Researchers at Lund University’s medical faculty received a combined 167,775 million crowns for 58 different research projects. The recipients were announced last week when the Swedish Research Council (SRC) decided upon which projects should be awarded funds.

The medical faculty at Lund University is the second largest recipient in the country, both in terms of research funding and the number of successful applications approved.

This year, the SRC awarded grants for a total sum of over one billion SEK for research in health and medicine. New this time around was that a new grant focussing on younger scientists was introduced. The money will go to special project grants aimed at young researchers in the beginning of their careers. In Lund, twelve young researchers were chosen as awardees.

Of the Bagadilico scientists Angela Cenci-Nilsson was the one who had made the strongest impression on the team of evaluators. Her research project “Harmful plasticity changes in the basal ganglia: focus on Parkinson’s disease and its treatment” was given 6,750,000 SEK for the coming five years, putting her among the top recipients nationwide.

Other scientists that were awarded grants within the Bagadilico environment were Maria Björkqvist and Gesine Paul. Maria Björkqvist received 2,4 million SEK for her project “Peripheral pathology in Huntington’s disease and its impact on disease mechanisms and biomarkers”. Cell therapy expert Gesine Paul was given 2,8 million SEK for her upcoming research efforts on “ Newly discovered perivascular stem cells in the brain - their contribution to regeneration and tumorigenesis”.

HOCKEY COACH RAISES MONEY FOR PARKINSON’S

About a month ago the head coach of southern Swedish hockey team Rögle, Björn Hellkvist, announced that he had to quit his job as a result of early onset Parkinson’s disease. In the end the symptoms were too frequent to combine with his coaching job. The over-medicating before games eventually became a strain on his everyday family life.

After announcing that he was suffering from Parkinson’s Björn has quickly become a spokesperson for the disease, showing up on television and in magazines promoting awareness for Parkinson’s. Recently he arranged a fund-raiser for Parkinson’s during a hockey game, raising 700,000 SEK for research purposes. The money was raised by the newly founded ‘Shaking Generation’, Björn Hellkvist’s fund-raising project for people with young onset parkinson’s disease.

PATRIK BRUNDIN SWEDBANK AWARD RECIPIENT

Patrik Brundin has been awarded the Swedbank Scientific Award in Memory of Amanda and Per Algot Mångberg. The prize is awarded for professor Brundin’s achievements in understanding the mechanisms behind neurodegenerative diseases. The motivation focuses mainly on professor Brundin’s two major research areas throughout his career, cell transplants and the prion-like spread of alpha synuclein.

On October 22nd Patrik received 50,000 SEK during the award ceremony at Umeå University.

SWEDISH PD FOUNDATION HOLDS LUND MEETING

On October 18th the Swedish Parkinson Foundation arranged a meeting in Lund on pump treatment and deep brain stimulation in Parkinson’s disease. 150 people had gathered to listen to and question Parkinson’s physicians and researchers.

Bagadilico’s Per Odin spoke about the treatments available for advanced Parkinson’s. Professor Odin, plying his trade in Germany as well as Lund, informed the audience on complements to the standard medication L-Dopa.

The three alternatives discussed were; apomorfin, a dopamine agonist that is taken by self-injection as the off-periods start. Another solution mentioned was the Swedish duodopa pump. The treatment is a combination of levodopa and carbidopa in the form of a gel that is administered directly into the small intestine through a surgically placed tube. The final treatment discussed was deep brain stimulation (DBS). DBS operations have been performed since the 1980s and seem particularly suited for patients suffering from severe cases of dyskinesia.

In his closing remarks Per Odin told the audience that while we are waiting for effective treatments in cell transplants and gene therapy the above-mentioned methods are being constantly refined. Giving one example, he stated that the duodopa pumps will get smaller and smarter. In his final statement professor Odin mad a plea that “all patients that can benefit from advanced therapies should receive them”.

