Brussels IVF

W20-E

SUPPLEMENT SR

INFORMATION ON THE USE OF GAMETES AND EMBRYOS FOR TRAINING PURPOSES AND SCIENTIFIC RESEARCH

SUPPLEMENT RELATING TO INFORMED CONSENTS A02 A03 D01 I07 I08 I09 I10 W01 W02 W03 W04

Dear Madam, Dear Sir,

As patient of Brussels IVF in UZ Brussel you have called on our expertise in the treatment of fertility problems. We sincerely hope that we will be able to help you fulfil your wish to have a child.

Since its creation in 1983, our centre has been driven by two strong engines: clinical practice, which is all about the patient, and (scientific) laboratory work, which supports and strengthens clinical practice. Thanks to this powerful combination, Brussels IVF - often together with the Centre of Medical Genetics (CMG) of UZ Brussel - has achieved several breakthroughs in the high-tech field of fertility medicine.

For medical progress, continuous scientific research is needed. However, such research is not possible without the contribution of patients who are prepared to donate reproductive material (oocytes, sperm, embryos).
The aim of this Supplement SR is to give you all the necessary information based on which you can then decide to donate any material for scientific research. This may be material that is unsuitable for your treatment or suitable material that has been stored for you by means of cryopreservation and that has passed the legal storage period or the storage period agreed with you. In other words, we only carry out research with oocytes, sperm and embryos which you cannot use yourself (any more).

This supplement is an integral part of the informed consents you sign as part of your fertility treatment at Brussels IVF. We hope that this information will help you reach a positive decision regarding the donation of gametes and embryos for training purposes and scientific research.

Prof. Hilde Van de Velde
hilde.vandevelde@uzbrussel.be
Responsible for the biobank and co-ordinator of the scientific research in the ART lab

WHICH SCIENTIFIC RESEARCH?

If you consent to donating reproductive human tissue for training or research, it can be used in the following five domains. More information about the domains and the accompanying projects is available from p. 5.
If you want to exclude one or more domains from your agreement for scientific research, you can do so by referring to the corresponding letter(s) in the informed consent.

I. Training of laboratory staff

To perform difficult techniques to a high standard, laboratory staff needs to be able to practise with real gametes and embryos.
This concerns techniques such as the micro-injection of oocytes, the freezing and thawing of gametes and embryos, the removal of one or more cells from embryos (embryo biopsy) and performing genetic tests on gametes and embryos.
Domain A – Laboratory techniques

II. Scientific research in five domains

Domain A – Laboratory techniques
Domain B – Embryonic development and implantation of the embryo in the uterus
Domain C – Genetic state of the embryo
Domain D – Embryonic stem cell research
Domain E – Genome modification

WITH WHICH GAMETES AND EMBRYOS?

In your fertility treatment we use your oocytes and sperm (gametes) to try to help you get pregnant. The fertilisation of the gametes produces possible embryos that can be transferred or frozen (cryopreserved) for later use.

- However, sometimes not all collected oocytes come into consideration for use in your treatment, or there may be superfluous sperm cells or embryos that are unsuitable for transfer or cryopreserving. See the possible causes of unsuitability further on.
  You decide on what happens with these gametes and embryos in the 'Informed consent for scientific research with gametes/embryos that cannot be used in your treatment' (W01 and W02).

- Gametes (oocytes or sperm cells) can also be used in research to generate embryos that will be genetically modified. In this case, you will need to give specific consent to do so (W03).

W20-E

INFORMATION ON THE USE OF GAMETES AND EMBRYOS FOR TRAINING PURPOSES AND SCIENTIFIC RESEARCH

- If during a treatment cycle more embryos are produced than can be transferred in the cycle and you don't want them cryopreserved, you have to decide if you want them destroyed or you want to release them for training purposes and/or scientific research. You do this in the 'Informed consent on the storage and destination of suitable supernumerary embryos in your assisted reproductive treatment (ART)' (A02).

- In the same A02 form you can decide to have your embryos cryopreserved. In this case you have to indicate immediately what use you give to the cryopreserved embryos if the legal or agreed storage period has expired or if you don't need them yourself anymore or can't use them. You can choose to release them for training and/or scientific research.

