The Czech – Norwegian Research Programme aims to enhance basic and applied research and cooperation between the partner scientific institutions by bilateral financial support. The programme operator in the Czech Republic is the Technology Agency of the Czech Republic (TACR), the donor programme partner in Norway is the Research Council of Norway.

Laboratory of the Biology and Pathology of the Eye, Institute of Biology and Medical Genetics, First Faculty of Medicine, Charles University and General University Hospital in Prague, obtained financial support from the Czech – Norwegian Research Programme for the project:

The establishment of advanced cell therapy for the treatment of limbal stem cell deficiency in the Czech Republic.

Project ID: TO01000099

Acronym: EYEFORTX-2

Duration: 01/2021 – 04/2024

Project Partners:

- Laboratory of the Biology and Pathology of the Eye, Institute of Biology and Medical Genetics, First Faculty of Medicine, Charles University and General University Hospital in Prague, Prof. Katerina Jirsova, PhD.
- Department of Ophthalmology, University Hospital Kralovske Vinohrady, Prague, Assoc. Prof. Pavel Studený, MD. Ph.D.
- Institute of Macromolecular Chemistry, Czech Academy of Sciences (IMC), Prague, Ing. Hana Studenovská Ph.D.
- The Norwegian Institute of Air Research, Prof. Dr. Mária Dušinská, Ph.D.
- Oslo University, Catherine Jackson Ph.D.

The overall project objective:

Limbal stem cell deficiency (LSCD) affects 3.3 out of 100,000 people in the EU (about 350-500 in the Czech Republic) and is often leading to a total blindness. The mechanism of the disease, which can be triggered by injury, such as chemical or thermal burn or have genetic etiology is shown in **Fig. 1.**

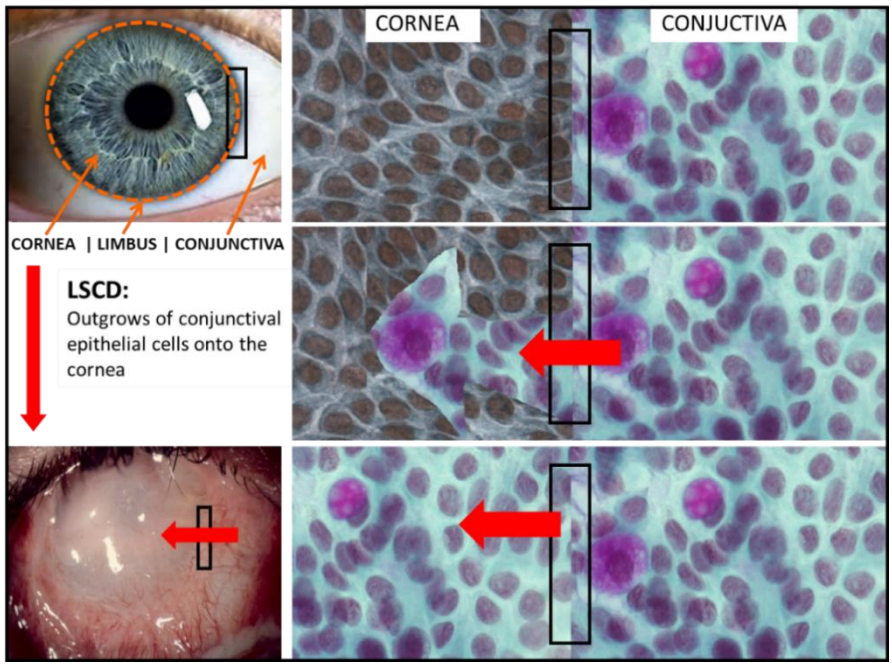

Figure 1. Limbal stem cell deficiency: Conjunctival epithelium extends over corneal surface (red arrows). Such condition originates as a result of progressive depletion or dysfunction of limbal stem cell population and leads to significant loss of vision or blindness.

Our aim is to restore the vision of patients suffering from both unilateral and bilateral forms of the disease. The treatment consists of replacing limbal tissue with the stem cells for the corneal epithelium. Only the presence of stem cells at the limbus can permanently assure a normal homeostasis, i.e. a transparent cornea, over which the opaque vascularized conjunctiva does not overgrow. The principle is schematized in **Fig 2.**

Developing cell-based therapy, i.e. the **Advanced Therapy Medicinal Products (ATMP)** with the presence of stem cells, requires a considerable funding, experienced top team, facilities such as tissue establishment and clean rooms, a top-quality equipped eye clinic, and rapid transfer of new technology into practice. Any delay in the chain: basic research -> applied research -> product development and approval -> clinical application increases the probability of ending up with obsolete experimentally developed treatments.

