Functional Activity of NLRP1 in Axon Pruning

Kiran Kelly-Rajan

During development of the nervous system, axon pruning allows neurons to selectively degrade their axons to refine connections, while keeping the soma intact. Like apoptosis, this process relies on caspase-mediated cell degradation as its effector mechanism, using caspases 3, 6, and 9. Apoptosis and axon pruning even share several upstream proteins, such as cJun and Bax, which are required for both processes to occur. Interestingly, the Deshmukh Lab has found that NOD-like receptor pyrin domain containing 1 (NLRP1) is required for axon pruning, as well as caspase 1. Recently, NLRP1 was found to be activated in a unique mechanism, involving autocleavage of an internal domain and proteasome mediated degradation which releases the active component of NLRP1 to trigger of caspase 1 activation. Autocleavage and activation of NLRP1 occurs in a sequence known as the function-to-find domain (FIIND). While NLRP1 was identified as crucial for axon pruning, it is unknown how NLRP1 is activated in this non-immune context. This experiment assesses whether the FIIND region is required for axon pruning to occur, the mechanism which was identified for its immune function.