At the beginning of next year, the first cell transplants for Parkinson’s disease are carried out in over a decade, anywhere in Europe. Scientists from around the globe will be closely following every step of the EU-financed TRANSEURO study. Many believe that the fate of cell therapy for Parkinson’s disease rests on the selected European scientists, including key personnel from Lund University, that are behind the TRANSEURO study.

On November 27th Bagadilico and Transneuro co-arrange a Parkinson Café that will take an in-depth look at the different stages of the study, from the bench to the bedside. Scientists integral to the implementation of Transneuro will talk about their experiences so far, and the future hopes that they tie to the project. From basic experimental research to clinical neurology and brain surgery, the invited speakers will give an inside view to the inner workings of the study.

The first years of the new millennium saw two disappointing American studies cast a long shadow over the entire field when many of the transplanted patients experienced serious side effects. In the wake of the failed U.S. trials it suddenly became a lot harder to motivate the pursuit of such an invasive therapy. Cell therapy for Parkinson’s disease appeared to have no future.

But what if these trials were designed to fail? Could perhaps more rigorous preparations, a more careful selection of patients and ten years of further development in this research area justify a new large-scale study? Bagadilico’s Anders Björklund and Roger Barker from Cambridge University thought so. Together they initiated a Europe-wide study that revisits past trials in an effort to develop safer and more efficient methods for neural transplants in Parkinson’s disease. The end result may shape the direction of Parkinson research in the 21st century.

LINE UP

Moderator - Göran Hermerén
Experimental scientist - Malin Parmar
Neurologist - Håkan Widnér
Brain surgeon - Stig Rehncrona

Sign up by e-mail to Jens.Persson@med.lu.se

**NEWS IN BRIEF**

**YOUNG INVESTIGATOR TALKS ON NOVEMBER 5th**

On November 5th, Luis Quintino, CNS Gene Therapy, will hold a talk in Segerfalksalen within the YIT scheme. See below for details on the seminar subject:

“Functional studies of resident microglia depend on the development of molecular tools allowing targeted genetic manipulations of this specific cell population. Endogenous microRNA (miRNA) can be exploited to achieve celltype specific expression of a transgene, by the incorporation of miRNA target sites in the transgene expression cassette. Here, we investigate if microRNA-9 (miR-9) regulated lentiviral vectors can be used to specifically target genetic modification to resident microglia in the rodent brain. Using a transgenic reporter mouse, we found that microglia lack miR-9 activity, while most other cells in the brain express miR-9. When we injected miR-9 regulated vectors into adult brain we found transgene expression specifically in cells with morphologies typical of ramified microglia. The majority of transgene expressing cells co-labelled with the microglia marker Iba1. Finally, we used this approach to visualise activation of resident microglia in an excitotoxic lesion model. In summary, the miR-9 regulated vectors described here is a straightforward and powerful tool that should have a broad use for functional studies of resident microglia.”

**NECTAR 2012 TAKES PLACE IN LUND**

The NECTAR (Network of European CNS Transplantation and Restoration) 2012 annual conference will take place at the AF Borgen in Lund, Sweden, on November 29th - 30th.

NECTAR was founded more than 20 years ago and celebrated its anniversary in 2010 in Freiburg at the 20th annual conference. NECTAR’s aim is to bring together European groups who share the common goal of protecting, repairing and restoring the central nervous system damaged through degenerative disease or injury. The main protagonists and now newer generations of scientists continue their research exploring cell transplantation and gene therapy as therapeutic strategies to improve the lives of patients with various neurological disorders.

To register for the conference, **CLICK HERE**

For details of the program, **CLICK HERE**

**CSRT RELEASES NEW BOOK - THE ATOMIZED BODY**

In December Bagadilico’s Cultural Research Team will release an anthology entitled *The Atomized Body - The Cultural Life of Stem Cells, Genes and Neurons*. The book release will be followed up by a workshop seminar in February. Date yet to be announced.

In *The Atomized Body* the authors examine the relations between culture, society and bioscientific research and show how our bodies’ singularized atoms indeed still are socially and culturally embedded. In today’s medicine, the biosciences are entangled with state power, commercialism, and cultural ideas and expectations, as well as with the hopes and fears of individuals. Therefore, biomedicine and biotechnology also reshape our perceptions of selfhood and life.
GENE THERAPY FOR PD

new study targets cell-specific delivery

During the past decade gene therapy has brought a lot of promise to the world of neuroscience. However, the fine-tuning of methods to achieve pinpoint delivery and desired genetic expression are still, for the most part, in a developmental phase. One challenge has been to carry the genetic material only to the specific cell that is targeted for therapeutic purposes. In a recent publication, Erika Elgstrand Wettergren and colleagues have shown that it is possible to develop disease relevant cell specific promoters, in essence keys to the genetic material inside the cell, that are highly specific for neurons and show a similar efficiency as conventionally used promoters.

