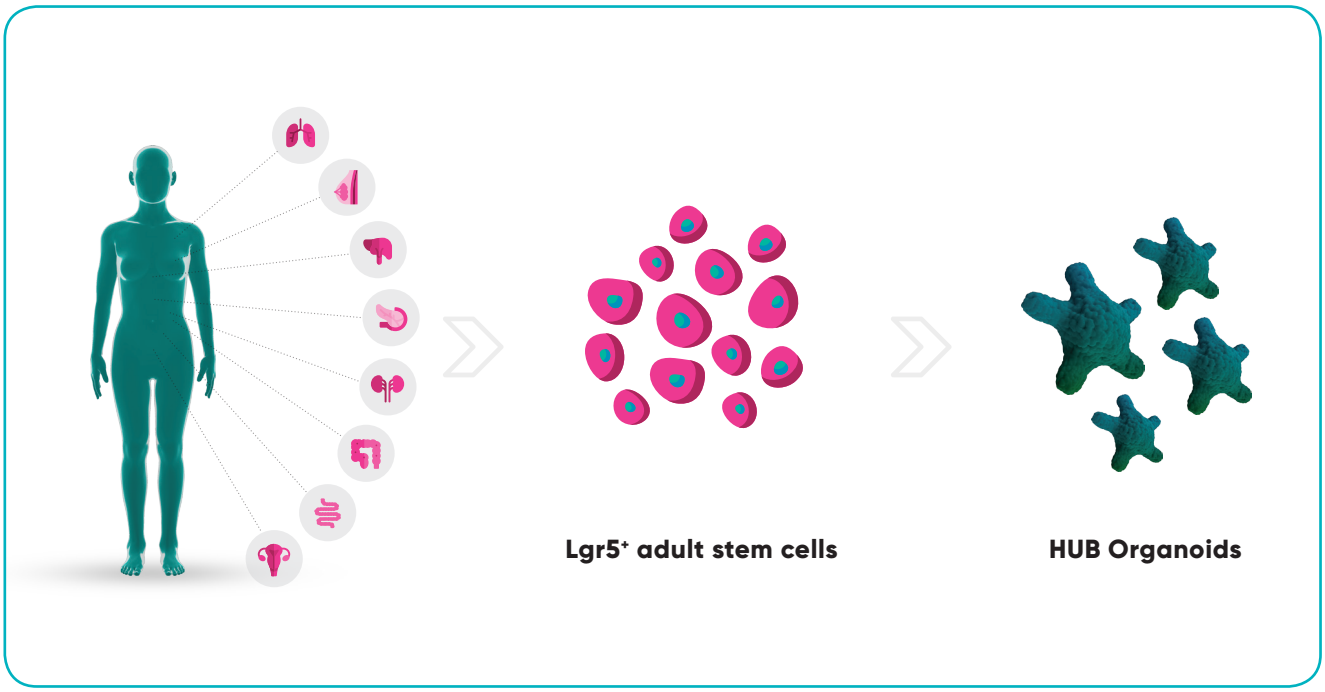
HUB Organoid Technology

Building in the discovery of the Lrg5+ adult stem cell marker, the Clevers` lab established that – when provided with organ-specific growth factors– single adult stem cells (ASCs) can be used to generate self-organizing, intestinal epithelial structures *in vitro*: The Organoid.

Clevers` group subsequently established protocols for the expansion of ASC-derived organoids, from many healthy and diseased (animal and human) organs. Importantly, long term culture of organoids maintains genetic and epigenetic stability (because no reprogramming or transformation is required). HUB has further developed, optimized and standardized the protocols for implementing organoid technology from a range of organs and diseases. The models are used for *in vitro* disease modeling, drug discovery and development, predictive diagnostics and personalized medicine.

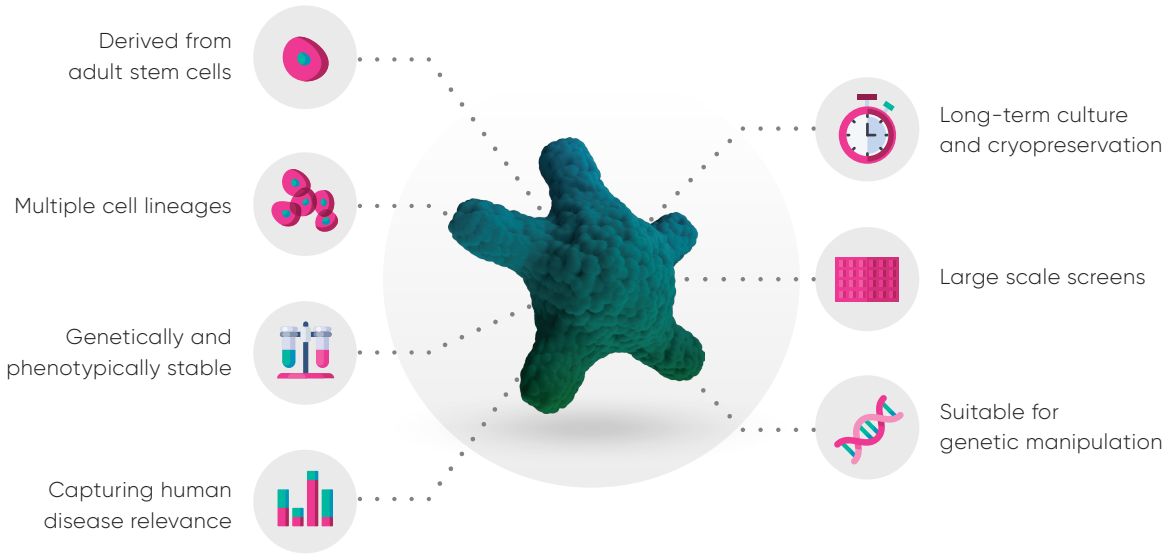
Important, the technology efficiency allows for generating organoids from any patient, with a very high success rate.

