Axonal PPAR promotes neuronal regeneration after injury

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Abstract

PPARγ is a ligand-activated nuclear receptor best known for its involvement in adipogenesis and glucose homeostasis. PPARγ activity has also been associated with neuroprotection in different neurological disorders, but the mechanisms involved in PPARγ effects in the nervous system are still unknown. Here we describe a new functional role for PPARγ in neuronal responses to injury. We found both PPAR transcripts and protein within sensory axons and observed an increase in PPARγ protein levels after sciatic nerve crush. This was correlated with increased retrograde transport of PPARγ after injury, increased association of PPARγ with the molecular motor dynein, and increased nuclear accumulation of PPARγ in cell bodies of sensory neurons. Furthermore, PPARγ antagonists attenuated the response of sensory neurons to sciatic nerve injury, and inhibited axonal growth of both sensory and cortical neurons in culture. Thus, axonal PPARγ is involved in neuronal injury responses required for axonal regeneration. Since PPARγ is a major molecular target of the thiazolidinedione (TZD) class of drugs used in the treatment of type II diabetes, several pharmaceutical agents with acceptable safety profiles in humans are available. Our findings provide motivation and rationale for the evaluation of such agents for efficacy in central and peripheral nerve injuries. Develop Neurobiol 76: 688–701, 2016

Keywords

PPARγ, regeneration, axon retrograde transport, dynein