NeuroCampus – Inside Out:

Anders Nykjær

Group leader at Nykjær Lab and Center Leader at PROMEMO, Dept. of Biomedicine

Nykjær Lab examines the function of the family of sortilin receptors in memory and mental disorders. They study how the proteins act in the healthy brain and why when dysfunctional this leads to cognitive deficits and psychiatric disorders.

Anders Nykjær. Photo: Karoline Klitgaard

Can you describe your research in a nutshell?
My research encompasses two major branches. One is focused on mental diseases while the other studies mechanisms underlying memory formation and recall. They are interconnected, since distorted memory is a frequent symptom in patients suffering from a psychiatric disorder.

Common focus for both branches is the sortilin receptor family, encompassing sortilin, SorLA, and SorCS-1, -2, and -3. These proteins are essential for memory function and mental health and show strong genetic association with risk of cognitive impairment and mental disease.

To reach our goals we use transgenic mice and fish, cell biology, neuroembryology, electrophysiology, mouse behavior, calcium imaging and dopamine sensors in living mice. These approaches enable us to understand how sortilin receptors affects neuronal communication in the healthy and diseased brain.

In 2018, we gathered a group of people from AU (Marco Capogna, Sadegh Nabavi, Poul Nissen, Magnus Kjærgaard and Hanne Poulsen) who all work with memory while using very different approaches. This became the starting point of our research center PROMEMO. Here, we study memory - spanning all the way from the underlying biophysics to in vivo studies of neural circuitry. In my lab, we specifically focus on the role of sortilins, which appear to be particularly related to forgetting.

The same sortilin genes that play a role in memory are connected with risk of mental disorders, linking our memory research to our research in mental disorders.
For example, one of our current projects focuses on the causal role of the receptors in the neurodevelopment diseases ADHD and autism spectrum disorder (ASD). Expression of the genes coding for SorCS-1, -2 and -3 that determines disease risk, are dynamically controlled and they exhibit functions that are specific to distinct stages in life. During development, these receptors enable neuronal wiring whereas in the adult brain they serve to control synaptic plasticity and, among other brain functions, in particular memory.
Using our genetically manipulated animal models, we closely study these connections.

What translational impact may your research have for people?
Understanding some of the underlying genetic mechanisms of mental disorders, particularly neurodevelopmental disorders, could be key in development of new drugs that activate or inhibit specific genes, thus constituting a more causative and specific treatment for mental disorders. Similarly, our studies of proteins in memory could be potentially important for discovering new ways of preventing the breakdown of memory e.g. in dementia.

How did you end up where you are today?
As a young medical student, I coincidently ended up talking to a medical doctor about research. I subsequently became affiliated with a professor who was immensely inspiring and took such good care of me as a student that I completely forgot to go into the clinics.
I think it is of the greatest importance to focus on the well-being, motivation and possibilities for young researchers. They are the ones that have to move the field along and moreover, often the ones with the good ideas.

What does a (local) strong neuroscience research network mean for you and your research?
The neuroscience community in Aarhus is essential for our research. Neuroscience at AU and AUH has increased extensively during the last decade, among other things due to the pull of DANDRITE. Without the strong network, the creation of PROMEMO with its many different ideas and approaches would never have happened.

We already have collaborations with the clinical department, i.e. PET Center and Ole Mors, but such interactions must be further strengthened and developed, as it is important that we get to know each other even better – particularly across basic and clinical science.

If you had unlimited resources to conduct a big, multidisciplinary neuroscience project, what would you like to do?
In line with our current projects, it would be very interesting to conduct studies using single cell mRNA-sequencing. It would allow us to answer completely new questions regarding memory. For instance: when you have a memory, do the specific cells activated during this memory look different that the ones that are not? Or do they look different compared to when they are not engaged in any memory processes? This would allow us to examine the causal roles of the sortilins more precisely.

I would also like to go clinical with our studies and hypotheses. Memory processes and mental disorders may be different in humans compared to mice and zebrafish, and it is essential to also study these effects of the genes and proteins in humans.

Contact:

- Anders Nykjær, PhD, Professor, Center Leader
- Address: Høegh-Guldbergs Gade 10, 1116-352
- E-mail: an@biomed.au.dk
- PURE profile

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