- During your treatment you can have gametes cryopreserved for later use or you can have this done as a separate (freeze) intervention. You give your consent for this in specific informed consent forms (I07, I09, etc.), in which – again – you immediately decide what needs to be done with the cryopreserved gametes if the legal or the agreed storage period has expired or if you don't need them yourself anymore or can't use them anymore. You can release them for training purposes and/or scientific research.

- And finally, gametes for scientific research can be from a donor.
  - In case of sperm it concerns a donor who specifically donates his sperm to create embryos for research in well-defined research projects.
  - In case of oocytes it concerns a donor who in an anonymous donation programme tries to help prospective parents become pregnant, and who gives up some of the donated oocytes for research.

The different types of gametes and embryos that may be released for scientific research are listed by numbers hereafter. You will find the numbers set out in this list preceding the description of each type of research. You can then work out the types of tissue that are used in the various types of research. .

1. Gametes

1a – Oocytes that cannot be used for fertilization because they have failed to reach the appropriate stage of maturation.
1b – Oocytes that cannot be fertilised during the treatment cycle and for which cryopreservation is not an option.
Oocytes may be impossible to fertilise in the IVF laboratory, the partner's ejaculate or testicular biopsy tissue[1] has not yielded any sperm and when the use of donor sperm is not an option for you as a couple.
1c – Oocytes made available by donors.
1d – Oocytes which have been frozen in the context of your treatment and are donated for scientific research after their predefined storage period.
1e – Sperm left over after IVF or ICSI.
1f – Testicular tissue.
1g – Sperm provided by a donor.
1h – Sperm frozen in the context of your treatment and donated for scientific research after the predetermined storage period.

If oocytes or sperm are released for scientific research they can be used – only with explicit permission of all donating parties involved – to create embryos. This is only done if the aim of the research can soly be achieved by creating embryos and subject to specific permission of the FCE, the Federal Commission for Medical and Scientific Research on Embryos in vitro *(see p. 4)*.

2. Embryos

2a – Embryos frozen as part of ART treatment and then donated for scientific research after the predefined storage period.
2b – Embryos of prospective parents who chose not to have their usable supernumerary embryos frozen.
2c – Embryos originating from abnormally fertilised oocytes. These therefore cannot be transferred to the uterus.
2d – Embryos of insufficient quality to be transferred to the uterus or cryopreserved.
2e– Embryos that have been genetically tested in the context of a PGT treatment[2] of the prospective parents and have been found to have a genetic defect.

Embryos are cultured in the laboratory no later than day 14 and are destroyed by the research technique.

1 In male infertility we sometimes try to collect sperm from a piece of tissue which we surgically remove from the testis or epididymis (a biopsy)
2 PGT or pre-implantation genetic testing means that we genetically examine embryos before they are eligible for transfer to the uterus.

W20-E

INFORMATION ON THE USE OF GAMETES AND EMBRYOS FOR TRAINING PURPOSES AND SCIENTIFIC RESEARCH

WHAT ARE YOUR RIGHTS WHEN RELEASING GAMETES AND/OR EMBRYOS FOR RESEARCH PURPOSES?

