The neuroendocrine serine protease inhibitor neuroserpin and synaptic plasticity in the pituitary of *Xenopus laevis De Groot DM*, Martens GM Department of Molecular Animal Physiology, University of Nijmegen, Nijmegen

The molecular mechanism underlying synaptic plasticity and the formation of new synapses remain largely unknown. Several classes of proteins are involved in changing the strength of a synapse, including extracellular proteases and protease inhibitors. Neuroserpin is a member of the serpin family of serine protease inhibitors and is expressed mainly in neuronal and endocrine tissue. We identified neuroserpin in our model system Xenopus laevis. This amphibian can adapt its skin color to the color of the background. This adaptation process provides the opportunity to manipulate the activity of the melanotrope cells in the neurointermediate lobe (NIL) of the pituitary, as well as their regulatory neuronal input in vivo in a physiological way. Neuroserpin protein was detected in Xenopus brain and NIL lysates. In NILs of white-adapted animals, one specific band of 55 kDa was recognized by an anti-neuroserpin antibody. Interestingly, in NILs of black-adapted animals a second band was identified. This additional band appeared after 5 days of adaptation to a black background. The nature of this second band is unclear, but currently experiments are performed to see whether it consists of a neuroserpin dimer or a complex of neuroserpin and a target protease. To study the physiological role of neuroserpin, we use the technique of stable transgenesis in Xenopus. By using specific gene promoters we can drive transgene expression specifically to the NIL or neuronal tissue such as the retinal ganglion cells that form the optic nerve. In this way, a GFP-neuroserpin fusion protein was overexpressed in these tissues. F0 animals were analyzed and an F1 generation was generated. These animals will be used to analyze phenotypic changes compared to wild-type animals. For example, adaptation experiments will be performed to examine the possible effect of neuroserpin on synaptic plasticity. Furthermore, microscopic studies will be done to visualize possible neuronal phenotypes. In addition, retinal ganglion cells of transgenic tadpoles will be cultured and examined in vitro. Our study may lead to a better understanding of the role of neuroserpin in synaptic plasticity.

Dorien de Groot, Department of Molecular Animal Physiology, University of Nijmegen, Geert Grooteplein Zuid 28, 6525 GA Nijmegen, The Netherlands, e-mail <u>d.degroot@ncmls.kun.nl</u>

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