The role of the promoter is not to direct the viral vector to the right cell or manage the entry into the cell body. This process is controlled by the protein envelop on the surface of the vector. Instead, the promoter is responsible for corresponding to the transcription factors inside the cell. When there is a match the process of expressing the therapeutic transgene can begin.

The much-used ubiquitous promoters, readable by every cell-type, are sometimes too blunt an instrument, expressing genes also in cells not necessarily intended for transcription. This can be corrected by expressing the transgene with better accuracy using cell-type specific promoters to, for example, target the neurons that are affected by the disease. The current study aims to develop such cell specific promoters for Parkinson’s disease.

Erika Elgstrand Wettergren believes that there has been a lack of evaluated cell specific promoters that are relevant for Parkinson’s disease.

- A vector system that is safe, specific and has an appropriate transgene expression level is needed to make gene therapy as beneficial as possible. The promoter plays an important role in these vector characteristics, but there is a lack of evaluated cell specific promoters for Parkinson’s disease.

The use of ubiquitous promoters that can be read by all cell-types may lead to certain problems for the patient. If the wrong gene ends up in the wrong cell it could cause serious side effects for the patient. The findings in the study now open up doors for other research groups to start new projects directed at developing new disease relevant cell specific promoters, not only for neurodegenerative diseases.

- I mean, this is a method study at basic research level. We want this technology to reach those who are working on Parkinson’s disease of course, but really it’s geared towards the entire field of gene therapy since the methods used in this study can be used to find promoters relevant for other diseases as well.
On this subject, staunch opponents or keen advocates are not hard to find. Often represented by people with strong convictions, beliefs that they would never give up, even if all arguments fail. But apart from those taking extreme positions, most people find themselves somewhere in between - on the one hand understanding the importance of research, on the other hand uncomfortable with animals being treated badly.

The most publicly accepted form of animal use in research is the scientific quest to understand, prevent or cure human disease. But already here we stumble upon a very important question - can animals actually predict human conditions? It is a simple, but important truth that “not all animals are humans, but all humans are animals”. From the outside, we may look very different but we should not forget that many fundamentals of life are shared in all living beings. Even our precious human DNA has 67% similarity to the DNA of such simple beings as earthworms. So even if (other) animals are not humans, they can be seen as human-like, at least in certain aspects. And this is precisely why we can use them as a “model”. The animal model is by definition never 100% the same as the “original, i.e. the human condition. Yet, it is representing the “original” in one or more critical features.

One of the main challenges for scientists concerned with brain-disorders is to investigate how “good” or “bad” their models are, the so-called validity of the models. A good animal model should, to a certain degree, imitate the human condition. If you investigate Parkinson’s disease, which shows clear motor symptoms in patients, you want to see at least some kind of motor deficit also in your animal models. And finally, a model needs to have a good “predictive validity” as well, meaning that a treatment that works in the human condition should be effective in the animal too. How well these criteria are met will vary from experiment to experiment, and a good scientist therefore tries to never depend on one model alone. This general blueprint for the functionality of animal models also suggests that they can always be improved through deeper investigation and understanding - not only concerning the disease to be modeled, but also pertaining to the biology of the animal that is used.

In fact, improving old models and developing better ones constitute a big part of work hours spent in biomedical laboratories today, especially for disorders of the human brain. We ourselves have been recruited to do our PhDs as part of a EU-network, Neuro-Model, that was funded by the European Comission to develop “model systems that translate to human pathology” of Parkinson’s and Huntington’s Disease (www.neuromodel.eu). Consisting of ten scientific partners, equally represented by academia and industry, this network has allowed us to understand the different needs for improved modeling of these diseases. We have learnt that research of fundamental brain function and dysfunction in disease demands different animal models than research aiming at improved treatments and therapies.

We, as many others working with animals, get asked quite often if it isn’t possible to replace animal models in research completely and use only computer models instead? The truth is: even though scientists foster progress in treating human diseases, we have only scratched the surface of what we need to learn in order to understand how the brain works. Much more information is needed before a realistic computer-model can be built, allowing us to study the brain. And it seems unlikely to happen in any foreseeable future – however it is not impossible. Until then, animal models remain the most valuable and promising tools in brain research.

Even if human brains are the most capable and complex objects to understand, we know that we use nothing less capable and complex to fulfill this task.