NeuroCampus – Inside Out:

Poul Henning Jensen

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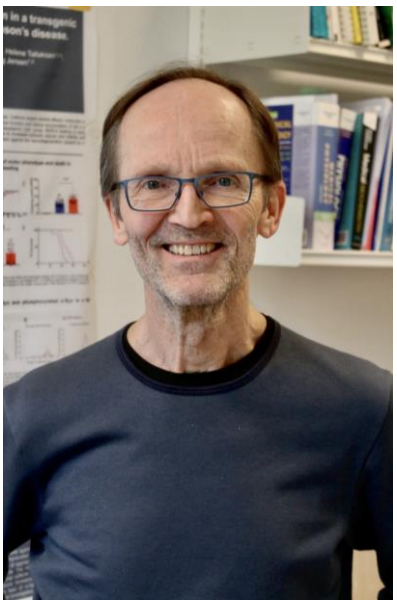
The Neurodegenerative Diseases Laboratory investigates the core mechanisms of neurodegenerative diseases like Parkinson's disease from molecules to single cells, animal models and humans. Focus is placed on how the mechanisms in the cells become dysfunctional at early points in disease progression and how these abnormalities can potentially be slowed down or even reversed.



Poul Henning Jensen. Photo: Karoline Klitgaard

Can you describe your research in a nutshell?
In my lab we study the core mechanisms of neurodegenerative diseases, particularly Parkinson's and Lewy Body dementia, all the way from molecules to the human organism.
One of current research project focuses on the aggregation of the protein, α-synuclein in Parkinson's disease. We use a research method in which we copy-paste α-synuclein aggregates from Parkinson's patients into animal or molecular models. In this way, we can study how the aggregation affects the mechanisms in the organism.
Among other things, this has led us to discover, that aggregated α-synuclein acquires a new function in the cell, in which it activates a Ca^{2+} pump and makes it hyperactive.
Rather than focusing on the aggregates, our labs focuses on investigating and understanding how they harm the nerve cells, e.g. via the Ca^{2+} pump. In this regard, we have conducted studies with different types of compounds, e.g. caffeine, in order to deactivate the pumps and down-stream effects of α-synuclein aggregation. The hyperactivated cells seems to be particularly sensitive to relatively small doses, and it may thus be possible to selectively affect the dysfunctional cells. We have found that doses of caffeine seems to have positive effects on the progression on Parkinson's disease and neurodegeneration in mice.

What translational impact may your research have for people?
In collaboration with Claus E. Olesen, also from Department of Biomedicine, we are testing whether these different compounds counteracting the hyperactivity of the Ca^{2+} pumps could potentially work as drugs against Parkinson's disease. Better understanding of the underlying disease mechanisms is an essential step for treating the diseases. We focus particularly on the fact that brain abnormalities and cellular dysfunction can be seen in Parkinson's patients a long time before the patient experiences the classical brain lesions and symptoms. Hence, we believe that an important focus in research in neurodegenerative diseases should be not only on mechanisms behind cell loss but also on the mechanisms behind their dysfunctions while still alive. This could enable us to both reduce cell loss and spreading, but also potentially to reverse some of the symptoms caused by dysfunctional cells that are not yet lost.

How did you end up where you are today?
I originally did a degree in medicine and were quickly drawn towards the world of research, in which you have countless possibilities for going your own directions and focusing on exactly what intrigues you the most.

What does a (local) strong neuroscience research network mean for you and your research?
A strong local community with people working in different fields and with different methods is very important for our research process. Many of the ideas that we come up with and want to test lie outside my own field of expertise. In Aarhus, we are lucky to have a closely connected network between different people, who are experts in very different fields and methods.
In our Parkinson's research, we collaborate closely with e.g. Marina Romero-Ramos who has great expertise in the use of animal models, Per Borghammer, who has great knowledge and skills when it comes to examining the neurodegenerative processes in patients via imaging, and Daniel Otzen, who is an expert when it comes to the behavior and aggregation of proteins such as α-synuclein
I believe that local and international collaborations play equal important roles. Local collaborations are crucial for the testing of hypotheses, while international connections with people from our own field is essential for the idea generation process and access to specialized techniques and reagents.

If you had unlimited resources to conduct a big, multidisciplinary neuroscience project, what would you like to do?
As mentioned earlier, I believe that Parkinson's disease progresses slowly for many, many years before the patients start to develop the characteristic symptoms.
I would like to conduct a longitudinal study of the different responses in different parts of the brain of our models, and thus investigate which mechanisms may be relevant at different points in the disease progression. This would require the use of some of the newest methods for studying cellular responses, which should be combined with collaborations with people who have access to actual patient brains – that is international collaborators.
We know that when it comes to Parkinson's disease it is crucial to make the diagnosis as early as possible and this kind of study would be important in order to discover biomarkers for the disease before the presence of symptoms.

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NeuroCampus – Inside out is a new initiative at Neuro-Campus Aarhus: Each month we will present interviews with group leaders and head clinicians from all corners of the NCA network. Stay tuned in our monthly newsletter or on our website: neurocampus.au.dk.