

Towards a Comprehension of the Structure of Mouse proNGF

Francesca Paoletti¹, Sonia Covaceuszach², Elisabeth Schwarz³, Milton Stubbs³, Rainer Rudolph³, Antonino Cattaneo^{1,2}, Dorian Lamba⁴,
¹SISSA-ISAS, Trieste. ²LayLine Genomics, Rome, Italy. ³Martin-Luther University Halle-Wittenberg, Halle (Saale), Germany. ⁴Istituto di Cristallografia - CNR, Trieste, Italy. E-mail: paoletti@sissa.it

The neurotrophin NGF (Nerve Growth Factor) is translated as a pro-protein of 27 kDa and cleaved by furin to mature NGF.

NGF is involved in the maintenance and growth of neurons, while the pro-peptide facilitates folding of NGF [1]. ProNGF is the predominant form of NGF in brain [2] and was found to be a high affinity ligand for p75 and to induce p75 dependent apoptosis [3]. The specific receptor for the proNGF is sortilin [4].

We focused on the biophysical biochemical characterization of the mouse proNGF, which was expressed in *E. coli*, refolded and purified. The native structure was proven by fluorescence and circular dichroism. The homogeneity of the protein preparation was tested through dynamic light scattering. We have started a robotic screening for crystallization conditions of the protein and are planning SAXS experiments.

[1] Rattenholl A., Ruoppolo M., Flagiello A., Monti M., Vinci F., Marino G., Lilie H., Schwarz E., Rudolph R., *J. Mol. Biol.*, 2001, **305**, 523. [2] Fahnstock M., Michalski B., Xu B., Coughlin M.D., *Mol. Cell. Neurosc.*, 2001, **18**, 210. [3] Lee R., Kermani P., Teng K.K., Hempstead B.L., *Science*, 2001, **294**, 1945. [4] Nykjaer A., Lee R., Teng K.K., Jansen P., Madsen P., Nielsen M.S., Jacobsen C., Kliemann M., Schwarz E., Willnow T.E., Hempstead B.L., Petersen C.M., *Nature*, 2004, **427**, 843.

Keywords: neurotrophin, protein refolding, biophysical biochemical characterization