ONLINE SEMINAR BY PROF. MARIO BORTOLOZZI

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June 4th, 2020 at 3:00 p.m.

Zoom Meeting ID: 947 1923 3989; Password: 469384

Title of the Seminar: **Biophysical investigation of the molecular pathogenesis of CMT1X neuropathy**

Abstract: Mutations of connexin 32 (Cx32) protein cause the X-linked form of Charcot–Marie–Tooth disease (CMT1X), a demyelinating peripheral neuropathy for which there is no cure. A growing body of evidence indicates that ATP release through Cx32 hemichannels in Schwann cells could be critical for nerve myelination, but it is unknown if CMT1X mutations alter the physiological mechanism that controls Cx32 hemichannel opening and ATP release.

Our study uncovered a link between CMT1X and Cx32 hemichannel dysfunction, suggesting a candidate peptide for treating the disease caused by the R220X mutation of Cx32. The investigation was carried out by a combination of *in vitro* fluorescence optical microscopy combined with patch clamp and *in silico* numerical simulations.

We recently complemented our biophysical approach by a cellular model based on induced pluripotent stem cells (iPSCs), derived from the same individual and differentiated into motor neurons and Schwann cells, which were subsequently co-cultured to mimic the peripheral nervous system.

Finally, we generated a mouse model carrying the R220X mutation which showed progressive demyelinating features compatible with CMT1X neuropathy.