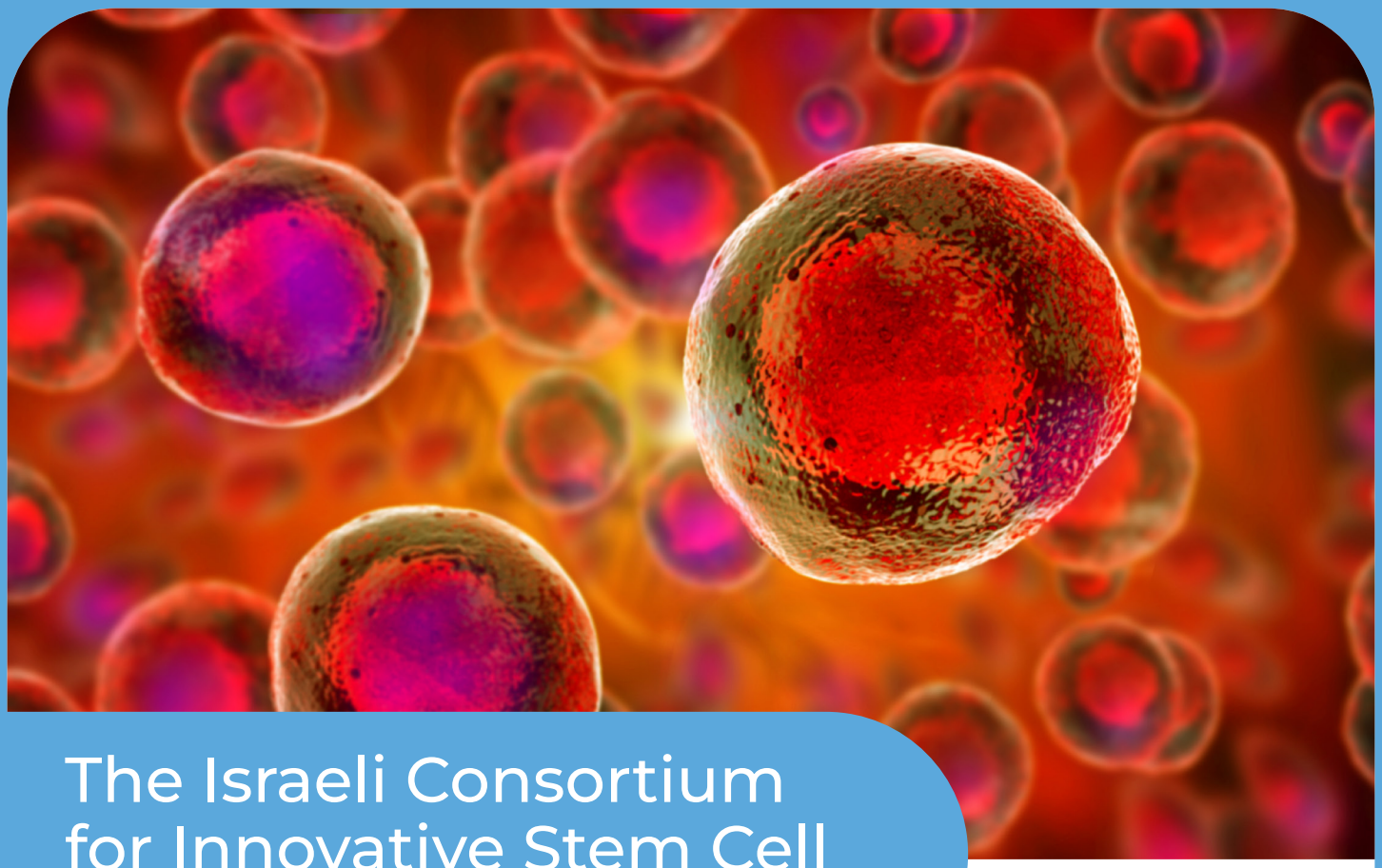


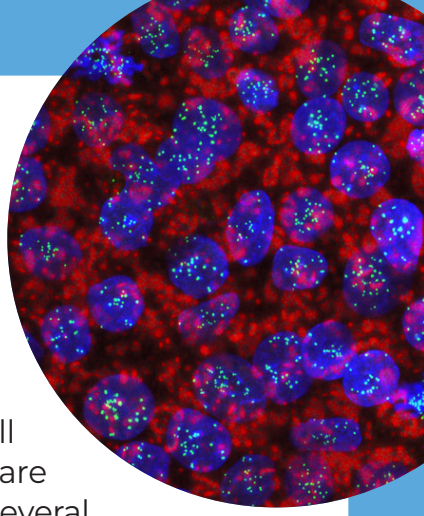
The Israeli Consortium for Innovative Stem Cell Research for Clinical Use

About Stem Cell Research

Human stem cell research is one of the holy grails of modern medicine. The use of regenerative cellular therapies holds extraordinary promise for treating diseases that today are considered incurable, since stem cells can potentially be used to regenerate the functioning of an organ that has been damaged by disease. Examples include the treatment of blindness caused by inherited retinal diseases or age-related molecular degeneration, faulty motor function due to Parkinson's or ALS, cognitive impairment from Alzheimer's, metabolic dysfunction related to diabetes or liver disease, cardiac problems from certain heart diseases, and more.

Two landmark breakthroughs in the area of stem cells have paved the way to a new era in regenerative medicine. In 1998, pluripotent human embryonic stem cells (hESC) were derived for the first time by Prof. James A. Thomson from the U.S. in collaboration with Prof. Joseph Itskovitz-Eldor from Israel. Shortly thereafter, Prof. Benjamin Reubinoff from Israel derived hESC for the second time, in collaboration with scientists from Australia and Singapore. In 2012, Prof. Shinya Yamanaka from Japan received the Nobel Prize for Physiology & Medicine for his historic achievement: discovering that mature human cells can be reprogrammed to become pluripotent stem cells (iPSC).

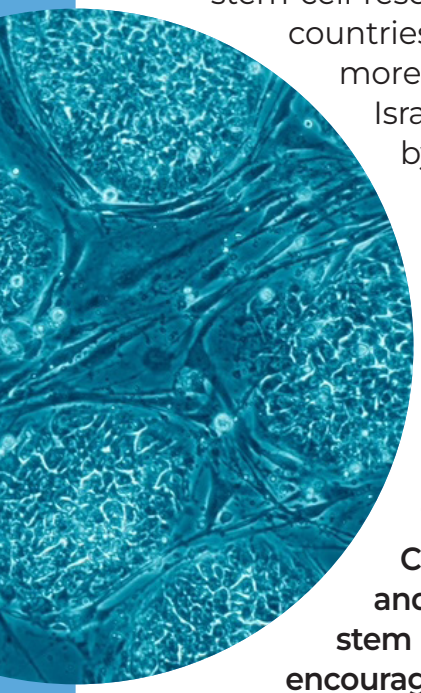
These two groundbreaking discoveries in stem cells biology – derivation of human embryonic stem cells and induced stem cells – paved the way to the development of human pluripotent stem cells as an unlimited source for human mature cells of any type for novel transplantation therapies. These scientific breakthroughs have led to the



establishment of thousands of research groups and biomedical start-up companies in Israel and around the world, investing tremendous efforts to advance stem cell research that can lead to novel therapeutic applications.

Although much progress has been achieved in the differentiation of hESCs and iPSCs into specific human cell types – such as heart muscle cells, retinal pigment epithelium cells of the eye, nerve cell and others – significant initial breakthroughs in clinical treatments are still at an early stage. In fact, despite several initial steps towards several clinical treatments, the scientific community's progress in the field of novel stem cell therapies has fallen short of expectations.

The Need for a Consortium



Israeli physicians and scientists have an international reputation as trailblazers in stem cell research and treatment, as evidenced by Israel's high ranking among countries that publish stem cell research (see table below). There are currently more than 30 research groups and biomedical start-up companies in Israel focusing on clinical human stem cell research. These are led by prominent physicians and researchers from top universities and medical centers. Their studies are at the forefront of global stem cell research.