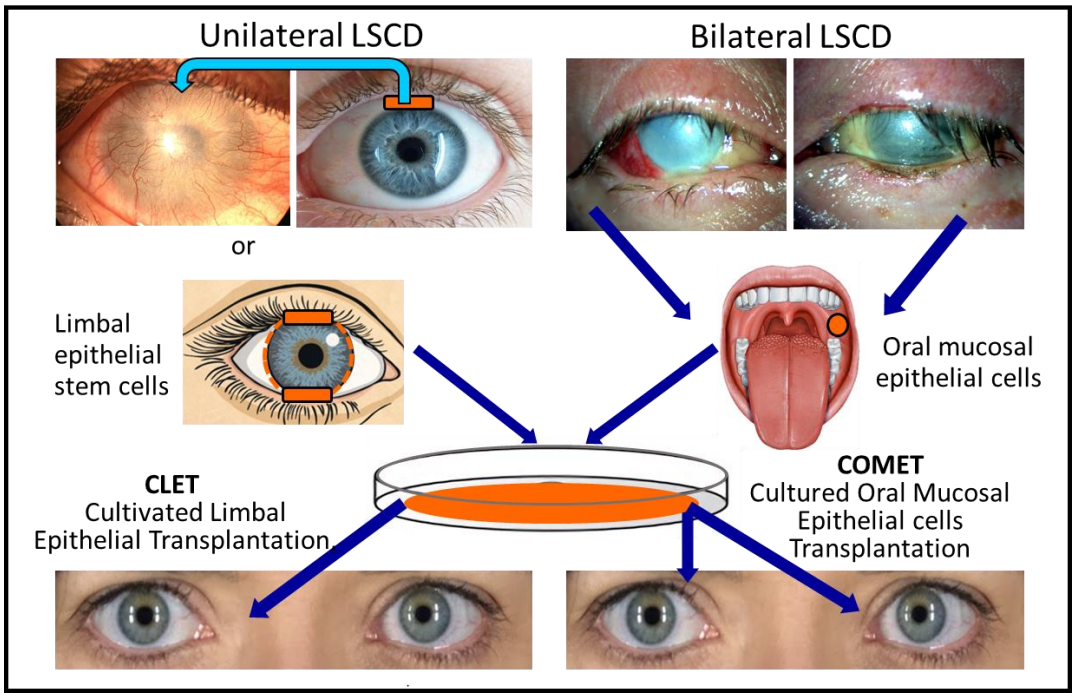

Figure 2. Treatment options for unilateral and bilateral limbal stem cell deficiency (LSCD). In **unilateral LSCD**, there is the option for direct transplantation of limbal tissue (blue arrow), retrieved from the paired healthy eye (risk and disadvantage of causing LSCD), or from a living-related donor (need for immunosuppression). Another possibility is the Cultivated Limbal Epithelial Transplantation (CLET)**,** a retrieval of a very small piece of limbus from the healthy patients' eye and its *ex vivo* culture to produce a cell sheet which will be used for grafting. In **bilateral LSCD**, there are no autologous LECs to retrieve and an one option is to retrieve and culture Oral Mucosal Epithelial Cells (OMECs) ex vivo, and then to transplant them onto corneal surface (cultivated oral mucosal epithelial transplantation, COMET). Alternatively, other autologous stem cells, e.g. hair follicle bulge-derived cells, can be used for such procedure.

The major goal of the project is to speed up the development of ATMP as much as possible and to start with treatment of unilateral and bilateral. One of the prerequisites for this rapid pace is the continuity of the results already obtained and the previous cooperation of the partners of the entire project team. This proposal is a direct continuation of the 'EYEFORTX-2' project, which has received an 'excellent' evaluation and whose results will be partly used in this project. The majority (65%) of innovation is already available from the latest call from Norwegian grants and follow-up work; some of the results have been further improved and, together with the newly acquired results, will be transferred to the preclinical (tissue facility – eye and tissue bank Kralovske Vinohrady University Hospital) and clinical practice (transplantation ophthalmological department of Kralovske Vinohrady University Hospital).

Research Team:

Our team consists of:

1) **scientists** (**cell and molecular biologists from CUNI (K. Jirova, V. Cabral) and OU**; scientists responsible for vitrification and long term storage of cells – **J. Bednar, CUNI**; scientists responsible for genome stability testing – **NILU (M. Dusinska, N. El Yamani, H. Fjeldstad)**; scientists responsible for new material for cell cultivation and their transfer into a diseased eye **(H. Studenovska**).

2) **pre-clinicians** (tissue and cell bankers, **K. Jirsova, M. Netukova**, and one ATMP banker/manager, planned to be hired)

3) **experienced clinicians M. Netukova and P. Studeny from KVUH**. The pre-clinicians and clinicians, together with the scientists, will be responsible for developing a procedure for applying cultured cells to the eye surface, selecting patients for treatment, ATMP transplantation, screening, and follow-up. They will also be responsible for the analysis and subsequent publication of the study results. The core team includes women (four out of five partners) and is relatively young. The team will include young scientists, namely Ph.D. student (2nd year) Victor Cabral MD, specializing in cell biology and pathology, and a second young scientist, a postdoctoral student, with a specialization in cell and molecular biology, will be employed in the near future. The team also includes other experienced scientists, lab technicians and administrators.

4) Cooperation with **CJ. Jackson, Oslo University** will also lead to the transfer of experience with cultivation methods, preparation and storage procedures that would have to undergo long-term development without such cooperation.

Contacts:

Principal Investigator: Katerina Jirsova, PhD., katerina.jirsova@lf1.cuni.cz, tel: 0022496 8006

Project Administrator: Kristyna Matejkova, DiS. kristyna.matejkova@lf1.cuni.cz, 0022496 4264

Links:

KAPPA funding programme for applied research, experimental development and innovation:

https://www.tacr.cz/en/kappa-programme

Project Promoter: www.cuni.cz

Project Information: https://starfos.tacr.cz/en/project/TO01000099#project-main