NEWS IN BRIEF
It all started with a chance e-mail to Switzerland. Deniz Kirik was fishing around for someone with the competence to update Lund’s PET-imaging facilities. The infrastructure in Lund did not have the proper equipment and Swedish patients had been flying in and out of London for PET-imaging trials for decades. What Deniz didn’t know was that the man answering his mail in Geneva would help kick off a string of events leading to a record-fast establishment of a new PET tracer module in Lund, ready-to-use in under twelve months. An idea that had been sitting on the drawing board for many years quickly became a reality. And at a sale price too.

- It turned out that the guy in Geneva who has been integral in helping us develop this knew other colleagues here in Lund from his post-doc time in UCLA. I didn’t know this when I contacted him. It also turned out that he had previously been working very closely with one of the advisors to the Lund Bioimaging Center, so I believe that his close link to Lund is probably what swayed him to help us build the module.

- Of course, we could have bought other machines, but it would have cost us several millions. We instead got this machine in place on a budget lower than 100,000 SEK, says Deniz Kirik, clearly pleased with the Biomagin Center’s latest acquisition.

The expertise offered by the team in Switzerland presented a unique opportunity to custom build add-ons to the existing PET-facilities at Lund’s hospital. The goal was to acquire the technology needed to create advanced tracers for experimental research, a capacity that was non-existent in Lund.

A few years earlier the Swiss scientists had developed a similar synthesis machine to the one that was now being upgraded at Lund’s cyclotron facilities. With the same technology in place in Lund the existing imaging site would be transformed. Previously only standard radiotracers for clinical use could be produced. Now, it would be possible to make advanced tracers allowing scientist to visualize detailed processes inside the brain. The proponents for the synthesis machine knew that such an upgrade would constitute a key edition to the overall biomedical research infrastructure at Lund University.

First test run successful

The security demands for producing tracers are rigor-
ous because of the radioactive components created in the process. The machinery involved is highly specialized and the materials can’t be handled on a normal bench, you have to work in a chamber, a heavily reinforced space called a hot cell. The hot cell is a shielded nuclear radiation containment chamber consisting of thick lead walls weighing several tons. This is where the radioactive tracers are generated. At the Lund facility these complex processes will be monitored by radiochemist Thuy Tran, a vital recruit for the future success of the project.

Thuy has already been working in the background for the last twelve months. She’s been the synchronizing factor here, communicating with the cyclotron unit as well as the collaborators in Geneva to make sure that all this was coordinated. She is also the one who will be making our tracers in the future, pushing the actual buttons, and these people are not easy to find today, says Deniz Kirik.

Thuy was involved a few weeks ago when the first test runs were made. An intense few days preceded the first ever synthesis for research purposes at Lund University. With the time, effort and money put in over the past year the group was anxious to see if the first images would reveal that the new tracer had actually worked. The results came quickly, and they were satisfactory. The images from the rat brains clearly showed the specific uptake in the striatum of the brain, exactly as the researchers had hoped and predicted. The hard work had paid off and the planning of new experiments immediately began.

Ushering in a new era

The successful tests signaled the start of a new chapter for the Lund Bioimaging Center. With the new technology in place Lund has become a more competitive research environment. The easy access to PET-imaging will allow researchers to tackle scientific problems from different angles. Critical imaging data will give further weight to scientific publications, as the added evidence grows stronger. The facilities will, simply put, make it easier for researchers to build a scientific case.

- We are broadening our toolset. This is to be viewed as a technology-enabling investment, which means that any research group will be able to contact the center and use PET imaging for their experiments. This is also relevant for many other brain diseases than just Parkinson’s. Quite simply, it’s helping us to do experiments better than we did before.

One of the first projects to utilize the new technology is a joint Bagadilico effort aiming to develop tracers that bind to dopamine receptors. If successful, the tracers will reveal the efficacy of different methods with the shared goal of re-enabling the brain to
make dopamine. The tracers will light up in the PET-image created, demonstrating the level of dopaminergic activity in the brain. For example, if you can show that the binding to the receptors has been normalized, you have most likely successfully corrected dopamine deficiency. If you are then able to correlate these findings with behavioral recovery in animals you have a strong case for a treatment with a clearly beneficial effect. These are important steps that are needed before a treatment can be tested in patients. In that sense, PET-imaging is a bridge between the laboratory and the patient, speeding up the process towards clinical trials.

