NeuroCampus – Inside Out:

Mai Marie Holm

Group Leader at Department of Biomedicine

Holm lab uses electrophysiological methods to investigate real time synaptic transmission and plasticity focusing on understanding underlying synaptic mechanisms in various diseases such as depression and ALS

Mai Marie Holm. Photo: Karoline Klitgaard

Can you describe your research in a nutshell?

In my lab, we use microelectrodes and advanced electrophysiological techniques for our studies in isolated brain tissue from rodents. This gives us the opportunity to visualize and investigate neuronal communication in brain tissue in real time - highly comparable to the events in the intact brain. I think that is very exciting! We manipulate the neurotransmission and trigger stimulation protocols mimicking the communication patterns in the living brain during learning and memory-related processes. We use rodent brain disease models to study isolated disease mechanisms. These studies are combined with carefully selected pharmacological tools and clinically employed drugs, and all together, this allows us to map the impact of brain diseases on synaptic transmission, plasticity, network activity, and investigate how pharmacological tools can potentially normalize these impacts.

What translational impact may your research have for people?

My motivation and ultimate goal is to contribute to the development of better treatments for future patients affected by brain diseases. More detailed knowledge about brain disease mechanisms will facilitate development of better treatment strategies, e.g. by targeting key molecules and normalizing imbalances. Research progress will improve our abilities to rescue impaired plasticity, improve learning and memory and potentially reduce the impairments, or slow the decline, caused by brain diseases.

How did you end up where you are today?

I started as a PhD student in molecular neurobiology in 1999, where I studied glutamate receptors expressed in Xenopus oocytes (frog eggs). I generated mutants to investigate conformational changes in the receptor complex in different functional stages and this was combined with complementary manipulations in the ligand done by collaborators from University of Copenhagen. I did a research stay at Emory University, Atlanta, US, where I was trained in an advanced ultra-fast ligand application system that was essential for my PhD studies and enabled me to afterwards establish the system in my PhD lab at AU. Working in this international research environment at Emory was highly stimulating and critically shaped my future career as a scientist. For my postdoc, I wanted to take a step closer to study the mechanisms happening in the intact brain. Employing advanced electrophysiology, I studied isolated rodent brain tissue from knockout and disease models. I contributed to the mapping of the functionality of novel neuronal receptors and the discovery of hippocampal impairments in a depression model. Now, as associate professor at Dept. of Biomedicine, I have the possibilities to pursue my combined interest from the molecular level to more complex neurophysiology.

What does a (local) strong neuroscience research network mean for you and your research?

A strong local network offers the possibilities and fast access to share ideas and discuss preliminary data and ways to progress our research projects. Strong local collaborations can complement your own expertise and speed up a project. Neuroscience groups often have common needs for research infrastructure and facilities. A local network can for instance facilitate collaborations on disease models breeding with no need to long-distance transport to national and international collaborators. Students and postdocs can run their project in labs with different areas of expertise within neuroscience - even in the same university campus. Additionally, I am course leader of the Graduate Neuroscience Course, which is a two-week PhD course covering a broad range of topics within neuroscience. The lecturers are almost exclusively local researchers, but all at very high international level.

A strong local research network allow us to attract high-ranking international experts for visits and inspirational talks. Importantly, it enables larger neuroscience focused events such as our annual Neuroscience Day, even at your home university.

If you had unlimited resources to conduct a big, multidisciplinary neuroscience project, what would you like to do?

I would love to further develop our functional studies in disease models of brain disorders, for instance by including simpler cellular models and perhaps even taking selected mechanisms to higher organisms. I would like to have access to a strong neuropharmacology group to provide the tools needed to target the different key players/molecular mechanisms we identify using our electrophysiological analysis. Furthermore, such projects rely on strong expertise in neuroanatomy to map anatomical changes and structural studies at the molecular level using X-ray crystallography. An advanced microscopy unit would be important for refined visualization and behavioral analysis to indicate impact on learning and memory tasks. Furthermore, the project should be conducted in close contact with the clinicians to enable back and forth exchange of relevant updated knowledge and details on relevant disease mutations, specific brain areas of disease activity, neuronal network imbalances, etc.

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