In a fresh report, a team of international scientists, including researchers from the University of Saskatchewan-Saskatoon, revealed an exciting discovery related to a new disease gene in Parkinson’s disease. Together with Saskatchewan Mennonite families the long-running study, presented during the 16th International Congress of Parkinson’s Disease and Movement Disorders in Dublin, Ireland, has identified an abnormal gene which leads to Parkinson’s disease.

“This discovery paves the way for further research to determine the nature of brain abnormalities which this gene defect produces,” says Dr. Ali Rajput, a renowned expert in Parkinson’s disease who has been working with the family in the study since 1983.

“It also promises to help us find ways to detect Parkinson’s disease early, and to develop drugs which will one day halt the progression of the disease.”

The study involved 13 of 57 members of one extended Saskatchewan family who had been diagnosed with Parkinson’s disease. Three other single cases from Saskatchewan and one family from British Columbia were also found to have the same mutation. All were of Mennonite background, a Christian group who share Dutch-German-Russian ancestry.

Rajput’s collection of more than 500 brains and nearly 2,200 blood samples from Parkinson’s patients has been key to the success of the study. The contributions of the Saskatchewan Mennonite family were also critical to see the laboursome study reach its conclusion.

“The whole-hearted and unselfish commitment of this family is remarkable,” Rajput said. “They went out of their way in every conceivable manner to help solve this mystery.”

The story is based on materials provided by the University of Saskatchewan.

BAGADILICO NEWS

MAY/JUNE, 2012

NEWS IN BRIEF

BAGADILICO PAPERS IN MEDIA SPOTLIGHT

A string of recently published Bagadilico papers have been widely quoted in media outlets in Sweden and abroad. Malin Parmar’s research group’s article, where they displayed a new technique that converts stem cells into brain cells, got a spread in the local newspaper Skånska dagbladet. Read a feature article on the study in this newsletter.

To read the article in Skånska Dagbladet, click here

Another study that turned heads worldwide reported on a new stem cell found in the brain. The cells were shown to be able to proliferate and form several different cell types - most importantly, new brain cells. Gesine Paul Visse and Patrik Brundin are two of the main researchers behind the study.

To read an article about the study in The Examiner, click here

A third study released, revealing new targets for cell transplantation in Parkinson’s disease, was led by Anders Björklund and Olle Lindvall.

To read an article about the report in Vetenskap & Hälsa, click here

BAGADILICO “PRION” STUDY JUST OUT

In a follow-up study to the report on prion-like spread of damaged proteins published last year, Bagadilico scientists present strong evidence for the case of an infection model explaining the spread of Parkinson’s disease in the brain.

Experiments in rat models uncover a process previously used to explain mad cow disease, in which misfolded proteins travel from sick to healthy cells.

“A major unmet medical need is a therapy that slows disease progression. We aim to better understand how Parkinson’s pathology progresses and thereby uncover novel molecular targets for disease-modifying treatments” explains Patrik Brundin, senior author of the study.

In the current study, published in the journal PLoS One, researchers were able to follow events in the recipient cell as it accepts the diseased protein. The experiments also show how the transferred proteins attract proteins in the host cell, leading to abnormal folding or “clumping” inside the cells.

This is a cellular process likely to lead to the disease process as Parkinson’s progresses, and it spreads to an increasing number of brain regions as the patient gets sicker” says Elodie Angot, lead author of the study and responsible for the revelatory rat model experiments

To read the article online, click here

THE ‘BIG’ QUESTION PUT TO SENIOR BAG SCIENTISTS

In a clip featured on the Bagadilico YouTube site some of our senior researchers ponder the future of Parkinson research in the future. Answering the question ‘What will Parkinson research achieve in your lifetime?’ they reflect on where the Parkinson puzzle is headed and what we might accomplish in the longer perspective.

To see the clip, click here.
Twenty years ago neuroscientists across the globe were in agreement, the adult brain could not produce new brain cells. In the early 90's this long-held theory was conclusively turned on its head opening up a promising research field soon to be coupled with great expectations. However, the differentiation process that sees neural stem cells develop into functioning brain cells is still, to a large extent, shrouded in darkness. In their efforts to pave way for new regenerative therapies scientists are working hard to break down this process, identifying what triggers and regulates each step of the journey towards the finished article, the fully integrated neuron. Bagadilico’s Johan Jakobsson may have stumbled upon an essential piece of the complicated puzzle.

