Company profile

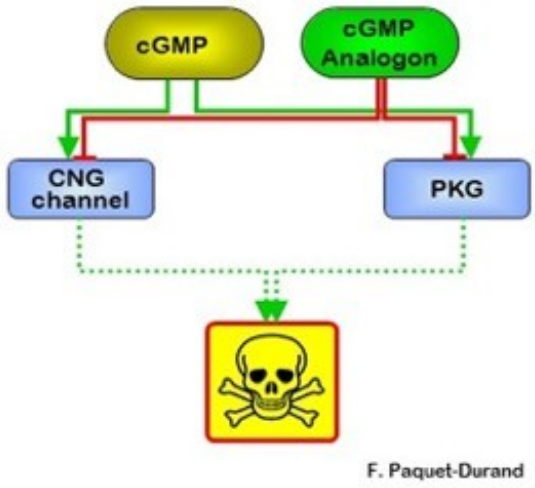
Mireca: a new drug for stopping the progression of eye diseases

A team of researchers from several EU countries has developed a new drug that stops the progression of hereditary retinal diseases. The project partners founded a company called Mireca Medicines GmbH in the city of Tübingen to bring the drug to market.

Prof. Dr. François Paquet-Durand (left), CSO, and Barbara Brunnhuber (right), CEO, are in charge of the company's destiny.

The awards speak for themselves: just a few days after its foundation, Mireca Medicines GmbH received the German BioRegions' Innovation Award. This was in April 2017, and in July the company was awarded first prize in the BioRegio STERN Management GmbH Science2Start idea competition. The reason for Mireca's clean sweep is the company's extraordinary potential. Biomedical research findings are rarely as unequivocal as those obtained by Mireca that can immediately be used therapeutically. The basis of this success is long-term research work mainly carried out at the Institute for Ophthalmic Research at the University Hospital of Tübingen. Prof. Dr. François Paquet-Durand has been studying retinitis pigmentosa (RP) for around ten years. RP is a

hereditary retinal disease characterised by the gradual death of the photoreceptor cells in the retina, leading to complete blindness in those affected.



The mechanism of action of cGMP (green arrows) in the photoreceptors can be stopped by an inhibitory analogue (red) – Mireca's drug is based on this mechanism. (CNGC = cyclic nucleotide gated channel, PKG = protein kinase G).
© François Paquet-Durand

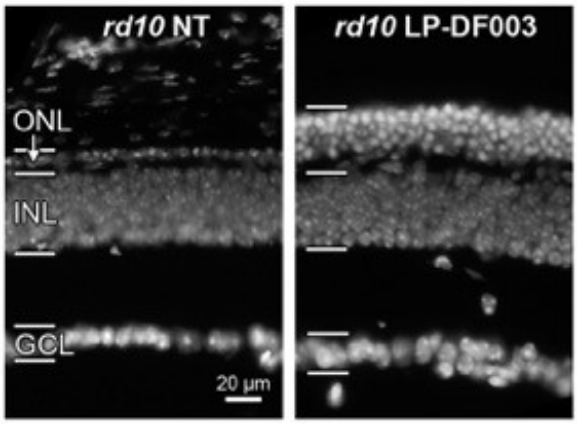
As part of a research project called DRUGSFORD (short for "Drugs for Retina Degeneration"), which was funded by the EU between 2012 and 2016, Prof. Paquet-Durand and his project partners found that the cellular signalling molecule cGMP (cyclic guanosine monophosphate) was a promising target for treating retinal degeneration. This was based on the knowledge that a broad range of mutations in various genes lead to an excessive supply of cGMP in the photoreceptor cells. A mechanism that has not yet been fully elucidated causes photoreceptor cells to die. The researchers came up with the idea of counteracting this using a therapeutic substance in the form of a cGMP analogue that binds to the same molecule (protein kinase G, PKG; and cyclic nucleotide gated channel, CNGC) as cGMP. However, this substance impedes the metabolic pathways and, as a consequence, prevents the death of retinal cells.