- In order to protect your privacy, we follow all legal provisions as set out in the Belgian so-called GDPR Act of 2018. Your name and other personal data – in case of a couple those of both partners – will remain strictly confidential to the researcher. The research material is encoded by means of a so-called pseudo-anonymisation, so that your clinical data also remain protected.
- This release of gametes and/or embryos is voluntary. You are entitled to refuse to release supernumerary reproductive material for scientific research. It will neither increase nor reduce your chances of success and your decision will have no effect on your subsequent treatment.
- Releasing gametes and/or embryos does not result in any financial benefit, nor does it entail any additional cost.
- You can withdraw your consent to use your supernumerary gametes and/or embryos for training purposes or scientific research, up till the moment the training or research begins.
- If you are a couple, this withdrawal is valid if requested by either of you.
- You must inform us of your decision to withdraw your consent in a written, signed document.
- Scientific research sometimes includes a genetic analysis of the studied oocytes, sperm or embryos. The research results are published in genetic databases, which are not publicly accessible. Only other scientists can access them and only with the consent of the original authors of the research. Nevertheless, and although this is very improbable, there is a theoretical possibility that another researcher can ascertain your identity based on the genetic data.
- In the informed consent form you can explicitly indicate whether you consent or not with the genetic analysis of your reproductive material and the accompanying publication of the research data.
- Scientific research is sometimes performed in collaboration with other research institutes or with companies in the private sector. In that event it may be necessary that your encoded personal data are shared with the researchers of the other institute. Your name and identity are never released however, not to our researchers, nor to third parties.
- By consenting to the use of your gametes and embryos for scientific research you are simultaneously consenting to the possible application for a patent for inventions that may result from the research to which you have consented.
- You fully understand this and waive all claims to any compensation.

HOW DO YOU GIVE YOUR CONSENT?

We request your consent for scientific research in the different informed consent forms belonging to your treatment. Take into account the following.

- For gametes you each decide separately: as a woman for the oocytes, as a man for the sperm.
- Embryos require a couple's joint decision.
  Obviously as a single prospective mother you decide for yourself.
- Gametes released for the purpose of scientific research remain irrevocably released from the moment of fertilisation. From that moment on, you will have no more obligations or rights concerning the released gametes.

- ○ If you tick the option 'consent for training of laboratory staff', the gametes and/or embryos can be used by the laboratory staff to practice techniques that occur in domain A.
- ○ If you tick the option 'consent for scientific research', the gametes and embryos can be used for said research, within the legal constraints we discuss on page 4.

Specifications of your consent

You can further specify your consent for scientific research in a separate section of the informed consent.

- You can indicate whether you want to exclude certain research domains or projects from your agreement, by filling out the letter(s) in the specified location of the excluded field of research or the number(s) of the excluded research project(s).
- You give your separate consent (or not) for a genetic analysis of your donated material and for sharing the genetic information with other researchers.
- Finally, you can decide whether to allow cooperation with other research institutions and private companies, and if so, with which ones. At positive decision you also have to agree that we share the necessary encoded personal data to the external researchers.
- If the gametes and/or embryos released for research are not suitable or not necessary at that time for scientific research or training purposes, they will be destroyed.

WHAT ARE THE REQUIREMENTS FOR SCIENTIFIC RESEARCH?

Most countries have strict laws on the use of human tissue and human embryos for scientific research. In Belgium this is governed by the law on research performed on embryos in vitro of 11 May 2003, published in the Official Gazette on 28 May 2003.

W20-E

INFORMATION ON THE USE OF GAMETES AND EMBRYOS FOR TRAINING PURPOSES AND SCIENTIFIC RESEARCH

This law stipulates the following (research) actions are prohibited:

- The implantation of human embryos into animals or the creation of chimeras[3].
- The implantation in humans of any embryos that have been used in research, except where the research was carried out with a therapeutic intent for the embryo itself or in the case of an observation method that does not harm the integrity of the embryo.
- The use of embryos, gametes or embryonic stem cells for commercial purposes.
- Conducting research or developing treatments aimed at the selection or improvement of non-pathological genetic characteristics for the human race.
- Conducting research or treatments for the purpose of gender selection, except for the purpose of preventing gender related diseases.
- Cloning of human reproductive tissue.
- Conducting research on embryos after the first 14 days of development, not including the period when frozen.

In addition, scientific research must meet the following conditions:
It has a therapeutic purpose or contributes to a better knowledge of (in) fertility, the transplantation of organs and tissues, the prevention or treatment of diseases.

- It is supported by the latest scientific findings and meets all metho–dological requirements of scientific research.
- It is conducted in or under the supervision of a certified laboratory associated with a university care programme for reproductive medicine or human genetics.
- It is conducted under appropriate technical and material conditions and under the supervision of qualified people.

These conditions are based on the guidelines for Good Clinical Practice of the ICH, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. These guidelines are included in the Declaration of Helsinki on the protection of individuals participating in clinical studies.

