

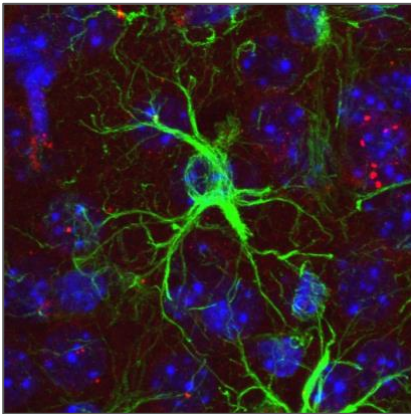
Master thesis project

Development of a new nanovector-mediated enzyme replacement therapy for Krabbe Disease: *in vitro* and *in vivo* testing

Dr. Marco Cecchini <marco.cecchini@nano.cnr.it>

NEST, Istituto Nanoscienze-CNR and Scuola Normale Superiore
Piazza San Silvestro 12
56127 Pisa (ITALY)
Phone: (+39) 050 509 459

Topic: Krabbe disease (KD) is a rapidly progressing childhood leukodystrophy triggered by deficit of the lysosomal enzyme galactosyl-ceramidase (GALC) and characterized by the accumulation of the cytotoxic sphingolipid psychosine (PSY) in the nervous system. Little is known about the exact molecular mechanisms by which PSY imparts toxicity and no cure is currently available for KD. Treatment is symptomatic and supportive only. Unfortunately, the systemic administration of GALC is not effective because of the presence of the blood brain barrier (BBB) that forbids the translocation of bulky proteins like GALC into the central nervous system. The NeuroSens group is developing a new strategy for GALC brain targeting based on polymeric nanoparticles functionalized with peptides for promoting the crossing of the BBB.



Objective:

- *in vitro* testing of the functionalized GALC loaded nanovector in primary murine and human Krabbe cells
- *in vivo* testing of the GALC loaded nanovectors in the natural mouse model of KD: the Twitcher mouse.

Methods: eukaryotic recombinant enzymes production, immortalized and primary cell cultures, standard fluorescence and confocal microscopy, fluorescent enzymatic assays, basic molecular biology techniques (SDS-PAGE, western blot, PCR, immunofluorescence), mice treatment and tissues characterization.

Further details on this research activity can be found in the website:

<http://web.nano.cnr.it/neurosens>

and in the following publications:

- Del Grosso, A., Antonini, S., Angella, L., Tonazzini, I., Signore, G., & Cecchini, M. (2016). **Lithium improves cell viability in psychosine-treated MO3.13 human oligodendrocyte cell line via autophagy activation.** Journal of neuroscience research, 94(11), 1246-1260.

- Voccoli, V., Tonazzini, I., Signore, G., Caleo, M., & Cecchini, M. (2014). **Role of extracellular calcium and mitochondrial oxygen species in psychosine-induced oligodendrocyte cell death.** Cell death & disease, 5(11), e1529.