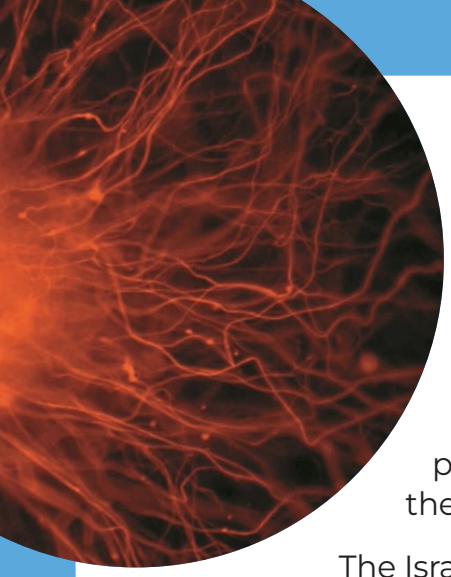
One of the main reasons for the slow pace of progress in this field both in Israel and internationally is the complexity encountered in obtaining highly efficient differentiation of pluripotent stem cells into pure populations of specific mature cells and their assimilation into recipient tissues under stringent regulatory conditions.

The new Israeli Consortium for Innovative Stem Cell Research for Clinical Use was recently established so that researchers can join forces and together overcome the key barriers on the road-map for developing stem cells for novel therapeutic applications. The Consortium aims to encourage synergy and the sharing of knowledge, thereby pushing forward applied research on a path towards achievements that will benefit humankind.

Although at first the Consortium will only include Israeli research groups, at a later stage researchers from other countries will be invited to join.

Top 10 countries in stem cell research published in scientific journals, per 1 million people

1. Singapore	**2. Israel**	3. Sweden	4. Finland	5. Denmark
6. Hong Kong	7. Australia	8. Switzerland	9. United Kingdom	10. Belgium



Objectives and Plan of Action

The newly established Consortium has defined very clear goals:

◆ Founding a National Stem Cell Biobank

A top priority is to establish a national biobank for pluripotent stem cell lines (embryonic and induced) that will be accessible to members of the Consortium as well as to others, for the purpose of conducting advanced research and developing therapies.

The Israeli National Stem Cell Biobank will derive iPSCs from patients' mature cells in collaboration with the research groups, providing them with the knowledge, methodologies, specific reagents, and laboratory infrastructure to develop iPSCs from patients to serve for modelling diseases and for testing novel therapies.

◆ Developing Universal Stem Cells

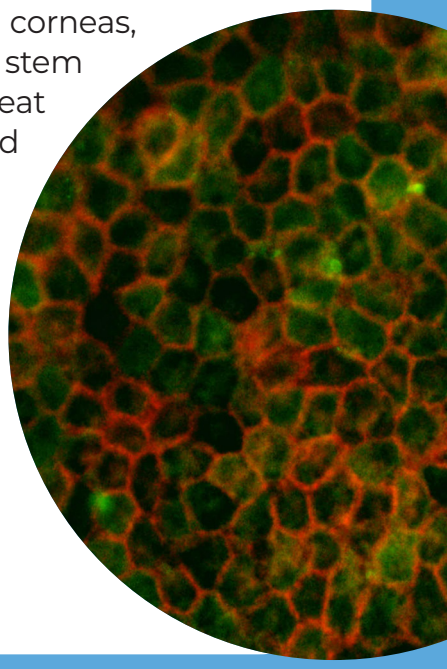
The Consortium is eager to accelerate the development of universal pluripotent stem cells that can be transplanted in humans without fear of being rejected by the immune systems.

