Bagadilico Task Forces
In May four task forces were granted money from the Bagadilico board. A prerequisite was to create new collaborations and explore novel projects with cutting-edge potential. PI Thomas Laurell will investigate acoustophoresis-based cell sorting for isolation of viable human neural progenitors derived from pluripotent cultures. PI Malin Parmar will look at the generation of iN cells from fibroblasts derived from individuals with point mutations or multiplications of the a-syn gene as experimental models of PD. Other projects include “A new approach to study the cellular mechanisms of graft-induced dyskinesia in identifiable striatal neurons” (PI: Angela Cenci), “Neuron-microglial interaction: Real time optical imaging on how microglia attacks neuronal components in alpha-synuclein overexpressing model” (PI: Jia-Yi Li).

New Bagadilico Money
Seven young members (Maria Björkqvist, Manolo Carta, Tomas Deierborg, Johan Jakobsson, Oskar Hansson, Martin Lundblad, Malin Parmar) brought in a total of 1 575 000 SEK from the Craaford foundation in May. Congratulations! Congratulations also to Ulrika Nordström for the two-year SSMF stipend!

New Bagadilico Papers


Upcoming Events
– mark that calendar!

June 8th at 12:00: Pre-lunch seminar in the Segerfalk lecture hall with Daniella Rylander. “Maladaptive plasticity of serotonin axon terminals in L-DOPA-induced dyskinesia.”

June 12-13th: All floors in the A-house, BMC, will be evacuated and locked when the MRI equipment on floor A09 is disinfected using (lethal) hydrogen peroxide vapor. A-building opens again Monday morning June 14th at 08:00.

June 23rd-24th: Maria Björkqvist is organizing a work-group meeting on biomarkers: “The European Huntington’s disease Network Biomarker working group meeting.”
Dr Ulusoy

Having finished the thesis carpentry with her “spikning” last month Ayse Ulusoy has now become Dr Ayse Ulusoy. It turns out that defending her thesis also schooled her in the noble art of party planning.

“Party planning is all parallel to the thesis work but has nothing to do with science. Luckily I had friends helping me out,” Ayse Ulusoy says. “I thought the date was good. It was close to a Turkish holiday so that my family could come, but I never thought about the Swedish holiday. Apparently it was ping-stafton and the Lundacarnival week. Everything was booked for either a party or a wedding.”

“During the defense it’s important to make sure the opponent understands how it’s going to happen. The customs are different. I also had to deal with other organization challenges for my opponents and guests. I thought of a strategy to prepare for his questions,” Ayse says, “but frankly, with all the things going on I didn’t have time.”

“For the first paper we created an animal model. There’s this whole storyline in the thesis. The last manuscript brings all the studies together. I made the final analysis while I was writing the thesis. It was a close call. I was working like crazy, writing and praying that I would get enough animals. Initially, our results did not have enough statistical power because of the small number of transgenic animals fitting the age criteria. Last minute I got the group together. I’m so happy it worked out!”

“In Parkinson’s disease there is a dopaminergic neurodegeneration. It is known why the symptoms are happening but it is not known why the cells are dying. One very important protein is alpha-synuclein.”

“We wanted to understand why alpha-synuclein was toxic for dopaminergic neurons. We thought it might be the dopamine itself that made the alpha-synuclein more toxic. We generated a vector to decrease the dopamine production in vivo, and also used a transgenic animal with increased cytosolic dopamine. Increased cytosolic dopamine increases alpha-synuclein toxicity. This is not a new hypothesis, but it is the first time it has been shown in vivo.”

“In another study we looked at L-DOPA induced dyskinesias. They are studied with lesions; you kill the dopaminergic cells. Killing cells decrease the dopamine. But then you don’t know if this is because the cells are dying or because the dopamine is decreasing? We were able to separate these two issues.”

“I’m here for another six months. Then I’ll go for a post doc. I have plans to go back to Turkey, but they are complicated plans,” Ayse smiles, “just like in my research.”
Two-photon Microscope

Elegant Machinery

The Bagadilico network has access to advanced expertise and equipment. This week we highlight the two-photon microscope.

“With a regular microscope you can focus up and down, but even light from out of focus will be detected obstructing your view,” says two-photon-mic-expert Håkan Toresson. “With this microscope you can select a thin focal plane and it will give you info from that plane only.”

“When you shine light on to a sample, this transfers energy into the tissue, energy that can cause damage. The two-foton laser emits light with longer wavelength and, hence, less energy, which can penetrate deeper into tissue without causing as much damage.”

Flourescent molecules are peppered with photons, and provided they are hit by two low-energy photons at the same time, they get excited, emit light and can be detected.

“The high, damaging energy is concentrated to the focal plane, the rest of the tissue is spared,” says Håkan Toresson. It takes at least three months to become an independent user of the microscope.

Please contact hakan.toresson@med.lu.se

Two-photon Microscope

* look at living tissue
* look at high depths (1 mm)
* reduced phototoxicity
* efficient light detection

Can’t get chips off your mind?

Last month Daniella Rylander received good news about two publications.

One paper was accepted into the Annals of Neurology and another paper published in Neurobiology of Disease. “I’m proud,” Daniella says. “I’ve spent a lot of time on the Annals-paper and my main PhD project is finally finished.” Daniella is not allowed to talk about the first article just yet because of a press embargo, but curious individuals are welcome to attend the pre-lunch seminar June 8th to find out more.

The second article has been out since May. It has a topic normally associated with Friday nights in the store snack lane: Glutamate!

Monosodium glutamate (MSG) has a bad health reputation but is responsible for the irresistible umami flavor encountered in chips, bouillon and Asian food. Apparently there are also glutamate receptors in the brain.

“Glutamate is a neurotransmitter that activates other cells when released. Individuals with Parkinson-related dyskinesias have too active glutamate signaling,” Daniella says.

“The only current treatment for dyskinesias are antagonists to glutamate receptors. We’ve looked at fenobam, an antagonist to the glutamate receptor mGluR5.”

“Fenobam was originally discovered in the seventies. It was tried out on people in another context, and found to have calming and pain-relieving properties. It wasn’t until about ten years ago that it was realized that it had an effect on this receptor. Then it became interesting for us Parkinson and dyskinesia researchers”

“We saw clearly that fenobam reduced dyskinesias in our rat model. But the rats didn’t turn into loose-limbed spaghetti; the effects of L-DOPA were still there. Our co-authors saw a similar effect in monkeys”

“To summarize, fenobam is a good candidate for future antidyskinetic treatments in Parkinson’s disease, and since it has previously been tested on humans, time can be saved.”

Photo: Anna Appelberg