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Infrastructure, education and innovation remain the main goals for MultiPark. The focus is, as always, on infrastructure that can be jointly used in our environment. Here we continue to build bridges with BAGADILICO for joint programs. We will continue with our popular noontime conferences coordinated by Tomas Deierborg and from 2016 also co-organize the ‘Frontiers in Neuroscience’ seminars previously organized by BAGADILICO alone. A new effort will be to start a neuroscience program for biomedicine masters students as well as 10th semester medical students. Another effort in education is to try to join the FENS graduate schools in neuroscience.

In innovation, the earmarked funding for an innovation officer were withdrawn by the university for 2016, but given the work by prof. Tadeusz Wieloch and others on innovation initiatives, MultiPark plans to support continued efforts that have grown out of the SIA application, while also keep an active local innovation group.

Some of the other budget items include an open call to support mid-level faculty without a fixed position, to allow for dedicated PET-scanner time for clinical research, to offer travel grants and to provide potential emergency funding for the TRANSEURO clinical trial. The experimental budget also sets aside some co-funding for our future senior MultiParkers, the PhD students.

MP EDITORIAL by Gunnar Gouras - With the new budget for 2016 in place, MultiPark continues to aim towards creating an environment in which cutting-edge progress can be made in Lund on the major neurodegenerative diseases of aging. The budget was divided among the major areas of experimental, clinical and health science research based roughly on the numbers of researchers in these areas. The board, with four external academics (Karina Fog, Carolina Graff, Davide Brooks and Håkan Billig), as well as one representative each from the faculty (Arne Lindgren) and SUS (Ingemar Peterson) has been increasingly active in the decision process. We thank them for their commitment. Input from our non-voting board members Johan Jakobsson (BAGADILICO) and Susanne Lindvall (Parkinsonsfonden), as well as our student representatives (Martina Svensson and Michael Jewett) are also highly appreciated.
You know, my view from the office is the same it was over ten years ago. It’s this concrete wall, which doesn’t offer much in the way of scenery. And it’s still grey. I wish they would have painted it white, he says jokingly, even though it’s quite clear that white would have been the better choice.

But now, at least I have my own office. I’m actually starting to like it very much, as it does not offer much distraction, it allows me to better concentrate on my grant writing, and design projects.

When he arrived here in 2002 he didn’t know quite what to expect, but what he had was motivation. Sweden and Lund was unchartered territory but he would soon settle in under the tutelage of Jia-Yi Li and Patrik Brundin. After a couple of years, with a PhD under his belt, it was once again time to spread his wings. This time with a small family as he had met his wife to be, Emma, at the university. Next stop, New York City.

Again I felt I needed to push myself, to discover new things, get additional skills, to develop further really. From a research perspective, I wanted to continue with stem cell research, but wanted to know more about the recent reprogramming discovery made by Nobel price winner Prof. Yamanaka. His discovery on reprogramming somatic cells into pluripotent stem cells enables unlimited access to cells that are affected in the brain, and model the disease in a dish. At that time there were only a few labs in the world working on this, and Project ALS Jenifer Estess Laboratory for Stem Cell Research was one of them. This laboratory was unique as it was completely privately funded. So, I wrote a grant application to the Swedish Brain Foundation and I got it. This grant contributed to my first year of studies in the Big Apple.

It is not without a hint of nostalgia that Laurent speaks about his time in the metropolis that is New York. With an apartment situated on 113th street, just northwest of Central Park, he fondly remembers weekends with his family in the green oasis, away from the hustle and bustle of Manhattan’s unrivaled tempo.

Of course, life with small children in a hectic city, combined with an ambition to deliver in a new, competitive
work environment is no small task.

- Many nights, perhaps too many, Emma and I would put the kids to bed and then I would take the subway back to the medical campus on 168th street to continue working. And then, if you missed the last subway at two in the morning you would have to wait until 5 am for the next one. These were long tiresome nights, but also very rewarding. One of my best memories from work at that time is actually watching the sun rise behind the New York skyline from inside the cell lab, with my very best friend Nuno, who often times had also missed the sub, during those early morning hours.

- I believe this was really one of the best places I could be to do the research that I was interested in, and I will never be thankful enough to Profs. Chris Henderson and Hynek Wichterle, as well as the Estess sisters Valerie and Meredith, for their constant mentoring and support. I felt privileged to find myself there, like I felt privileged to do my PhD with Jia-Yi and Patrik.