SCIENTIFIC RESEARCH AT THE UZ BRUSSEL – BRUSSELS IVF

It goes without saying that scientific research at UZ Brussel meets all the requirements of the specified law and that all studies are carried out in accordance with the guidelines of the ICH/GCP (*see above*).
Moreover, every research protocol for which human gametes or embryos can be used has received a favourable recommendation before the research begins from the two authorised committees in this area:

- the Medical Ethics Committee of UZ Brussel (LCE) and
- the Federal Commission for Medical and Scientific Research on Embryos in vitro (FCE). The FCE must ensure that all legal requirements are met.

In most cases the research that we describe here is conducted by scientific staff at Brussels IVF laboratories. However, we also collaborate with other researchers.

- Genetic research mostly takes place in the laboratories of the Centre for Medical Genetics (CMG) of UZ Brussel, for example. Together, the CMG and Brussels IVF make up the PGT clinic, where we try – by testing the embryos genetically before they are transferred to the prospective mother's womb – to help couples with genetic problems to have a child free of the genetic defect.
- We also work with the Human Stem Cell laboratory (hESC lab) and with the REGE, REIM, FOBI and BITE research groups of the Vrije Universiteit Brussel (VUB).
- If the scientific research is done in collaboration with a foreign research institute or a private enterprise it must also be approved by the ethics committee of the institute to which the cryopreserved human tissue has been donated and by the FCE.

Hereafter is a brief description of the scientific projects Brussels IVF is involved in and in which we use human gametes and/or embryos.

3 Chimeras or hybrids are creatures made up of cells of different creatures.

W20-E

INFORMATION ON THE USE OF GAMETES AND EMBRYOS FOR TRAINING PURPOSES AND SCIENTIFIC RESEARCH

DOMAIN A – LABORATORY TECHNIQUES

Research material: 1a, 1b, 1c, 1d, 1e, 1f, 1g, 1h, 2a, 2b, 2c, 2d, 2e
This domain is about the research in itself, but also includes the training of laboratory staff. The aim is to improve existing techniques in the fertility clinic and to develop and validate new procedures in the following sub-domains.

- Laboratory techniques to fertilise an oocyte outside the body (IVF and ICSI).
- Conditions under which embryos grow well outside the body.
- The best way to freeze and store embryos.
- The technique to remove a few cells from the embryo for genetic diagnosis (embryobiopsy).
- The refinement and fine-tuning of existing techniques to check DNA mutations, hereditary disorders and chromosomal abnormalities in embryos.

DOMAIN B – EMBRYONIC DEVELOPMENT AND IMPLANTATION OF THE EMBRYO IN THE UTERUS

Embryonic development starts when the oocyte is fertilised by a sperm cell. A fertilised oocyte develops into a multicellular embryo, a morula and a blastocyst.
Research into embryonic development and implantation in vitro is aimed at understanding why embryos grow poorly or do not implant. Our aim is a better understanding of the function of the genes and proteins that play a crucial role in early embryonic development.
We hope this will lead to better diagnosis and treatment of couples with fertility problems.

Project 16 – Investigation of trophectoderm regulators playing a role in human embryo implantation

ADV080 – LCE (BUN 143201939165, permit 6/03/2019)
FCE (permit 29/04/2019, completion date 29/04/2024)
Research material: 2a, 2b, 2c, 2d, 2e

Project 16 focuses on the implantation of the embryo. In humans, the implantation mechanisms are not well known, which means that implantation failure is the main limiting factor in an IVF programme.
In this crucial stage in human reproduction – on day seven after fertilisation – the embryo and the endometrium must interact perfectly. The process – for which both the embryo and the endometrium have to be optimally prepared – consists of three steps.

- Apposition, i.e. the initial loose attachment between the embryo and the endometrium.
- Adhesion, or the stronger attachment of the embryo to the endometrium.
- Invasion, when the embryo penetrates the endometrium.

