

DANDRITE Topical Seminar by postdoc Mikhail Paveliev

Thursday 30 March 2017
10:15-12:00

Aud. 6, building 1170, 3rd floor
Ole Worms Allé 3, 8000 Aarhus C



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A role for the extracellular matrix in neurotrophic factor signaling?

Neurotrophic factors (NTFs) and extracellular matrix (ECM) are the two groups of tissue signaling molecules that are required for proper development of CNS and for its function in adulthood. Both neurotrophic factors and ECM are actively used for the development of therapies promoting posttraumatic regeneration in the injured brain and spinal cord. There is exceptionally strong demand for those new therapies as regeneration normally fails in the adult human CNS and such injuries lead to lifelong disabilities. Interestingly, the two major regulators of CNS regeneration – NTFs and ECM interact intensely with each other via direct molecular interactions and via signaling crosstalk. In our recent study we tested the NTF pleiotrophin (also known as HB-GAM) as a drug candidate for the treatment of CNS injuries. Pleiotrophin (like BDNF and many other NTFs) binds with high affinity to chondroitin sulfates – the major component of the brain ECM. We demonstrate that chondroitin sulfates are required for the ability of soluble pleiotrophin to induce neurite growth in cortical neurons. At the same time chondroitin sulfate by itself is known to act as a major inhibitor of axonal regeneration in the injured CNS in vivo. We used multiphoton imaging of regenerating dendrites and axons in living injured brain and spinal cord to demonstrate that pleiotrophin converts the chondroitin sulfate-containing posttraumatic scar ECM from inhibitor into a potent activator of axonal and dendritic regeneration. This type of functional interaction between NTFs and ECM may also have broader physiological implications in brain plasticity and learning.