After a few years in the U.S. a new opportunity came knocking. A position where he would be able to start his own research group was announced at Lund University and Laurent jumped on the chance. The position was that of junior group leader at MultiPark. This was a chance to define his own research lines for the future. With a Swedish wife and children fast approaching the school-age it also seemed like a sensible choice from a family perspective.

- Since I came back here I wanted to work with iPSC-technology and develop human models that would allow me to better understand brain diseases. It has been painstaking work during these 4 years, trying to get our models done, but now it is done, thanks to all the lab members. “Make your models first, it will be stressful and difficult, but once they’re there, they will be a great resource and you will be able to deploy exciting projects”, I was told many times.

- Now we have started many collaborations and begun to produce publications which will be beneficial to the environment. Today, everything is indeed in place and we need to recruit. The projects are there, and so are the tools and the collaborators.

Laurent doesn’t view his new title as badge of honor. More so, it’s to be viewed as a door opener and a natural next step allowing him to move forward in his career, and employ additional PhD-students to join his research group. Also, it lends some weight to future grant applications, and further career opportunities. Being an associate professor also involves many more responsibilities, which he is not taking lightly.

When asked if there has been a party to celebrate his appointment he offers a look of bewilderment. The thought hadn’t yet crossed his mind.

- Perhaps we should. It’s just been work, work, work. But you know, seeing the members of the lab succeed in their work is a true reward in itself.
What initially sparked your interest in medicine and science?

- I started hanging with the wrong crowd in high school. We went to public lectures with scientists from Lund who came and gave talks in Halmstad where I grew up. I became interested in astronomy. I spent long cold nights in the middle of a field with a telescope that I borrowed from school, counting the moons of Jupiter.

What was your inspiration for becoming an MD and a scientist in matters concerning the human brain?

- In high school I read a lot of popular science books. Tor Nørretranders “Märk världen” was important. Discussions with friends about the mind inspired me a lot. After high school I took a few semesters of math and history before I realized that medical school could be a great mix of science and humanities.

Why Alzheimer’s disease in particular?

- Alzheimer’s is a melting pot of unmet social, medical and scientific problems. But my first projects were on other diseases. I did some work on multiple sclerosis and inborn errors of metabolism. And I still find the continuum between neurodegenerative diseases very interesting and important.

Do you have any role models, inside or outside the research community, that have inspired you to get where you are today?

- My PhD and postdoc advisors have all been very inspiring, although they have had quite different styles. I also want to mention the Swedish 18th century researcher Peter Forsskål. He was a senior scientist on a Danish expedition to the middle east, one of the grandest and most expensive Scandinavian research projects ever, described in the book “Det Lyckliga Arabien” by Thorkild Hansen. They were delayed for weeks because of a storm which kept pushing them back into Helsingör. Forsskål barely noticed and immediately started doing a catalogue on Danish seaweed and molluscs. I just can’t stop thinking about that.

Last year, you received an award from the Swedish queen. How was that experience and what did it mean to you?

- It was a true honor for me to be the first recipient of this new price. It provided funding for my projects and the queen seemed very interested in our work.

Before Lund you did your postdoc in the US at the University of California. What initially brought you there and how was it to work at a top American university?

- I had been to San Francisco a few years earlier on holiday and loved the city. So when the opportunity...
came to spend a few years there with funding from Vetenskapsrådet it was an easy decision. I had great liberty at UCSF to explore topics that I found interesting.

Could you share some highlights from your time in the U.S., professional and personal?

- The professional highlights were the interactions and conversations with several key researchers in my field, which have changed my way of thinking about Alzheimer’s disease in important ways. Personally I made several close friends. I loved to explore the nature in Northern California. And I now understand baseball.

What was the key in bringing you to Lund university?

- The opportunity to combine clinical work and research at an advanced level.

What has been your main research lines to date and what projects are you focusing on going forward?

- My key research lines have been the use of biomarkers, initially only biofluid markers but since my postdoc also different neuroimaging markers, to study early clinical stages of Alzheimer’s disease. My main focus for the future is to develop methods and create studies to explore the very initial development of Alzheimer’s disease in humans, with a focus on the interaction between different types of pathologies, i.e. amyloid and tau and the downstream effects of these pathologies on brain structure and function.