Patient-Derived Organoids (PDOs) are excellent surrogates of patients, capable of taking on the function of the tissue of origin and modeling a wide range of diseases in the areas of oncology, infectiology, genetics and metabolism. In addition to the development of multiple organoid models for human diseases, HUB has also generated large PDO biobanks of human tissue – including small intestine, colon, pancreas, lung, breast, kidney, and liver. Since its discovery, HUB and Clevers have shown that the organoid technology can be used for all epithelial tissues. Living organoid biobanks not only capture the genetic diversity of healthy human populations, they also reflect the spectrum of individual variations that exist within a defined disease group.



Key Features of HUB Organoids

"The only *in vitro* model that combines short- and long-term culture with genetic and phenotypic stability resulting in direct translation of *in vitro* data to patient response.''



Key Advantages of HUB Organoids over Standard *in vitro* Models

- generated from adult stem cells – recapitulating organs` function, genetics and morphology of the organ they were derived from *in vivo*.
- physiologically relevant modeling of healthy and diseased tissue biology.
- rapid development and long-term expansion while maintaining genetic and phenotypic characteristics.
- amenable to cryopreservation, gene editing, and all molecular, cell-biological and biochemical techniques used in cell line models.
- unlike embryonic (ES) or pluripotent (iPS) stem cell derived organoids, HUB Organoids are derived directly from patients (tumor) and therefore are capable of capturing heterogeneity in diseases such as cancer.
- unlike ES or iPS stem cell derived organoids, HUB Organoids are highly specialized for the tissue in which they reside, e.g. colon stem cells can only produce colon organoids.

"The only *in vitro* model that faithfully recapitulates the multi-lineage identity of an *in vivo* organ, while maintaining the capacity for long-term expansion with superior genomic and phenotypic stability."

Research & Therapeutic Potential of HUB Organoids

Traditional preclinical models allowed for biological understanding of diseases and treatments but fell short when it comes to predicting clinical responses. This is mainly due to genetic alterations acquired by cells to accommodate *in vitro* growth, the very few patient samples that have been established as cell lines, and the fact that animal models represent animals, not humans. HUB Organoid Technology captures both disease biology as well as the patient specific (epi)genetic phenotype. Therefore, for the first time, a preclinical model directly represents the treatment outcome that can be expected in the patient on the clinic.

HUB Organoids are changing the field of:

- drug & target discovery
- drug development
- cancer & other disease modeling
- safety studies
- personalized medicine
- clinical trials
- patient stratification & biomarkers
- diagnostics

Applications of HUB Organoids

- living organoid biobanks: HUB organoids capture disease relevance and heterogeneity of the patient population in the lab.
- database: HUB Organoids enable data-driven target discovery and drug development.
- drug discovery and development: HUB Organoids allow generation of drug efficacy, safety, and mechanistic data.
- preclinical clinical trials: HUB Organoids allow patient stratification on biobank collection in the preclinical phase with clinical trial accuracy.
- predictive diagnostics: HUB Organoids represent individual patients and therefore enable designing targeted and personalized therapies.
- companion diagnostics: HUB Organoids can serve as ultimate biomarker for specific drug treatments.

A patient in the lab

What we offer

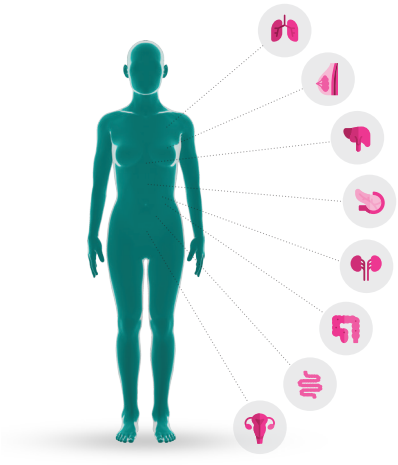
A Patient in the Lab

The HUB Organoids model system is currently the only one of its kind that has proven to be representative of individual human patients. The overall high attrition rate within drug development is largely due to a lack of patient relevance in existing preclinical model systems.

Since the breakthrough of Hubrecht Organoid Technology, we now have the ability to establish a laboratory model of any epithelial disease, from any patient: a 'patient in the lab'.

Organoid Models & Biobank

To improve and support your research, HUB offers clinically relevant organoid models for various diseases, including cystic fibrosis, cancer, toxicology, and infectious diseases. Additionally, HUB has used patient materials to create living organoid biobanks that represent a variety of organs and disease models. The living biobanks are an expanding resource of highly characterized organoids for different organ systems, allowing for the integration of molecular, genetic and clinical patient data. HUB Organoids as a functional test will greatly help predicting patient response combining molecular, genetic and clinical patient data.



HUB Organoid Biobank

- *In vitro* drug testing
- Safety studies
- Disease model development
- Organoid characterization
  - DNA / RNA seq
  - IHC
- Biobank
- Clinical trials
- Preclinical trials
- Assay development
  - FIS
  - Cell viability and cytotoxicity
  - Immuno-oncology

Services

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