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Taking advantage of adeno-associated viral vector (AAV) transduction, We expressed the neural cell adhesion molecule L1 in the spinal cord of adult mice after compression injury. Expression of L1 was observed up to 10 mm rostral and 10 mm caudal to the lesion center 5 weeks after infection, the longest time period studied. L1 expression was not detectable in the fibronectin-positive lesion core. Overexpression of L1 improved motor functional recovery. Using Western blotting we found that the expression of the neurite outgrowth inhibitory chondroitin sulfate proteoglycan NG2 was drastically decreased in AAV-L1 treated spinal cords, along with reduction of the reactive astroglial marker GFAP, suggesting that besides acting as a neurite-ougrowth promoting molecule, overexpression of L1 in all neural cell types of the spinal cord promotes functional recovery by reducing inhibitory mechanisms.

Currently we are carrying out the experiments about the time course of the L1 expression transduced by the AAV vector. We are going to detect the L1 levels with Western blot in the injured mouse spinal cord 1 week, 2 weeks, 3 weeks and 5 weeks after the AAV transduction. This experiment will demonstrate when the earliest onset of the L1. Besides this, we are also checking the corticospinal tract axons regeneration and serotonergic axons regeneration in AAV-L1 as well as in AAV-GFP transduced mice. These are to find out the morphological basis of the improved locomotor functional recovery. Meanwhile, the experiments of detecting microglia in AAV-L1 and AAV-GFP transduced mice are being carried out. This is to demonstrate whether L1 overexpression is able to influence the immunological response in the injured spinal cord.

In summary, the data we got matched the prediction that L1 overexpression mediated by AAV was capable of improving the locomotor recovery. We have been carrying on the experiments to elucidate the underlying mechanisms of this improvement. Up to now, it is reasonable to think that the downregulation of the inhibitory molecules such as NG2 and inhibitory cellular components such as reactive astrocytes might be partially responsible for this achievement.