Where do you see yourself and the field of AZ research in ten years?

- We all hope that there will be treatments available that may provide some disease-modifying effect. Such treatments will not only change clinical practice but may also give us a better understanding of the contributions and interactions of all the different players in the neuro-pathology. We will need to define how to optimally use such treatments for primary or secondary prevention. And how to use them in very old people, which will be the majority of the patients, and whose neuropathology may be quite diverse and complicated. Rapid development of novel biomarker technologies will allow us to study more and more of the different aspects of AD in vivo in humans.

Besides from research, what are your other passions?

- I still read a lot outside of work, both fiction and popular science. I love to travel. My wife and I took three months off between US and Lund, and travelled in South America, which was amazing. More recently I have become involved as a volunteer helping immigrants with their Swedish homework, it has been interesting and rewarding.

Tell me a surprising fact about yourself that most people might not be aware of.

- A few years back I did some acting with an amateur theater company. Our director was dead serious, and had written this play about terrorism, refugees and existentialism etcetera. My character had a very complicated name, none of the other actors ever learnt how to say it properly. I was dressed all in white and I was essentially the devil.
INCREASED CHANCES FOR EARLY DETECTION OF ALZHEIMER’S DISEASE

BY BJÖRN MARTINSSON - A method for detecting early signs of Alzheimer’s disease using amyloid PET imaging works as well as the previously used cerebrospinal fluid sample method. This is the conclusion of a new Lund University study — the most thorough and extensive undertaken in the field so far.

The most commonly used tools for investigating early signs of Alzheimer’s disease in Swedish public healthcare are various cognitive memory tests and computed tomography. For several years it has also been possible to carry out an analysis of a cerebrospinal fluid sample which increases the chances of early detection. So far, however, only patients in memory clinics have been offered the test.

Recently, a method known as amyloid PET was approved for clinical use in Sweden. A special substance which binds to a protein in the brain, beta-amyloid, is administered to the patient. This amyloid is a marker for Alzheimer’s changes, which are then mapped with PET imaging.

Opinions have long been divided as to whether cerebrospinal fluid samples or PET imaging are the best tools for detecting early-stage Alzheimer’s disease.

“In the study, both the cerebrospinal fluid sample and the amyloid PET scans were able to identify approximately 90 per cent of the patients who would be diagnosed with Alzheimer’s later on. Our conclusion is therefore that the two methods work equally well to achieve this aim. One can thus choose the method on the basis of cost, expertise or patient preference,” says Sebastian Palmqvist, MD, PhD, at Lund University.

Both methods are also good at identifying which individuals are healthy and unlikely to develop Alzheimer’s disease within the next ten years. However, when the diagnosis is reached without reference to a cerebrospinal fluid sample or amyloid PET imaging, its accuracy can drop to 60-70 per cent.

Late detection of Alzheimer’s disease is not only a problem for today’s healthcare, but also for the development of future treatments.

“Previous drug trials to evaluate new treatments for the presence of amyloid in Alzheimer’s cases failed, partly because treatment began too late in the course of the disease. With two accurate tools for early diagnosis, we can identify suitable participants at an early stage of Alzheimer’s disease. This will considerably increase the chances of being able to prove a positive effect for new drugs,” concludes Oskar Hansson, associate professor and neurologist at Lund University.

The research data originates from the Swedish BioFINDER study. 122 healthy elderly participants and 34 patients with mild cognitive impairment who developed Alzheimer’s disease within three years were investigated in the article. The study was then repeated in an American population group of 210 individuals. The new findings are presented in the American journal Neurology.
What initiates the accumulation and the spread of toxic alpha-synuclein is still very much up for debate. It has previously been reported that in MSA pathology, toxic clumps of alpha-synuclein are found in oligodendrocytes, whereas in PD they accumulate in neurons. The prevailing theory to date on how toxic alpha-synuclein spreads in PD is through a virus-like cell-to-cell transfer, from neuron to neuron. How it accumulates in MSA pathology, in oligodendrocytes, we still don’t know. The current study, published in the journal Stem Cell Reports, might offer a clue. Mehdi Djelloul, first author of the study, and colleagues show here that alpha-synuclein is endogenously produced in the early development of oligodendrocytes.