Deniz Kirik believes that this is just the beginning of an era where bioimaging will continue to grow in importance. He tells me that as imaging becomes more common it will help scientists capitalize not only on successful experiments, but on failures too.

- If you review clinical trials that have tested novel therapeutic strategies for PD, you’ll find that most of these tests have yielded negative results. Some of those trials reveal interesting biological readouts, they generate new questions or new hypotheses, which suddenly open up doors even on the end of a failure. If you end up in a negative trial without imaging data you may find it difficult to explain why the experiment failed. Whereas if you have collected images you can then start formulating questions, new questions that you didn’t think about from the beginning.

In his efforts to develop Lund’s Bioimaging Center, Deniz Kirik has been a tireless worker. Now that the pieces are starting to fall into place it seems that his energy is only picking up. Anxious to put the new facilities to the test he is determined to generate solid scientific results within the first year.

- Nothing should prevent us from being the most advanced site for PET-imaging in Sweden, hopefully in less than five years. What we have done here is to trigger a late awakening. Our goal now is to catch up.
On October 31st, at three o’clock in the afternoon, Swedish time, a diverse group of people from all over the world sat down in front of their computers, in office chairs or by their kitchen tables, to take part in the first Bagadilico webinar on Parkinson’s disease. A multinational grouping - consisting of Swedes, Dutchmen, Brits and Norwegians - had converged to try to cobble together a live broadcast with the goal of sparking a discussion across continents. The web statistics afterwards suggested that goal had been reached. When the last cameras and microphones had been packed away it was clear that visitors from 124 cities worldwide had taken part in the inaugural webinar.

The headliners of the day were Bagadilico’s Patrik Brundin, Angela Cenci-Nilsson and Gesine Paul. The trio’s talks stretched from the excitement and uncertainties of experimental science to the organizing of ongoing trials in cell therapy. In an effort to give life to the age-old seminar set-up each talk was followed by a discussion initiated by questions from the on-stage Parkinson’s Movement panel and the live audience. Before soon online participants were also taking part in the debate, sometimes stumping the scientists with their well-informed questions.

The webinar format inspired a conversation encompassing different actors and groups within the global Parkinson community, giving a voice to all who wanted to engage in the debate. Young scientists were perhaps the most active group on the live chat, while the live audience included many patients with advanced stages of Parkinson’s. Senior researchers were also weighing in on the web discussion and Patrik Brundin, on stage with his laptop comfortably placed in his lap, took upon himself the dual role of interrogator and defendant as he posted comments on the chat while answering increasingly sophisticated questions in front of the cameras.

Alpha Synuclein – the main culprit?

Patrik Brundin was also the one who kicked of proceedings with his talk on the role of alpha-synuclein in the disease progression of Parkinson’s disease. Professor Brundin has been a pioneer in describ-
ing how the mutated protein travels from cell to cell, triggering the slow breakdown of motor neurons in the basal ganglia region of the brain. His working hypothesis is that the misfolding of alpha-synuclein, and the prion like spread of this sick protein, could be what sets of the negative chain of events leading to Parkinson’s disease. The Brundin research group has been able to tie early symptoms of Parkinson’s – such as sleep disorder, loss of sense of smell and constipation – to the development of harmful clumps of aggregated alpha-synuclein in the areas of the brain governing these functions, suggesting that the spread of the sick protein is an important key to understanding the enigma of where Parkinson’s disease may first start.

After his presentation Patrik Brundin was hit with questions from around the world. One question, that always seems to pop up in these settings, and understandably so, was; “When will this research lead to a viable therapy in the clinic?” Professor Brundin answered, somewhat tentatively; “It’s of course difficult to say, we are in the early stages here, but I always say five to ten years because I believe that to be a fair description of what is probable, but the answer is of course that I don’t really know”.