To gain a better understanding of implantation, and implantation failure in particular, an in vitro model for implantation in humans has been set up. Human embryos are grown in the presence of human endometrial cell lines or biopsies.
Using molecular biological techniques and a microscope, we examine the role played by adhesion molecules, growth factures, hormones and the immune system during the three phases of implantation.
By fostering or preventing implantation in vitro, we hope to discern the factors that play a crucial role. In this way we hope to understand the causes of implantation failure and recurrent miscarriage.

Project 25 – Assessing the impact of SARS-CoV-2 infection during pregnancy on obstetric and foetal outcome

AdV085 – LCE (BUN 1432020000258, permit 7/12/2020,
FCE (permit 7/12/2020, completion date 7/12/2025)
Research material: 1a, 1b, 1c, 1e, 1g, 2a, 2b, 2c, 2d, 2e

The respiratory disease COVID-19 (CO-rona VI-2 rus D-isease 2019), caused by the novel severe acute respiratory syndrome (SARS) coronavirus (CoV), named SARS-CoV-2 or 2019-nCoV, has resulted in thousands of infected patients since December 2019.
Although SARS-CoV-2 infection does not always result in COVID-19 and most people of reproductive age show few or no symptoms, scientific knowledge of the effect of SARS-CoV-2 infection during pregnancy is scarce. Infection during the final weeks of the third trimester appears not to have any adverse effects for mother and neonate. However, a recent study has reported an increased risk of maternal and neonatal complications if the infection occurs early in the third trimester. Moreover, very little is known about the consequences of infection during the first or second trimester of pregnancy. Finally, whether transmission of SARS-CoV-2 occurs from mother to embryo/foetus (vertical transmission) is still a matter of much debate.

The aim of project 25 is to investigate:

- whether vertical transmission of SARS-CoV-2 occurs during embryonic development (i.e. during early embryogenesis), and
- whether/how this may harm the developing embryo.
  In other words, we are investigating the susceptibility of human oocytes and embryos to SARS-CoV-2 infection and its impact on embryonic development in vitro.

W20-E

INFORMATION ON THE USE OF GAMETES AND EMBRYOS FOR TRAINING PURPOSES AND SCIENTIFIC RESEARCH

Project 26 -Exploring the first lineage segregation in the human embryo: is GATA3 the gatekeeper of trophectoderm differentiation? (FWOGATA3)

ADV087 – LCE (BUN 1432021000526, permit 03/10/2021)
FCE (permit 06/12/2021, completion date 05/12/2026)
Research material: 1a, 1b, 1c, 1d, 1e, 1g, 2a

Project 26 concerns the study of the first different developments in human embryos prior to transfer. This development starts at the stage of compaction, when the contact between the cells becomes stronger and the outer cells become polarised.
Then, on the fifth day of development in the laboratory, a blastocyst is formed in which two types of cells or cell lines can be distinguished: an outer layer of cells or trophectodermal cells (which will develop into the placenta) and an inner cell mass (which will later develop into the baby). This moment of development is called the first differentiation within embryogenesis.
In this project, we study how this polarisation is induced and how it contributes to the development of two different cell lineages.
Using time-lapse image capture, immunostaining and RNA analysis, we are also studying the role of GATA3, a specific protein that plays an important role in the formation of trophectodermal cells.
Finally, we also intend to study the role of the signaling cascade (in particular, the "Hippo pathway") that ensures the development of the different cells during this first phase of differentiation. This will help us to better understand why some embryos develop better than other ones.

Project 27 – Inhibitor treatments and microscopy in human embryos to understand cell fate specification in early human embryonic development (CREPE)

AdV090 - LCE (BUN 1432021000539, permit 03/08/2021)
FCE (permit 06/12/2021, completion date: 05/12/2026)
Research material: 2a

Project 27 studies the early development of different cell types, or differentiation, in human embryos prior to transfer. On day five, the fertilised oocyte develops into a blastocyst, in which two cell types or cell lineages can be distinguished: an outer layer of trophectoderm cells (which will develop into the placenta) and an inner cell mass (which will form the embryo). Then, on the sixth or seventh day, the inner cell mass will continue to develop and form two new cell lines. At that moment we can distinguish the primitive endodermal cells (which will form the yolk sac) and the epiblast cells (which will later develop into the baby).
In this project, we study how DNA processes regulate these different developments in young human embryos. We aim to gain knowledge by suppressing the regulatory mechanisms in the embryo with small molecules, using immunostaining and by determining the RNA sequence in human embryos that we keep in lab culture up to day 14. This helps us to better understand why some embryos develop better than other ones.