We wanted to see if oligodendrocytes themselves could offer an alternative, or complementary explanation to alpha-synuclein pathology, beyond the theory of cell-to-cell transfer. Could the alpha-synuclein have an autonomous origin within these cells? It seems that they may. However, our experiments also show that once matured, the oligodendrocytes stop producing alpha-synuclein. So, the next step for us will be to see whether we can shed further light on if, and how, oligodendrocytes play an active part in driving disease progression, says Laurent Roybon, research team leader.

Within the study a range of different disease models has been produced. Of particular interest are the ones developed through iPSC-technology, a method where mature human cells, skin cells for example, are reprogrammed back to the stem cell stage and then further guided towards becoming brain cells, replicating the ones found in a person suffering from a particular disease. These models can now be used to further study the role of alpha-synuclein in MSA and PD.
In short, which were the main subjects addressed during the café?

- The overarching themes were the person-centered perspective and prioritized areas for the evaluation of treatment, from the perspective of people with PD and health care professionals. We focused on particularly on the areas considered highly prioritized according to various studies (our own and others). These are quality of life, walking ability, mobility, sleep, fatigue, depression, fluctuations and ability to perform daily activities.

You both speak about highlighting the patient perspective through various assessment instruments. Are we seeing a trend in outcomes research to focus more on the patient’s individual experience?

- There is a clear international trend of involving patients in research in different ways in order to make the research and research results more relevant to the people that they primarily concern. This relates both to what the research concerns and how to evaluate the results of clinical trials. The latter has been found to be one of the ten top-priority research areas - along with finding better therapies relating to sleep problems, balance, and mobility - among people with PD, according to a recent large British study. The experience and knowledge of patients are important for understanding the consequences of living with a progressive disease. It is therefore vitally important that patients are involved in the processes of treatment and evaluation. If the evaluation instruments are based on what is relevant and important to patients, better treatment methods will follow.

Why is it important to communicate your research results in a direct dialogue with people with PD?

- It was very important for us to present our results. First and foremost, it was a way for us to give feedback to the participants in our previous studies, and thus thank so many of them who have given us a lot of knowledge through sharing their experiences. We wanted to show what we had arrived at and how our results can hopefully benefit people with PD. In addition, the discussions gave us an added perspective that is of value for our continued work. Judging by the spontaneous reactions and comments during the seminar it seemed that we were also able to offer something to the participants.

- All in all, it was valuable to get feedback directly from the people who participated in the café and the concluding Q & A was both interesting and rewarding. The discussion itself was also a sign that there is a great belief and confidence among patients and relatives that the research will lead to new, effective treatments. Our participants were very well informed and engaged, and this is something we believe is important for the continued development of productive research.

Did you get any specific feedback from the café participants?

- Yes, we received very nice feedback after our presentations. There were several who could identify with the results of the different studies. Especially when we explained the importance and meaning of walking ability, there were several who could identify with the outcomes presented in the study. They believed that it correctly reflected the lived experience of their daily lives and that we also had managed identified their emotional reactions to these situations.
NANOWIRES OFFER HOPE OF IMPROVED BRAIN- AND RETINA IMPLANTS

Neurons thrive and grow on a new type of nanowire plate developed by researchers in nanophysics and ophthalmology (eye diseases). The results suggest that future brain- and retina implants could become more effective and also reduce risk that they lose their effectiveness over time, which is a problem today. The findings are published in the Journal ACS Applied Materials & Interfaces.

By implanting electrodes in brain tissue, it is possible to stimulate and capture signals from different areas of the brain. These kinds of brain implants, or neuro-prostheses as they are sometimes called, are used in Parkinson’s disease and other neurological diseases. Tests are ongoing in other areas, such as depression, severe cases of autism, obsessive-compulsive disorder and paralysis. Another research line pursued is for retina implants to be able to replace the light-sensitive cells that die in retinitis pigmentosa, and other eye diseases.

Today’s electrodes, however, are cumbersome. One problem is that the body interprets the implants as foreign objects which leads to the electrodes being encapsulated and the signals becoming weak.

