Understanding the molecular mechanisms of neurodegeneration is the overarching research theme of my lab, with the long-term goal of developing new therapeutic approaches for currently incurable neurodegenerative diseases. To this aim, we pursue an integrated approach at different scales, from the molecular to the cellular to the system level, also exploiting newly developed experimental tools and technologies.

We have discovered a pathway that causally links alterations in the NGF signaling in the adult brain to the development of a progressive neurodegeneration of the Alzheimer’s type. This provides the rationale for a new NGF-based therapeutic approach for Alzheimer’s disease, aimed at re-establishing the NGF homeostasis. However, developing an NGF-based drug requires solving the issue of the potent pain-inducing actions of NGF. Inspired by the rare genetic disease HSAN V (Hereditary Sensory Autonomic Neuropathy type V), we have developed “painless NGF” (hNGFp), a variant of human NGF that preserves its full neurotrophic properties, while having a tenfold reduced pain-sensitizing activity. This hNGFp molecule is currently being developed towards its clinical testing in man.

The broad effects resulting from interfering with NGF in the brain, and the broad neuroprotective actions of NGF when delivered to the brain, cannot be explained by NGF known actions on its neuronal target cells. This opens the question as to what is the cellular basis of these broad effects: which are the NGF target cells in the brain? Today we shall provide an answer to this question by describing the results of recent work in the lab.

Simona Capsoni (Associate Professor of Physiology at the University of Ferrara and at Scuola Normale Superiore) will describe a new mechanism, mediated by astrocyte and microglia cells, underpinning the broad and potent anti-amyloidogenic and neuroprotective actions of nasally delivered hNGFp to Alzheimer’s mouse models.

Alexia Tiberi (third year PhD student in Neuroscience at SNS) will show how NGF steers cortical microglia cells to a neuroprotective and anti-inflammatory phenotype. I will then step in, to
illustrate recent work, demonstrating that astrocytes are biosensors of ambient NGF levels and respond to reduced NGF levels by acquiring a neurotoxic A1 reactive phenotype.

Finally, Francesco Gobbo (last year PhD student in Neuroscience at SNS) will describe SYNACTIVE, a new method to visualize active synapses in vivo and to express optogenetic probes selectively at potentiated synapses. This will allow to interrogate neuronal circuits and neuron-glial interactions with synaptic optogenetic probes under physiological and neurodegeneration conditions.

Martedì 19 Dicembre 2017 ore 17 (Aula Magna, Scuola Medica)