Project 28– Defining signaling pathways regulating cell fate decisions during human peri-implantation development (LINDIF)

AdV088 - LCE (BUN 1432021000572, permit 01/09/2021)
FCE (permit 06/12/2021, completion date: 05/12/2026)
Research material: 2a

Project 28 involves the study of the development of different cell types, or differentiation, in human embryos prior to transfer.
On day five, the fertilised oocyte develops into a blastocyst, in which two types of cells or cell lineages can be distinguished: an outer layer of trophectodermal cells (which will develop into the placenta) and the inner cell mass (which will form the embryo). Then, on the sixth or seventh day, the inner cell mass will continue to develop and form two new cell lineages. At that moment, we can distinguish the primitive endodermal cells (which will form the yolk sac) and the epiblast cells (which will later develop into the baby).
In this project, we want to determine which pathways, or signaling cascades, are involved in this primary differentiation. We will visualize this by means of immunostaining and RNA-seq determination. Pathways already well known in mice will be modified with small molecules up to day 7 of embryogenesis (the moment of implantation in women).
This helps us to better understand why some embryos develop better than other ones.

Project 30 – Optimising endometrial assembloids for human embryo implantation (EUTOPIA)

Adv093 - LCE (BUN1432022000093, permit 17/04/2022)
FCE (permit 13/06/2022, completion date 13/06/2027)
Research material: 2a

To gain a better understanding of implantation, and implantation failure in particular, we developed a new in vitro model to study implantation in humans, called assembloids. The model is made of endometrial epithelium and stromal cells. Human embryos are grown in the model in absence and in presence of small inhibitory molecules in order to investigate signaling pathways that may play a role in implantation.
Using molecular biological techniques and a microscope, we examine the role played by adhesion molecules, growth factures, hormones and the immune system during the three phases of implantation (apposition, adhesion and invasion).
By fostering or preventing implantation in vitro, we hope to discern the factors that play a crucial role. In this way we hope to understand the causes of implantation failure and recurrent miscarriage.

W20-E

INFORMATION ON THE USE OF GAMETES AND EMBRYOS FOR TRAINING PURPOSES AND SCIENTIFIC RESEARCH

DOMAIN C – GENETIC STATE OF THE EMBRYO

This domain studies techniques to examine the DNA of embryos before they are returned to the uterus.
The best-known application is pre-implantation genetic testing (PGT), in which we remove a few cells or a little tissue from the embryo for analysis in the lab.
There are two main reasons to genetically examine embryos:

- To prevent embryos with a genetic disorder from being transferred in a fertility treatment.
- To find out which genes play a role in embryonic development and implantation.

Project 23 – The origin of mitochondrial DNA mosaicisms in human embryonic development

AdV076 – LCE (BUN 143201731657, permit 7/06/2017
FCE (permit 26/02/2018, completion date 26/02/2023)
Research material: 2a, 2b, 2d, 2e
Mitochondria are the components in our cells responsible for the production of energy. They have their own DNA. Mutations in mitochondrial DNA can not only lead to hereditary disorders, but play an important role in our general state of health and ageing process.
Project 23 studies the possible differences in the mitochondrial DNA of each cell of the same embryo. The aim is to determine whether different cell lines develop during early development with different mutations in the mitochondrial DNA and when this happens.

Project 24 – The mitochondrial genome in the oocytes and granulosa cells of ART patients

LCE (BUN 143201939997, permit 24/04/2019, completion date 24/04/2023)Research material: 1a, 1b
The aim of project 24 is to determine whether there are differences in the mutations in oocytes of women who need fertility treatment for different reasons. Our hypothesis is that the oocytes of women with an unknown reason for infertility carry more mutations than those of fertile women. To study this, we mapped the complete mitochondrial DNA of both the oocytes and the granulosa cells surrounding the oocyte.