- The finesse of our nanowire structure is that the group of cells, glial cells, which tend to encapsulate the electrodes do not do this here, says Christelle Prinz, a scientist of nano physics who developed the technique together with Maria Thereza Perez, a scientist in ophthalmology.

- I am very pleasantly surprised by these results. In previous lab studies conducted, glial cells usually become attached to the electrodes, she says, adding that tests so far only have been made with cultured cells (in vitro) but the researchers hope to soon be able to go ahead with experiments in rodents (in vivo).

The explanation for glial cells not encapsulating the electrodes here is because the researchers have developed a small plate where fields of super thin nano-wires are interspersed with blank spaces. While nerve cells and their processes are climbing around the nanowires, the glial cells mainly occupy the flat spaces in between (see picture below).

- The different cell types still interact with each other. This is key, otherwise the nerve cells do not survive because the glial cells provide them with important molecules. The plate is made of the semiconducting material gallium phosphide where each outgrowing nanowire only measures 80 nanometers (billionths of a meter) in diameter.

What looks like a bed of nails are actually nanowires. Each out-growing wire measures 80 nanometers (billionths of a meter) in diameter. The green objects climbing up the nanowires are neurons.
- The students attending the club see how talented researchers are in different areas of our environment and they see opportunities for cooperation. We have a number of examples of partnerships that have emerged from the Seminar Club. When a new issue or problem comes up in your everyday work you now have, through the Seminar Club, a name and a face of a person with expertise in a certain area that may be able to help you. Without doubt this is time well invested, says Tomas Deierborg.

At the beginning of 2015 Tomas Deierborg and Maria Björkqvist took the helm at the LUN Graduate School. Their vision has been to tailor courses to meet the needs of all students under the MultiPark and BAGADILICO umbrella. Maria Björkqvist admits the inherent challenge in developing a schedule that offers equal access and opportunity to all young researchers within the environment. Some courses have to, by definition, be aimed at a smaller target group. That includes, for example, the recurring technical workshops where methods for operating cell-sorting machines are taught by Anna Hammarberg.

An example of a course that should have a much wider appeal was announced recently. This six-day event is focused on innovation in medicine. The aim of the course is to give participants a fundamental introduction to entrepreneurship, innovation and commercialization. Lectures will put emphasis on the entrepreneurial process as well as the examination of practical examples brought forward by the students themselves.

Jörgen Adolfsson of the Sten K. Johnson Centre for Entrepreneurship has been instrumental in setting up the course. He will also lead a number of the lectures. With a strong track record as an entrepreneur in his own right he hopes to be able to help participants develop their own research-based ideas into commercializable products, either through the creation of a new venture or through collaboration with established organizations.

- We hope to inspire students to develop their ideas further with the ultimate goal to convert their research into actual social benefit. Ideally, they will receive the tools necessary to create a business that can take a product or service to the community. Once the course is completed, we hope to have broadened the participants’ horizon on the possibilities of where they can take their own research. In some cases they may even consider a new career path as an entrepreneur, says Jörgen Adolfsson.
The last time a similar course was held at BMC was seven years ago. It seems a long time considering the high level of experimental neuroscience carried out at LU laboratories. One would think that opportunities of innovation would be plentiful in an environment flowing with such creativity. However, the translation of scientific discoveries to commercializable products is a tricky one. Not least in Sweden has this been a divide that seems infuriatingly difficult to bridge. A phenomenon sometimes referred to as the Swedish paradox. The expression refers to Sweden being the world’s biggest spender in research in relation to our GDP but with a limited output in terms of economic gains. USA and Japan are often hailed as shining examples at the other end of the spectrum. So to is our neighbor to the east, Finland.

- Perhaps this is in part a sign of a certain self-image among Swedish researchers in medicine. Compared to certain other countries we are perhaps not accustomed to thinking in terms of entrepreneurship and business to the same extent. Also, entrepreneurship as a discipline at Swedish universities is a fairly new concept. But I feel that this is changing and we want to help push that change, says Jörgen Adolfsson.

- We hope that researcher leaders also decide to join the course. Our guest lecturers are top names in their respective fields. It is the most ambitious course we have ever organized and I believe it should be time well spent for everyone who decides to take part, says Maria Björkqvist.
Many people with Parkinson’s disease eventually experience walking and balance difficulties, despite adequate medication. Moreover, some patients cannot fully take dopamine-based medication, as dopamine can lead to side effects.

