

# An integrative structural biophysics approach to study the interactions between ATP and neurotrophins

*Tuesday, 26 September 2023 14:45 (15 minutes)*

The talk will present the application of an integrative structural biology approach to the field of neurotrophins. The prototype of the neurotrophin family, Nerve Growth Factor (NGF), is essential for the development and maintenance of neurons and is crucial in immune and endocrine systems and in the pain pathway. NGF precursor, proNGF, whose pro-peptide is an intrinsically unstructured domain (IUD), is endowed with different biological properties. The binding to TrkA, p75NTR and sortilin receptors activates the NGF/proNGF signaling pathways. Much is known about NGF in neuronal physiology. However few reports described essential endogenous ligands as modulators of NGF biology.

Recently, the binding of ATP to NGF was identified. To determine the molecular elements of this binding, we used integrative structural biology with solution NMR and a set of complementary biophysical and computational methodologies, to unveil for the first time the binding cartography of ATP to NGF [1] and proNGF [2]. The used methodologies will be briefly presented, as well as the scientific results. Our results prove that ATP is responsible of a modulating quinary interaction with NGF, and that ATP binding induces a change in the conformation and/or dynamics of proNGF, predominantly in the IUD pro-peptide. These results, thus, pinpoint ATP as a likely molecular modulator of NGF and proNGF signalling, in health and disease states, and help providing an explanation for the neurotrophins' biology in neurodegenerative conditions.

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**Session Classification:** Session