

Poster presentation

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## Compartmentalized NF-kappaB activity in the axon initial segment

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The transcription factor NF-kappaB plays a pivotal role in the development and maintenance of the central nervous system and its constitutive activation in neurons has been previously reported. NF-kappaB is post-translationally activated upon phosphorylation of the IkappaBalpha inhibitory protein by the activated IkappaB kinase (IKKalpha/beta) and the subsequent degradation of IkappaBalpha by the proteasome. Recently, we had demonstrated an unexpected accumulation of three components of the NF-kappaB cascade in the axon initial segment (AIS): Activated IKK, phosphorylated IkappaBalpha and phosphorylated-p65(Ser536). These are all associated with detergent-insoluble cytoskeletal components of the AIS. We observed further compartmentalization as pIKKalpha/beta primarily associated with the membrane cytoskeleton, whereas pIkappaBalpha was sequestered to fasciculated microtubules. Colchicine-induced depolymerization of microtubules was associated with reduced sequestration of pIkappaBalpha in the AIS, which could be blocked by use of proteasome inhibitors like Mg-132 or Lactacystin. Concurrently, enhanced nuclear immunoreactivity for the NF-kappaB subunit p65 was noted. Using NF-kappaB-dependent reporter gene assays, a significant increase in NF-kappaB activity was observed after depolymerization of microtubules and this was inhibited by the microtubule-stabilizing drug paclitaxel. The use of transiently transfected, photoactivatable-GFP p65 fusion proteins will allow us to specifically analyse the compartmentalized signal transduction pathways in unique spatial and temporal resolution. Taken together, these observations provide strong evidence for compartmental-

ized activation of NF-kappaB in the AIS and modulation of neuronal NF-kappaB activity by microtubule dynamics.