The current research findings verify similar data from a previous study by other researchers, which was performed on brain tissue from a small number of deceased patients.

“The strength of our study is the number of participants, and the fact that they are alive. Because many suffer from several parallel diseases at the final stage of their lives, it is difficult to analyse samples from deceased persons”, explains Oskar Hansson, reader at Lund University and consultant at Skåne University Hospital.

The findings, published in the journal Neurology, were made when the researchers used a broad approach when looking for mechanisms to increase understanding of how Parkinson’s disease works.

“The measurements showed clear connections between markers of angiogenesis in the brain and walking or balance difficulties among the participants. We also noted an increased permeability of the blood-brain barrier, which leads to blood components potentially leaking into the brain and causing damage”, says Oskar Hansson.

The first part of the study included 100 Parkinson’s patients and 38 healthy control persons at Skåne University Hospital in Malmö. Through a cerebrospinal fluid sample, several different proteins that indicate formation of blood vessels in the brain were measured. To ensure the results, two additional groups of patients of approximately the same size were also tested.

“Medication for angiogenesis already exists. If we can confirm our results in further studies, these drugs can be tested on Parkinson’s patients in the future”, says Oskar Hansson.

Before it may be time to test the drugs in clinical studies, Oskar Hansson and his colleagues plan on conducting an animal study, to gain further knowledge about the mechanisms that are believed to cause problems for Parkinson’s patients, and to enable a selection of the most appropriate drugs to use.

The research was conducted in collaboration with the University of Gothenburg, Sweden, the Mayo Clinic in Scottsdale, Arizona (US), and others. The studies were made possible thanks to the support from the European Research Council (ERC), Swedish Research Council (VR), Parkinson Foundation in Sweden, MJ Fox Foundation for Parkinson Research, Region Skåne through ALF funding, etc.
ROGER BARKER
FROM CAMBRIDGE TO LUND

BY JENS PERSSON - To some extent, we are all products of our environment. As far as choosing your own profession goes, Roger Barker is not. Raised all over Britain, his father a wheeling and dealing businessman, young Roger’s path towards academic prowess was all but paved. Once his older brother got a D on a chemistry paper, which included a snarky comment in red ink from the teacher. At that moment, Roger thought that science probably wasn’t for him either. As fate would have it, he would later become one of the world’s leading clinical scientists in his field. MultiPark’s newly appointed Guest Professor could just as easily have veered towards studies in history, for he is a curious man with an apparent thirst for knowledge. It just so happened that medicine combined his interest in people with his knack for solving practical problems.

Him ending up in Lund is much less of a surprising story. In 1986 he qualified as a neurologist with a special interest in diseases tied to the basal ganglia. It was around this time that the world-renowned first fetal cell brain transplants were taking place in Lund with Olle Lindvall and Anders Björklund at the helm. Roger Barker followed the trials with fascination. He would soon contact the team in Lund and embark on a partnership that has only grown stronger over the years. Walking up Sölvegatan the other day he suddenly remembered sending letters asking for reprints to that very address, almost 30 years ago.

- This place has been something of a Mecca for the transplantation area for many years now. I’ve been fortunate that they have been so welcoming and that we have developed a fantastic partnership over the years. The great advantage for me today is that although Cambridge is a fabulous place to work and the science is unparalleled in many respects, in this particular area, neural transplantation, we don’t have that depth, he says.

The clinical trials in the TRANSEURO program - cell therapy for Parkinson’s disease (PD) with fetal cells - are now underway. Finally. It has been a long and often bumpy road towards completion. Bringing a complex and invasive therapy to the clinic has been a more challenging task than Roger Barker perhaps expected. While his patience and determination has been tested a number of times, we have now arrived at the final step where transplants are being performed in Cambridge. The operations in Lund should commence shortly.

- On May 18th the first operation was performed. Since then, another five transplants have been completed. This adds up to three complete patients since each patient requires two transplants, one on either side of the brain. So far there have been no complications and we’ve had no problems at all really. The immunosuppression that the patients are on has required bit of finessing in some cases but it has not a big issue.