The recent revolutionary breakthrough in genomic editing paves the way for two main approaches that are currently being developed worldwide to avoid immune rejection of transplanted allogeneic stem cells. In one strategy, the HLA molecules on the surface of the stem cells, which provoke their immune rejection by the recipient, are ablated. Another strategy would be the insertion of genes that can repress immune rejection into the cells, and that shield them from the immune system. The development of universal hPSC lines would serve as a global “off-the-shelf” unlimited stem cell resource for the development of safe cellular products that will not be rejected after transplantation.

Eventually, the Consortium aims to establish a national and international biobank of universal stem cells for clinical and research use, and for treating patients in Israel and around the world.

◆ Establishing a National Repository for Tissue-Specific Stem Cells

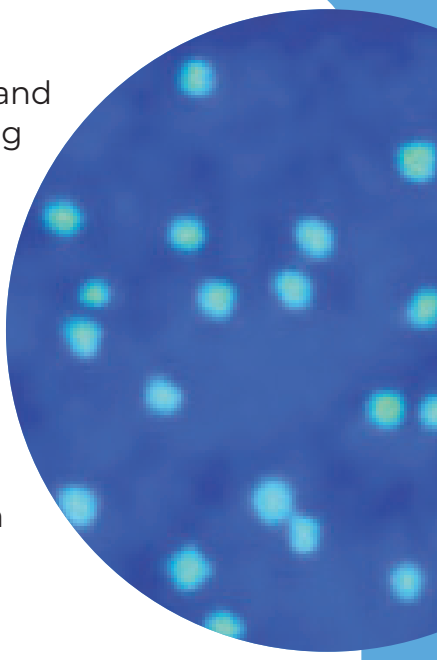
Many tissues in the body, including those in the kidneys, skin, corneas, digestive system and other organs depend upon their specific stem cells for proper functioning. These stem cells can serve to treat pathologies of the tissues and therefore can be harvested and used for treatment when needed. Such treatments already exist for corneal transplantation and for treating severe burns, blood cancer and other conditions.



These specific tissue stem cells can be used to create an organoid that mimics the original organ and can be used to study pathological mechanisms of diseases and testing new treatment modalities. The national repository will serve researchers in Israel and abroad who wish to study organ-specific diseases and develop new treatments.

◆ Creating a Scientific Sharing Platform

The Consortium will actively promote stem cell research and transplantations in all fields of medicine, for the purpose of developing treatments for a wide range of diseases. As such, the Consortium will foster collaboration among experts in this field in Israel, many of whom are at the forefront of global stem cell research but currently have little contact with each other. In addition, it will provide continuous guidance and support to research groups studying different diseases.



The new collaborative approach that facilitates sharing knowledge will undoubtedly accelerate the research process and bring about vital breakthroughs. Ultimately, stem cell research taking place in Israel is expected to form a vanguard of global trailblazers.

Leadership

The Consortium is headed jointly by Prof. Ido Perlman and Mr. Ohad Lahav. Members of the steering committee include prominent top-tier scientists and physicians with world-class expertise in this field. Among them:

◆ **Prof. Benjamin Reubinoff –** Hadassah Medical Center

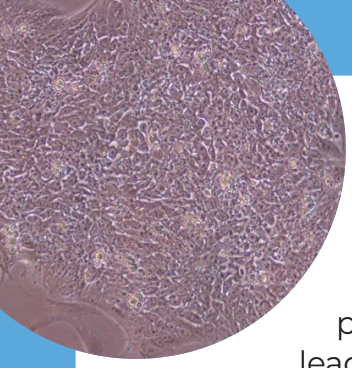
Prof. Reubinoff is the former Chairman of the Department of Obstetrics and Gynecology and the Director of the Sidney and Judy Swartz Stem Cell Research Center at Hadassah's Goldyne Savad Institute of Gene Therapy. He is also the co-founder and CSO of Cell Cure Neurosciences Ltd. He has been among the world pioneers in the derivation of human embryonic stem cells. In collaboration with a retina specialist, Prof. Eyal Banin, he developed a clinical trial for the transplantation of Retinal Pigment Epithelial (RPE) cells derived from hESCs, for preventing the loss of central vision of patients suffering from age related macular degeneration (AMD).