The search for a suitable analogue was rather like looking for the proverbial needle in a haystack and was the first of several hurdles the project had to overcome. Paquet-Durand explains: "We used a three-stage system to search for substances that have the ability to interfere with PKG or CNGC and prevent the death of the photoreceptors. A Bremen-based company called BIOLOG Life Science Institute Forschungslabor und Biochemica-Vertrieb GmbH tested a variety of substances for their ability to bind to PKG. Promising substances were then sent to the University of Modena in Italy where other partners tested whether the substances could prevent the death of cells in cell cultures resembling photoreceptor cells. The researchers identified 15 promising substances that were then sent to partners at the University of Lund in Sweden who used organotypical retina explant cultures to confirm that the substances did in fact prevent cell death."

Blood-retinal barrier – drugs used for treating retinal diseases must be able to pass this barrier

The successful API (active pharmaceutical ingredient) candidates from these tests were the starting point for another hurdle that had to be overcome. The challenge was to find a way to deliver the drug to the retina where it exerts its effect. Using drugs in this area is not easy, as the

retina is shielded by the blood-retinal barrier which is impermeable to many molecules. This is where a Dutch project partner, 2-BBB Medicines BV from Leiden, came into play. The company, which specialises in the development of molecular drug delivery systems, packed suitable substances into liposomes that are able to overcome the blood-retinal barrier. "This was not easy to achieve. There are around a dozen factors such as molecule size and structure, the number of charges and lipophilicity that need to be taken into account," says Prof. Paquet-Durant. In the end, five substances were tested at the Institute for Ophthalmic Research at the University Hospital of Tübingen for their ability to stop photoreceptor cells dying in vivo as well. One substance turned out to be particularly effective and was developed further. A company called SP Process Development AB from the Swedish city of Södertälje was another partner in the DRUGSFORD project and, together with BIOLOG, went on to develop a GMP drug development process.



Cross-section through untreated (NT) and treated mouse retinas. Significantly more photoreceptors survive in treated than in untreated retinas. ONL = outer nuclear layer (i.e. photoreceptor layer), INL = inner nuclear layer, GCL = ganglion cell layer.
© François Paquet-Durand

Towards the end of the EU-funded project, all the partners were delighted with how the cooperation had gone and with the success achieved and agreed to continue working together on further developing the treatment. "We had such good data that all the project partners agreed to establish a company in order to test the drug in a clinical trial and eventually place it on the market. All the project partners are now shareholders of Mireca Medicines GmbH and all results and related patents have been transferred to the company. In the coming years, Mireca will prepare the market launch of the drug," says Paquet-Durant, CSO of Mireca. Barbara Brunnhuber, who became aware of the DRUGSFORD project and the planned start-up company through personal contacts at an industry meeting, was brought on board as the company's CEO. Brunnhuber helped drive forward the establishment of Mireca Medicines GmbH and accompanies the transfer of the research results to industry with her concentrated skills as a chemist, engineer, business economist and consultant. Peter Rall from the "Senioren der Wirtschaft" working group is now the business administrator for the young company. "The original plan was that Peter Rall would only provide support in the founding phase, but because the cooperation worked out so well, he is continuing to provide administrative support," says Paquet-Durand.

Manpower: the entire team from the research project is now involved with Mireca

"We hope to be able to place the drug on the market within the next eight to ten years. This would be relatively quick and this is partly due to the fact that our drug and its use for the treatment of

retinitis pigmentosa is eligible for a European Medicines Agency (EMA) process that facilitates the development and authorisation of medicines for rare diseases (orphan medicines). As early as 2015, the project team obtained organ drug designation status for the drug under development," says Brunnhuber. The team prepared a clinical trial protocol, which has already been reviewed and accepted by the EMA. The clinical trials will be carried out at the University Eye Hospital in Tübingen. The team has already tested the drug candidate under GLP (good laboratory practice)-like conditions, which are cheaper and less complex than the real thing, and sufficient for this phase of development. The next stage includes the preclinical testing of the drug under real GLP conditions. At present, the Mireca team is working on sourcing funds for the next development and testing stages, and is in contact with potential investors. "We hope to conclude the first round of financing in the near future, and will immediately start pharmaceutical development," says Brunnhuber. Paquet-Durant is already thinking about another research venture: "At the same time, we will explore whether and how we can use our patents to develop APIs for other retinal diseases."

Article

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Further information

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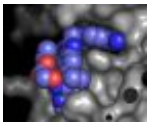

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