Roger admits that being at the heart of things - acting as a link between basic scientists, clinicians and the authorities - has been a steep learning curve. Apart from the inherent logistical challenges of gathering the right cells at the right time, the job has involved frequent discussions with state representatives concerning ethical issues as well as details regarding the operating instruments. Regulations have changed over the past few years and the program has had to change with them, demanding an added workload for Roger and his colleagues.

Getting TRANSEURO to this point is not the end of the road. The endgame is to make cell therapy for PD an affordable and accessible treatment on a global scale. Realizing this vision will most likely require further successful cell therapy trials using brain cells derived from stem cells. Turning to stem cells will allow the production of the motor neurons required to be ready for transplantation at any given moment. This program has been running parallel to TRANSEURO over the last couple of years and major advances has given scientists hope that clini-
cal trials could get off the ground in three years.

While these developments should offer some hope to people with Parkinson’s, taking a therapy from first clinical trials all the way to the patient often requires navigating in unchartered waters for scientists and clinicians who are most comfortable conducting their businesses in labs or doctor’s offices.

- If you perform a first study that works in patients then you have to perform a bigger study and ultimately a definitive study before it can become a therapy. This whole journey is complicated and needs to be carefully planned in advance. It brings with it commercial pressures and partnerships. It’s fairly easy to perform an academic study but being able to fund it further and later supplying it to the greater population is another thing entirely. And if you don’t have Big Pharma or anyone else behind you, you haven’t got a therapy. These processes demonstrate how you ultimately translate from the lab to the clinic. It’s not always science but it’s actually challenging in a positive way.

To Roger, these are exciting times as he feels he is learning a lot about interacting with the commercial sector and the regulatory authorities. Being at that place where the hard facts of science meet the less stable truths of politics and business has brought some realizations home for him. He now better understands the great many factors that have to align for a therapy to go all the way to the clinic. Clearly, it has been a voyage of discovery for him and while one might suspect that the backlashes would have left him slightly cynical about the whole thing he very much takes it in stride.

- So much of this is new to everyone but the scientists and clinicians working on it. The regulatory authorities don’t know what this is and yet my interactions with them have been very encouraging and they really want to work with us. One thing that can keep you awake at nights that you can take this to the clinic and show that it works but ultimately Big Pharma may tell you that this is a one off therapy for PD and you can just as well have deep brain stimulation (DBS) surgery instead. And then you’ve developed a therapy, which no one really can afford to use. Here lies the challenge in working with the commercial sector, at some point you’ll lose control of your project and the market will decide. They can always close down the program.

Being a realist and an optimist are not a contradiction in terms for Roger. Rather, his optimism seems to be born out of a belief that although the process might be tedious and cumbersome at times, change and progress is readily achievable if you do your homework and stay the course.

The expertise he has now gathered working in an area that could only be described as the weakest link of the translational chain, the place between first clinical trials and the marketplace, will be a welcome addition to MultiPark. This is normally where new therapies go to die and with MultiPark’s ambition to be a vehicle for translational science, Roger Barker’s credentials should make him an ideal match for the network.

With a background at Oxford and Cambridge one might suspect that Roger Barker would carry himself with that air of aloof restraint often applied when caricaturing the British upper class. The fact is he is neither upper class nor reserved in his ways, rather he is approachable and enthusiastic. Perhaps it has something to do with his family, an eclectic range of characters as it turns out. He paints the picture of a family from humble beginnings where people sought their own paths in life. His mother left school at 14, his uncle became a clergyman in South Africa during the violent years of apartheid, his one brother a policeman, the other an alcohol salesman and his sister a lawyer and a devout Christian. The colorful gallery of persons in Roger’s life has likely allowed him to become a more empathetic doctor. He believes strongly that the doctor and the patient are the same.

- When you start your career in medicine the patient is often seen as another species almost. But what’s absolutely guaranteed is that you at some point will become the patient so the first thing to understand is that a patient is not just a case of PD or heart attack, they’re a person. Everything is about relationships, it’s about getting the trust of the patient, getting to know the patient, empathize with them. Not to have this; I’m the doctor, I tell you what to do.

