Text: Louise Hagbard, Ph.D. Photo: Ulf Sirborn

STEM CELL INNOVATORS

OUTI HOVATTA

"I applied for an ethical permit and became the first researcher in Sweden to derive hES cells from donated IVF embryos."

OUTI HOVATTA, Ph.D.

PROFESSOR EMERITA
OBSTETRICS AND GYNECOLOGY, ESPECIALLY ASSISTED REPRODUCTION, KAROLINSKA INSTITUTET, SWEDEN

ABOUT: Professor emerita Outi Hovatta has been researching fertility for nearly 40 years. She was the first to apply for an ethical license to derive and grow embryonic stem cells in Sweden. Her group in Stockholm is also among the foremost in the world when it comes to developing completely clean lines, which can be used for future treatments. Prof. em. Hovatta has helped countless infertile couples and derived over 30 different human embryonic stem cell lines.

Prof. em. Hovatta graduated as a medical doctor and holds a Ph.D. in reproductive science from the University of Helsinki in Finland. She worked as a specialist obstetrician and gynecologist at Helsinki University Hospital and then became the chief physician and founder of the infertility clinic, the Family Federation of Finland. Prof. em. Hovatta did a postdoctoral research period at the Imperial College School of Medicine at Hammersmith Hospital in London and was a visiting professor at the University of Geneva, Switzerland. Between 1998 and 2013 she was chief physician of the fertility unit at Karolinska University Hospital Huddinge in Stockholm, Sweden. She held a professorship in Obstetrics and Gynecology, especially Assisted Reproduction at Karolinska Institutet in Stockholm, Sweden, and was a senior professor before retiring in 2016.

Outi Hovatta has published over 300 original articles and reviews and has been an authority within the pluripotent stem cells community.

KAROLINSKA INSTITUTET

Karolinska Institutet was founded in 1810 is Sweden's single largest centre of medical academic research and offers the country's widest range of medical courses and programmes. It is one of the world's foremost medical universities and since 1901 the Nobel Assembly at Karolinska Institutet has selected the Nobel laureates in Physiology or Medicine.

↑ Biopsy of human embryo. Photo: Mona Sheikhi

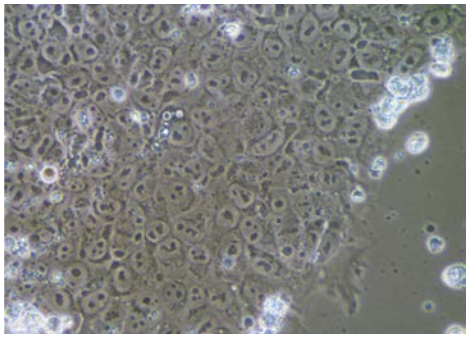
Tell me how you started your research career within pluripotent stem cell research!

"I have always been a clinical researcher, so it began already during my studies at the University of Helsinki. I was interested in reproductive science and did research on testicular development, how the testis cells behaved in cultivation. So, in 1998 when we saw that it was possible to grow embryonic stem cells, I thought that would be a natural continuation of my work within the fertility research field. I was chief physician at the fertility unit at Karolinska University Hospital Huddinge in Stockholm, Sweden so I had good access to embryos that were left over from *in vitro* fertilization treatments. I applied for an ethical permit and became the first researcher in Sweden to derive hES cells from donated IVF embryos."

"Already from the start, we had the idea to use these cells for cell therapy applications. That is why we wanted to get rid of all animal-derived components. Most stem cell researches were using mouse fibroblasts as feeder cells, but we chose to use human foreskin fibroblasts. However, feeder cells were quite hard to work with and I was looking for a way to culture hESC without the need for feeders. I discussed this with my colleague, professor Karl Tryggvason, who I knew well from when I worked as

IN VITRO FERTILIZATION

***In vitro* fertilization (IVF) is a procedure used to treat fertility or genetic problems and assist with the conception of a child. IVF is the most effective form of assisted reproductive technology. During IVF, mature eggs are retrieved from the ovaries and fertilized by sperm in a laboratory dish. The fertilized egg, the embryo, is then implanted into the uterus three to five days following fertilization.**



↑ hES cell line HS983 cultured on LN521. A fully characterised line from a single blastomere.
Photo: Liselotte Antonsson

“I believe that Swedes have a very positive attitude toward stem cell and cell therapy research.”

Human embryo. Photo: Mona Sheikhi

Single isolated blastomeres of 8-cell stage embryo. Photo: Liselotte Antonsson

a medical doctor in Finland, and he suggested that I test the recombinant laminin proteins that he was machining in his lab. So, we did a test, culturing hESC on laminins, and it was a success. Compared to working with feeder cells, it became so much easier to culture human embryonic stem cells on laminin substrates. We got much more robust results, and we did not have to put time and effort on growing human fibroblasts from different donors. When Karl later founded BioLamina, it became possible to get ahold of these defined, animal component-free laminin substrates for research. We have been using Biolaminin substrates since then and I consider them essential for clinical research."

Do you feel that it has been difficult to get ahold of embryos for research?

"No, not at all. There are regulations in Sweden that allow 5-year storage of frozen IVF embryos. If the parents do not have any need for these embryos, they can choose to either discard them or donate them to research purposes. I would say about 90% of all parents donate their embryos. I believe that Swedes have a very positive attitude toward stem cell and cell therapy research. I think the reason for that is that it's a part of the education system. Medical research is actively discussed in school."

What has been your biggest inspiration?

"When I was young, I always knew I wanted to become a researcher. I was torn between two research fields, to study biology or to study medicine. I chose medicine because of my father. He was a professor at the Institute of Technology in Helsinki in Finland, and he was under the impression that it was easier to get funding at the medical facility. I got accepted to both facilities but chose medicine and I have never regretted it. I really enjoyed being a clinician. Now I'm retired and have moved back home to Finland where I'm closer to my children and grandchildren, which I am very happy to have in my life. I will also get more time to be with them and to read and write. I will never give up research and will continue to follow the progress within this field. I'm in regular contact with my former research group and I assist them in small things, like reading their manuscripts."

What do you think about the future of pluripotent stem cell-based therapy?

"I think it has great potential but currently it's too early to say to what extent and for with disease. There is still a lot of research to be done in this field. There are a few clinical trials ongoing that look promising, but there have also been a few catastrophic attempts. I think the biggest hurdle we face is safety, to make sure that the cell products transplanted will behave normally and do not form tumors. We have to be able to control that."

What is your impression of the collaboration with biotech companies, like us?

"It has been very positive and has enabled part of my research. The collaboration with Karl Tryggvason has also been very important. It has generated grants and our research has generated publications in high impact journals."

Is there something you are extra proud of?

"I am very proud of the human embryonic stem cell lines we have generated. I am also proud of the stem cell-based research we've done within the group. That we have been able to generate dopaminergic neurons and retinal pigmented epithelial cells. Cells that hopefully will have a clinical application in the future."


BioLamina
REVOLUTIONIZING CELL CULTURE