A Novel Role for ROS in Neuronal Growth Cone Motility and Guidance

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Reactive Oxygen Species (ROS) not only have toxic effects when in abundance, but also have signaling functions in a number of cellular processes including differentiation, apoptosis, synaptic function, cell adhesion and migration. Whether ROS also act as signaling molecules controlling directional movements of neuronal growth cones during development and regeneration is unknown. We have recently found evidence that ROS affect dynamics and organization of the actin cytoskeleton in growth cones. Lowering cytoplasmic ROS levels in growth cones inhibits actin assembly at the leading edge, reduces retrograde F-actin flow as well as neurite outgrowth. Furthermore, we determined that a major source of ROS mediating these functions is NADPH oxidase (NOX) and not mitochondria. Immunolocalization of the NOX2 and p40phox subunits reveal the presence of a NOX2 complex in Aplysia growth cones. Interestingly, in unstimulated growth cones a significant fraction of the cytosolic subunit p40phox is associated with F-actin and not the plasma membrane. Stimulating growth cones with the adhesion protein apCAM increased NOX2/p40phox colocalization, suggesting adhesion-mediated NOX2 assembly and possibly activation. We are currently investigating downstream targets protein of redox signaling as well as upstream regulators. Our results support the novel hypothesis that ROS produced by a specific source, NADPH oxidase, regulate directional growth cone movement via controlling actin dynamics.