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Prof. Gurcharan KAUR

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Venue - Zoom

Speaker - Prof. Gurcharan KAUR, PhD, FIAN, FNASc,
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Title - Unmasking therapeutic potential of a key neuroplasticity marker, PSA-NCAM: Our lab's journey

Abstract - The carbohydrate moiety polysialic acid (PSA) post-translationally added on the 5th Ig like domain of Neural Cell Adhesion Molecule (PSA-NCAM) is a key neuronal plasticity marker in both health and disease. With an aim to exploit the immense therapeutic potential of PSA-NCAM, our recent studies using drug re-tasking approach have focused on identification of synthetic PSA mimetics from NIH library of small molecules. 5-nonyloxytryptamine oxalate (5-NOT), Venorelbine and Epirubicin have been reported by our lab as potential PSA mimicking compounds and amongst these three molecules, 5-NOT was found to significantly promote functional recovery after spinal cord injury in mice. In order to further augment the beneficial effects of 5-NOT in neuroregeneration, we further used biomaterial-based approach using functionalized collagen-laminin (C/L) scaffolds and hydrogels impregnated with 5-NOT. In the *in vitro* 2D culture paradigm, 5-NOT in combination with C/L was observed to promote neurite outgrowth, migration and fasciculation in cerebellar neuronal cells, whereas, the cells in 3D culture systems demonstrated more ramification and complex Sholl profiles. Further, 5-NOT promoted the survival and neurite length of cortical neurons when co-cultured with glutamate challenged astrocytes. A paradigm of spinal cord compression injury in mice was further used with immediate, intraoperational application of C/L hydrogels impregnated with 5-NOT. The mice receiving 5-NOT containing C/L hydrogels demonstrated ~75% recovery of motor functions after 14 days of injury. Further, this effect was shown to be dependent on Erk-MAPK pathway of cell survival. The pre-clinical data based on biomaterial approach gave new insights for the role of PSA mimetic, 5-NOT containing hydrogels as growth and endurance promoting agent to speed up recovery after adult CNS injury.