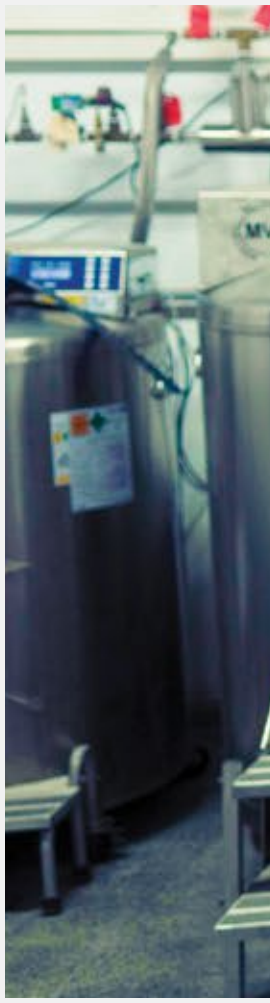
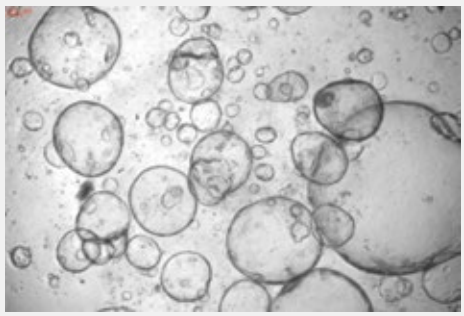
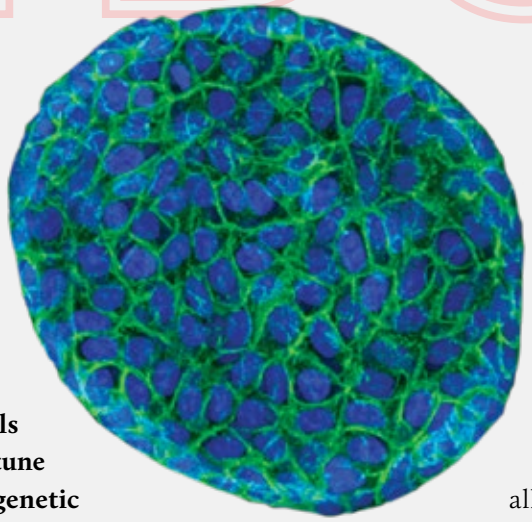
ORGANOIDS

THE KEY TO PERSONALIZED MEDICINE





Organoids derived from human pancreatic ductal adenocarcinoma



Organoids derived from human colon mucosa

"Organoids, which are miniature versions of tissues grown in the laboratory, are driving a revolutionary change in the way diseases are studied and patients are treated. We can grow organoids from a patient's own cells which can be used to develop and fine-tune treatments based on the individual genetic and molecular profiles. Combined with other technologies such as genome analysis, organoids are paving the way for true personalized medicine that will lead to more effective treatments, and considerably reduce healthcare costs," says Dr. Myriam Grunewald, director of the Hadassah Organoid Center (HOC) and an expert in cardiovascular biology and aging.

Dr. Liron Birimberg-Schwartz, clinical director of HOC and a gastroenterologist, adds, "As a research center within Hadassah, our goal is to offer an organoid-based platform as a point-of-care testing to allow healthcare providers to quickly test multiple drugs or drug combinations and advise on the optimal drug regimen for each patient in a timely manner."

The Hadassah Organoid Center was established on the initiative of Prof. Eyal Mishani, head of the Hadassah Research and Development Division, with a vision to use organoid technology as a tool to bridge

(l-r) Dr. Myriam Grunewald with MSc students Debora Duran and Widad Samman

the gap between basic science and clinical practice.

"To make an organoid, we start with a small sample of cells, from a patient's own tissue, healthy or diseased, and provide them with the right nutrients and conditions to grow and differentiate into the desired cell types," say Debora Duran and Widad Samman, both MSc students under the guidance of Dr. Grunewald. Cultivated in three dimensions, organoids mimic the complex structures and functions of real tissues, allowing the study of human biology and diseases as never before. Samman is studying how to target hard-to-treat head and neck cancers, while Duran is cultivating retinal organoids to investigate degenerative retinal diseases. "Importantly, organoid cultures allow almost infinite in vitro expansion of the tissue and its cryopreservation until future use, while maintaining genetic heterogeneity and epigenetic features of the original tissue," adds Dr. Naama Sznajder, the HOC laboratory manager.

> **"Today, organoid technology is at the forefront of basic and translational research and the US Food and Drug Administration (FDA) has recently approved the first drug to enter clinical trials on the basis of efficacy data derived only from these advanced cell models."**
>
> **- Dr. Myriam Grunewald, Director of the Hadassah Organoid Center**

The potential applications of organoids are vast and varied. Organoids can be used to screen drugs for efficacy and toxicity, reducing the need for animal testing and accelerating the drug discovery process. They can also be used to study the effects of environmental factors such as toxins or radiation on tissues, and to develop personalized treatments for patients based on their individual genetic and molecular profiles. Moreover, organoids can serve as platforms for studying developmental biology, infectious diseases, and cancer biology, among other fields.