### Doing away with dyskinesia

Next to take the stage was Angela Cenci-Nilsson, a world-renowned authority on the role of L-DOPA induced dyskinesia in Parkinson’s disease. She has been a leading presence in the field for a number of years and her research group has been integral in the development of animal models for dyskinesia, helping to move a number of laboratory discoveries to the clinic. Professor Cenci-Nilsson talked to the audience about her latest research targets for reducing L-DOPA induced dyskinesia.

**One such target** is the effort to block the overactivation of glutamate signals, which have been linked to the development of dyskinesia. The dopamine in our brains fine-tunes the signal strength of important neural circuits and the loss of dopamine in Parkinson’s disease can create an imbalance between these different signal systems. With L-DOPA treatment additional changes occur in this complex neural circuitry. One target for professor Cenci-Nilsson is now to develop a drug that stops the glutamate overactivation by blocking a glutamate receptor called ‘mGluR5’.

“If we can block this glutamate receptor we could prevent the negative effects and im-
prove the dyskinesias resulting from L-DOPA medication. Several clinical trials are now ongoing to evaluate the effects of mGluR5 antagonists in L-DOPA treated PD-patients. Two phase-2 trials have already reported significant positive results”, explained Angela Cenci-Nilsson, before she opened up to questions from the web visitors and the live audience.

Cell therapies of tomorrow

The final presentation of the day was delivered by Gesine Paul, a neurologist and scientist who divides her time between the clinic and cell therapy experiments in the lab. Dr Paul talked about the exciting potential that cell transplants could have for Parkinson’s patients. Illustrated by a video from the world famous transplants performed by Olle Lindvall and Anders Björklund in the late 80’s, where a person that has undergone a transplant shows clear motor function improvements years later, she effectively demonstrated the possible impact that this research field still could have for future therapies.

However, the field of cell therapy has always attracted its fair share of skeptics. Ethical issues relating to the use of aborted fetuses as well as doubts concerning the cost effectiveness and logistics of cell therapy are routinely used as arguments for shelving the method as a viable, universal therapy for Parkinson’s patients.

Dr Paul was the first to admit that these arguments are not unfounded and that there is still a long way to go before we can see the technique benefitting patients on a larger scale. “Over the past decades a number of patients have received cell transplants. In some, the transplanted cells survive, grow and significant clinical improvements can be seen for many years after the transplant. Yet, in others, the therapy not only fails, but the patient develops side effects” explained Gesine Paul, underlining the complexity inherent in taking cell transplants from the lab to the clinic.

After admitting that the field of cell therapy has plenty of obstacles yet to pass, Dr Paul instilled some new hope in the audience. A wide-ranging, multinational research program – TRANSEURO – is now aiming to develop a best practice for cell therapy. Being part of the Lund TRANSEURO team, Gesine Paul was clearly hopeful that the ongoing study, already performing multicenter clinical trials, will help push the field ahead to a new phase of cell therapy trials in Parkinson’s disease.

As the afternoon turned to evening and the Swedish autumn sun gave way outside the tall windows of the Pufendorf Institute all three scientists took the stage for the final debate. The stage was shared with the three representatives from the Parkinson Movement - Jon Stamford, Sara Riggare and Paul de Ross – and there was no shortage of subject matter as the six of them began touching on the topics of the day.

The lively debate ended on a surprising note as the Bagadilico scientists were put on the spot by an unexpected question from a web visitor. Paul de Roos read the question; “If you rubbed a bottle and a genie appeared, what PD-related question would you ask him?” Patrik Brundin hesitated before deciding upon the question “at what specific event does Parkinson’s disease actually start?”. Gesine Paul took it one step further by suggesting the question “What is the perfect therapy for Parkinson’s?”, admitting that the answer to that question would put her and her colleagues effectively out of a job.