◆ **Prof. Benjamin Dekel –** Sheba Medical Center and Tel Aviv University

Prof. Dekel holds the Kleinman Chair in Nephrology at Tel Aviv University and heads the Pediatric Stem Cell Research Institute and the Pediatric Nephrology Department at Sheba Medical Center, Tel Hashomer. He chairs the Israeli Society for Stem Cells and is the director of the Segol Center for Regenerative Medicine at Tel Aviv University. Prof. Dekel is known internationally as one of the most innovative and highly recognized investigators in the field of human renal stem cell biology and regenerative medicine, applying new therapeutic cellular protocols that can delay the need for dialysis and kidney transplantation.

◆ **Prof. Noam Shomron –** Tel Aviv University

Prof. Shomron heads the Functional Genomics Laboratory at Tel Aviv University's Medical School, as well as the Digital Medicine team at Tel Aviv University's Innovation Lab. Prof. Shomron is the Director of the Rare Genomic Institute-Israel, assisting those who suffer from rare genetic disorders. His research team combines AI and computational methods in order to explore the regulation of gene expression mainly by small RNAs and to reach a global systems view of the mechanistic roles they play in health and disease.



◆ **Prof. Ido Perlman –** Technion–Israel Institute of Technology
Prof. Perlman served as Dean of the Technion Graduate School and Dean of the Technion's Rappaport Faculty of Medicine. He is an expert on retinal functioning and headed a research project that used induced pluripotent stem cells from patients to study the cellular mechanisms leading to loss of central vision in people suffering from an inherited disorder damaging the macula region (Best Disease) of the human retina.

◆ **Prof. Nissim Benvenisty –** Hebrew University of Jerusalem
Prof. Benvenisty is the Director of the Azrieli Center for Stem Cells and Genetic Research at the Hebrew University of Jerusalem. He is an expert on tissue engineering, the biology of stem cells, human genetics and cancer research; a member of the steering committee of the International Stem Cell Initiative; and on the Board of Directors of the International Society for Stem Cell Research (ISSCR).

◆ **Prof. Lior Gepstein –** Rambam Health Care Campus
Prof. Gepstein is the Director of the Cardiology Department at Rambam Health Care Campus, as well as Professor of Physiology and Medicine (Cardiology) at the Technion's Faculty of Medicine, where he holds the Edna and Jonathan Sohnis Chair in Tissue Engineering and Regenerative Medicine. His research group was among the pioneers in developing unique cardiomyocyte differentiation strategies from human embryonic stem cells and human induced pluripotent stem cells.

◆ **Prof. Mordechai Shani –** Sheba Medical Center
Prof. Shani served as Director General of the Sheba Medical Center for 33 years and helped found the School for Health Policy at Tel Aviv University. He also served two terms as the Director of the Israeli Ministry of Health and is the Founder and Chairman of the Management Committee of the Gertner Institute for Epidemiology and Health Policy Research.

◆ **Prof. Aaron Ciechanover –** Technion–Israel Institute of Technology
Prof. Ciechanover is a highly distinguished Israeli biochemist who won the Nobel Prize in Chemistry in 2004 for characterizing the method that cells use to degrade and recycle proteins using ubiquitin – which enabled a breakthrough in the research of cancer and other diseases. He is currently a Technion Distinguished Research Professor in the Rappaport Faculty of Medicine and Research Institute at the Technion.

Budget

The Consortium's **five-year budget is $50 million**. This is the amount required for implementing the Plan of Action detailed above, which includes the following projects:

- Establishing and maintaining a National Stem Cell Biobank
- Developing universal stem cells
- Establishing a repository for tissue specific stem cells
- Supporting innovative, high-potential research projects
- Recruiting leading researchers to work in this field at Israeli research and medical institutions
- Advocating and increasing awareness about the importance of this initiative

We welcome contributions of all levels, and all donors will be recognized for their generosity

For more information, please contact Ms. Nadine Hollander, nadine@eyes.org.il, +972-54-4230012