Prof. Tamar Peretz, a senior oncologist and cancer researcher at Hadassah, sees the organoid technology as a genuine breakthrough. "Because each patient has a unique response to established treatments for a disease, it is crucial


Dr. Liron Birimberg-Schwartz

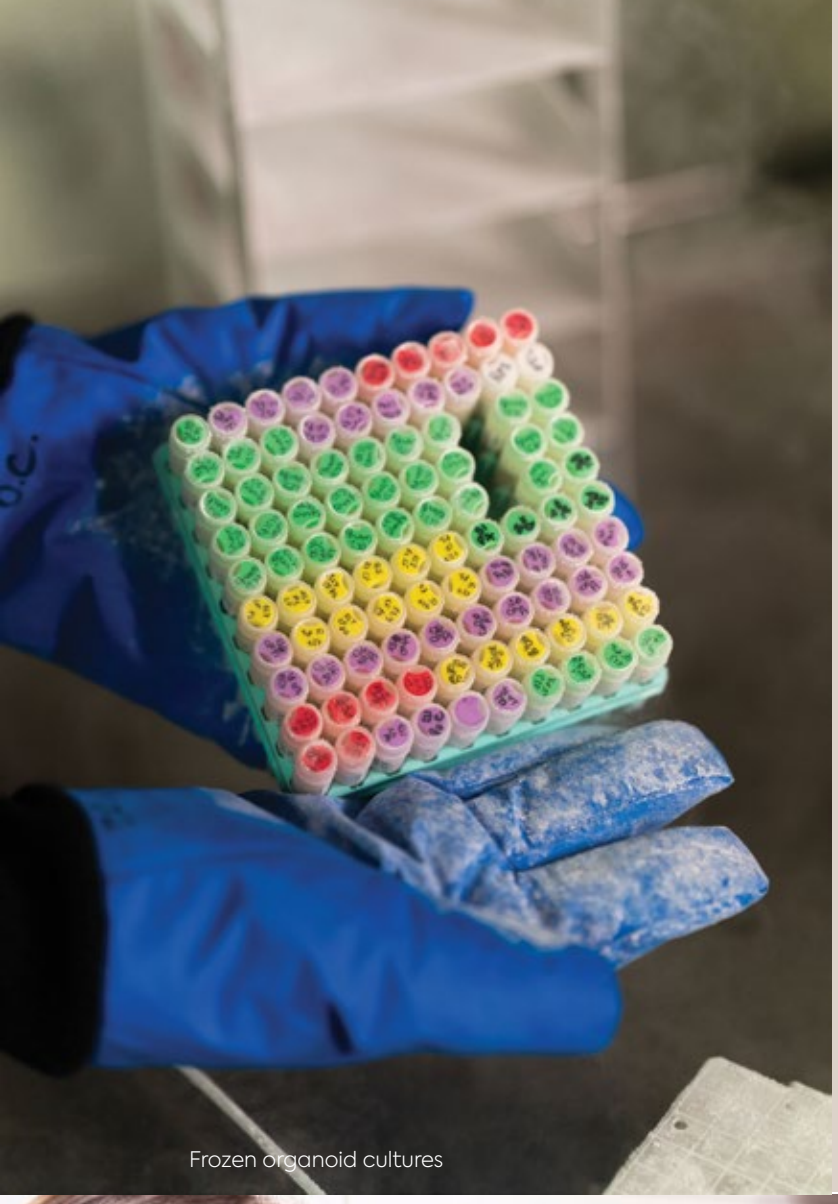

Dr. Naama Sznajder

The mission of the Hadassah Organoid Center (HOC) is to serve every medical center in Israel – predicting treatment outcomes and rapidly identifying the most effective personalized precision therapy for each patient.

to have a preclinical model that can accurately predict the response. It will save precious time for patients with aggressive cancers who cannot afford the traditional trial and error approach," Peretz explains. She recently turned to the HOC to identify a therapy, that includes repurposing of an FDA-approved drug, for a 42-year-old mother of young children, suffering from a type of breast cancer which had metastasized to her lungs and is currently untreatable. The HOC team was able to grow organoids from the patient's lung pleural effusions - a world first - since she was too weak to undergo another biopsy. Collaborating with Hadassah oncosurgeon Dr. Ori Wald, and colleagues, the HOC team is producing organoids derived from lung cancers that are currently untreatable. These organoids serve as a testing platform for new anti-cancer drugs developed by researchers at the Hebrew University, targeting specific mutations.

"Organoids will also play a central role in regenerative medicine," adds Grunewald. By combining organoids with advanced technologies such as gene editing and 3D printing, and by improving their complexity by co-culturing other cell types to provide organoids with vasculature, innervation (stimulating a nerve or an organ to activity), and other stromal elements, we can engineer functional tissues for transplantation.

"We are collaborating with Dr. Shay Porat, a Hadassah gynecologist, to explore the possibility of using endometrium-derived organoids to repair a damaged uterus, thanks to a generous donation from Prof. Neri Laufer," she adds. Organoids can also help us to understand the mechanisms of tissue aging and age-related diseases and to develop strategies to promote healthy aging and extend lifespan.



Frozen organoid cultures

Israel's First Organoid Biobank

The Hadassah Organoid Center has created the first organoid biobank in Israel, serving the scientific community, including academic research scientists, clinicians, and biotechnology companies in Israel and worldwide. This biobank provides a comprehensive biorepository of organoids derived from a variety of human tissues, representing diverse genetic backgrounds, taking advantage of the vast heterogeneity of the population treated at Hadassah. Biopsies are obtained from healthy or diseased organs including esophagus, stomach, small intestine, colon, rectum, pancreas, breast, lungs, endometrium, ovaries, fallopian tubes, and prostate. Where possible, diseased and adjacent healthy tissues are collected from the same patient. Organoids are cultured and expanded, frozen, thawed on-demand, and cultured again to either answer a basic scientific question or to help a physician decide which drug to prescribe for the best outcome.

The HOC presently partners with academic laboratories and pharmaceutical companies, both local and international, primarily to screen drugs that could potentially treat cancer, cystic fibrosis, inflammatory bowel diseases, and retinal degenerative diseases.

www.hadassah-organoids.co.il

MSc student Debora Duran