- Especially when you go into these clinical trials you need to realize it involves both you and them, it’s a journey you go on together which means you get to know them very well and at one level you become good friends. They are the brave ones going through all of this while you’re fortunate to give them the opportunity. So for me, medicine has always been about trying to help people, be honest with people. To be realistic while at the same time giving people hope and learning as you go along. I’ve done it for 30 years but you still learn from people. Humility is very important in this profession.
THE BRAIN FORGETS IN ORDER TO CONSERVE ENERGY

BY INGELA BJÖRCK - Our brains not only contain learning mechanisms but also forgetting mechanisms that erase “unnecessary” learning. A research group at Lund University in Sweden has now been able to describe one of these mechanisms at the cellular level.

The group’s results, published in the international journal Proceedings of the National Academy of Sciences of the United States of America (PNAS), explain a theoretical learning phenomenon which has so far been difficult to understand.

The premise is that human or animal subjects can learn to associate a certain tone or light signal with a puff of air to the eye. The air puff makes the subject blink, and eventually they blink as soon as they hear the tone or see the light signal. The strange thing, however, is that if the tone and the light are presented together (and with the air puff), the learning does not improve, but gets worse.

“Two stimuli therefore achieve worse results than just one. It seems contrary to common sense, but we believe that the reason for it is that the brain wants to save energy”, says brain researcher and professor Germund Hesslow.

His colleague Anders Rasmussen, who performed the present study, has previously shown that when the brain has learnt a particular association sufficiently, certain neurons that act as a brake on the learning mechanism, are activated.

“You could say that the part of the brain that learned the association (a part of the brain called the cerebellum) is telling its ‘teacher’: ‘I know this now, please be quiet’. When the brain has learnt two associations, the brake becomes much more powerful. That is why it results in forgetting, usually only temporarily, however”, explains Germund Hesslow.

Maintaining unnecessary association pathways requires energy for the brain. The researchers believe that this is the reason for the brake mechanism – even though in this case it happened to be a little too powerful.

The Lund researchers were able to describe how the nerve cells learn and forget through studies of animals, but believe that the mechanisms are likely to be the same in the human brain. Therefore, these findings are of fundamental interest for both brain researchers and psychologists. They could also be of practical interest to educators.

“Obviously, it should be important for teachers to know the mechanisms by which the brain erases the things it considers unnecessary. You do not want to accidentally activate these mechanisms”, says Germund Hesslow.
This technology would make it possible to understand brain function in both healthy and diseased individuals.

“There are several elements that must go hand in hand for us to be able to record neuronal signals from the brain with decisive results. First, the electrode must be bio-friendly, that is, we have to be confident that it does not cause any significant damage to the brain tissue. Second, the electrode must be flexible in relation to the brain tissue. Remember that the brain floats in fluid inside the skull and moves around when we, for instance, breathe or turn our heads.

The electrode and the implantation technology that we have now developed have these properties, which is unique”, says Professor Jens Schouenborg who together with Dr Lina Pettersson led the project.

The Lund researchers’ tailored electrodes, which they call 3-D electrodes, are unique in that they are extremely soft and flexible in all three dimensions, in a way that enables stable recordings from the neurons over a long time.

The electrode is so soft that it deflects against a water surface. In order to implant such electrodes, the researchers have developed a technique for encapsulating the electrodes in a hard but dissolvable gelatine material that is also very gentle on the brain.

“This technology retains the electrodes in their original form inside the brain and can monitor what happens inside virtually undisturbed and normally functioning brain tissue”, says Johan Agorelius, a doctoral student in the project.

Until now, developed flexible electrodes have not been able to maintain their shape when implanted, which is why they have been fixated on a solid chip that limits their flexibility, among other things. Other types of electrodes that are used are much stiffer. The result in both cases is that they rub against and irritate the brain tissue, and the nerve cells around the electrodes die.

“The signals then become misleading or completely non-existent. Our new technology enables us to implant as flexible electrodes as we want, and retain the exact shape of the electrode within the brain”, says Johan Agorelius.

“This creates entirely new conditions for our understanding of what happens inside the brain and for the development of more effective treatments for diseases such as Parkinson’s disease and chronic pain conditions than can be achieved using today’s techniques”, concludes Jens Schouenborg.

FACTS ABOUT THE ELECTRODES

The electrodes are made of 4 um gold leads and individually insulated with 4 um parylene. The array of electrodes consists of eight flexible channels, designed to follow the movement of the brain. Both the electrode and implantation technology, which have been tested on rats, are patented by NRC researchers, in Europe and the US, among other places.