Project 29 – The origin of chromosomal abnormalities in human preimplantation embryos (eMOSAP)

AdV091 - LCE (BUN1432021000647, permit 24/11/2021)
FCE (permit 17/01/2022, completion date 16/01/2027)
Research material: 2a, 2e

After years of research on embryos obtained after IVF, we know that many (more than half) of them carry chromosomal abnormalities. After transfer in the womb most of the embryos with a chromosomal abnormality will not survive. Even after years of intensive research we still don't know what causes these abnormalities. This project aims to bring about change in this regard.

We are investigating why there are fewer chromosomal abnormalities in 5-day-old embryos than in 3-day-old embryos.
We investigate as well whether there are differences between the way the embryo eliminates abnormal cells in the inner cell mass (which will later on grow into the baby) and in the outer cells, or trophectoderm (which will grow into the placenta). To this end, we will use embryos that have been genetically tested and have already received a diagnosis of 'normal' or 'abnormal'. This approach will lead to us being able to predict with greater certainty than before, which embryo will grow into a healthy baby and which will not.

The research also examines whether or not the method of biopsy for genetic testing affects the embryo. Two different biopsy methods that are currently used in the IVF laboratory are compared. On the one hand, we investigate whether the cells in the biopsy sample remain in good condition (DNA intact) for genetic diagnosis. On the other hand, we are investigating the effect on the rest of the embryo after biopsy. This will help us to determine the biopsy method that is most promising.

W20-E

INFORMATION ON THE USE OF GAMETES AND EMBRYOS FOR TRAINING PURPOSES AND SCIENTIFIC RESEARCH

DOMAIN D – EMBRYONIC STEM CELL RESEARCH

A human embryo of about five days old (the blastocyst) contains unique stem cells that, under certain conditions, can develop into any type of cell in the human body, such as nerve cells, muscle cells, blood cells, oocytes (oocyte cells) and sperm.
This research wants to investigate whether these stem cells can be used in the future to replace damaged cells in diseases such as Parkinson's, heart failure and diabetes.

DOMAIN E – GENOME MODIFICATION

The aim of this research is to determine whether it is possible to modify the DNA of a human embryo safely and efficiently. This can be useful for two reasons:

- To avoid serious diseases by correcting the gene responsible for the disease.
- To conduct scientific research on genes that play a crucial role in early embryonic development. We do this by eliminating them and studying their effects on embryonic development.

Project 31 – Exploring the first lineage segregation in the human embryo: is GATA3 the gatekeeper of trophectoderm differentiation? (FWOGATA3_CRISPR/Cas9_WP2)

Adv096 - LCE (BUN 1432021000526, permit 26/04/2023)
FCE (permit 12/06/2023, completion date 12/06/2028)
Research material: 1a, 1b, 1c, 1d, 1g

Project 31 involves scientific research, which aims to gain a better understanding on the function of the genes that play a crucial role in the first five days of human preimplantation embryo development when two cell types appear in the embryo: (1) the inner cells, called the inner cell mass (which will grow into the proper embryo and later on the baby), and (2) the outer layer of cells or trophectoderm (which plays a major role in the implantation process). Malfunction of these genes is often associated with poor embryo development, but the underlying mechanisms remain unknown. Our aim is to identify these mechanisms by characterizing the function of specific genes including GATA3, which is a major regulator in trophectoderm formation.
In our research, we will use oocytes and sperm released for research to create embryos using the ICSI procedure. During the ICSI procedure, molecular biology tools (CRISPR/Cas9) will be introduced inside the embryo. These tools are able to modify the DNA sequence in order to inactivate specific genes; we aim to modify genes that play a key role during preimplantation embryo development. Following inactivation of a gene, we will characterize its function by studying subsequent effects in embryo development and by performing genetic analysis and immunostainings. Embryos carrying modified genes are never used for Medically Assisted Reproduction or transferred back in the uterus; they are destroyed by the research.