**IBSCA research seminar**

Lecturer **Prof. Eran Perlson**
Dept. of Physiology and Pharmacology,
Sackler School of Medicine,
Tel Aviv University

**Title:**

# ALS as a subcellular mislocalization disease

## Abstract

Amyotrophic Lateral Sclerosis (ALS) is a lethal adult-onset motor neuron disease. Although the disease's etiology is not fully understood, it is thought to involve subcellular alterations in RNA metabolism. Recently, using both *in vitro* and *in vivo* ALS models, we demonstrated that alterations in miR126-5p regulates the secretion of muscle destabilizing factors such as Sema3A near MNs axons and facilitate a non-cell-autonomous mechanism underlying axon/NMJ degeneration in ALS. Here, we hypothesize that alterations in the spatial localization of Sema3A can lead to opposite effects in MNs biology. This complexity has to consider in ALS disease. While Sema3A at MNs cell somata activates survival and axon growth, at the distal axon, Sema3A results in axon degeneration. Furthermore, in MNs caring ALS C9orf72 and $SOD^{G93A}$ mutations, Sema3A application at the axons increase the interaction between CRMP4 and Dynein, which leads to a retrograde death signal and MNs loss. Thus, we discovered a novel mechanism underlying ALS pathology, in which spatial alterations of Sema3A signaling control motor neuron health.