In a new article, his research group reports on the key role played by microRNA in adult neurogenesis. In experiments with mice they have shown that a microRNA, playing an important role in gene regulation, is turned on when the stem cell begins its transformation towards brain cell. When turning off the microRNA the stem cell did not become a neuron, instead it developed into a glial cell, also known as a helper cell. Understanding the fine-tuning function of microRNA in adult neurogenesis will put us one step closer to unveiling one of the main mysteries of neuroscience.

To be specific, we are talking about miRNA-124, the small RNA molecule that Johan Jakobsson’s lab has been investigating for a few years. They have long suspected that miRNAs play an important role in gene expression but even they were perhaps a little bit surprised by the key role miRNA 124 seems to play in the birth of neurons in the adult brain.

- It seems like they are truly essential in adult neurogenesis, carrying some sort of switch-on mechanism at the very beginning of the process. Proof to this was exhibited when we turned off the miRNA and the stem cell developed into a glial cell instead. You could perhaps compare their role to your stereo amplifier. When you adjust the switch, even slightly, you get a completely dif-
Replacing lost cells

Scientists are still only scratching the surface when it comes to grasping the complex concept of adult neurogenesis. Upon hindsight, Johan Jakobsson hopes that mapping the role of miRNAs will be viewed as a major break in the case. The long-term prospects surrounding this discovery concerns the possibilities of creating or stimulating the birth of new neurons in culture dishes as well as inside the human brain. If successful this method could help replace lost brain cells in diseases such as Parkinson’s, Alzheimer’s and stroke.

- **In the longer** perspective, this is what we are hoping that the study will lead us towards. What it tells us already today is that it confirms the claim that miRNAs play very important roles in the cell. There has been a debate within the scientific community whether this is actually the case. This is one of several recent studies suggesting that they are essential in controlling gene transcription in the cell.

**The multi-purpose of miRNA**

The newsy part of the study is undoubtedly related to the possible future benefits within regenerative therapies. But the results also show promise within the general field of studying microRNAs. The complexity of the experiments has forced the team to develop new, highly technical, methods. These advanced techniques will be valuable also for studying the function of micro-RNAs on a broader scale.

- **These methods** can be used to study in which cells in the brain a specific micro-RNA is active. This will allow us to perform studies looking at their role also in memory and learning processes. Because microRNAs seem to be important not only in neurogenesis, but also for how neurons integrate and communicate in many parts of the brain.

**So, what do** these new pieces of the puzzle tell us. Are we one step closer to connecting all the dots? The answer is yes. And no. We now know more about the differentiation process but the revelations in this study at the same time suggest that it is more complicated than we originally thought. As science often goes, one answer poses several new questions.

To read the study, click here
From Stem Cell to Brain Cell - New Technique Mimics the Brain

A new technique that converts stem cells into brain cells has been developed by researchers at Lund University. The method is simpler, quicker and safer than previous research has shown and opens the door to a shorter route to clinical cell transplants. By adding two different molecules, the researchers have discovered a surprisingly simple way of starting the stem cells’ journey to become finished brain cells. The process mimics the brain’s natural development by releasing signals that are part of the normal development process. Experiments in animal models have shown that the cells quickly adapt in the brain and behave like normal brain cells.

“This technique allows us to fine-tune our steering of stem cells to different types of brain cells. Previous studies have not always used the signals that are activated during the brain’s normal development. This has caused the transplanted cells to develop tumours or function poorly in the brain”, says Agnete Kirkeby, one of the authors of the study.

Since the method effectively imitates the brain’s own processes, it reduces the risk of tumour formation, one of the most common obstacles in stem cell research. The quick, simple technique makes the cells mature faster, which both makes the transplant safer and helps the cells integrate better into the brain. The results of the study bring stem cell research closer to transplant trials in the human brain.

“We have used the new protocol to make dopamine neurons, the type of neuron that is affected by Parkinson’s disease, and for the first time, we are seriously talking about these cells as being good enough to move forward for transplantation in patients. The next step is to test the process on a larger scale and to carry out more pre-clinical safety tests”, explains Malin Parmar, research team leader.

The research is presented in the report ‘Generation of regionally specified neural progenitors and functional neurons from human embryonic stem cells under defined conditions’ in the journal Cell Reports.

The study has been conducted as part of the EU 7th Framework Programme project NeuroStem-cell.

To read the study, click here