HDAC1 mediates p53 deacetylation in dorsal root ganglia after sciatic nerve transection

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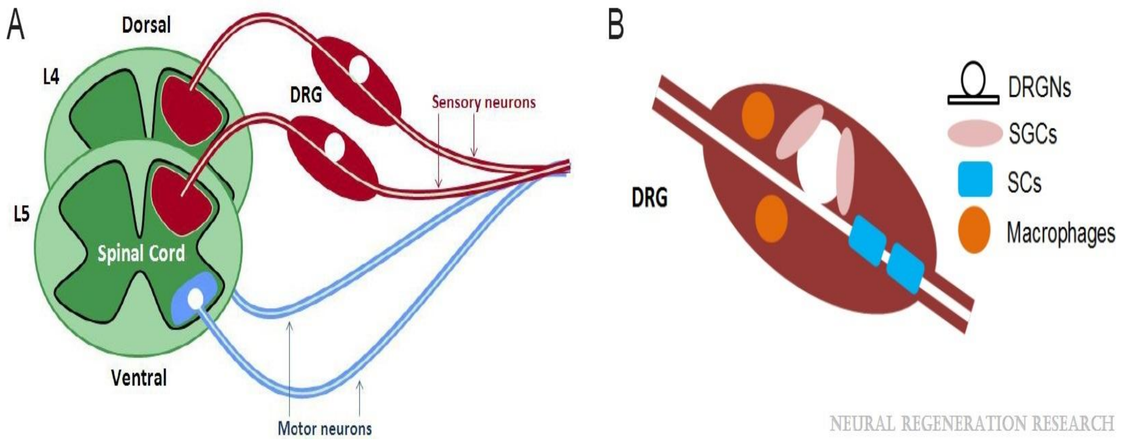
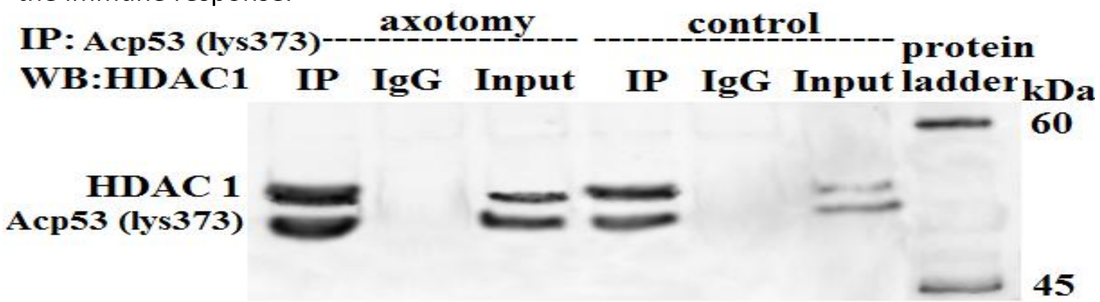
Background and aims. Neurotrauma is among the main causes of human disability and mortality. In our previous works, immunofluorescence microscopy and immunoblotting showed the overexpression of HDAC1 and HDAC2 in the dorsal root ganglia (DRG) at 1-4 hours after sciatic nerve transection as the earliest proapoptotic event. This was followed by the upregulation of proapoptotic protein p53 at 24 hours post-axotomy. In DRG neurons, HDAC1 was initially upregulated at one hour post-axotomy but then redistributed together with p53 from the nuclei to the cytoplasm at 24 h post-axotomy. Administration of sodium valproate, a non-selective inhibitor of I class HDACs, prevented axotomy-induced p53 cytoplasma translocation and reduced overexpression of p53 in the axotomized DRG. To examine the possible interaction between HDAC1 or HDAC2 and p53, we performed co-immunoprecipitation and Duolink® proximity ligation assay (PLA®) for endogenous HDAC1 or HDAC2 and p53.

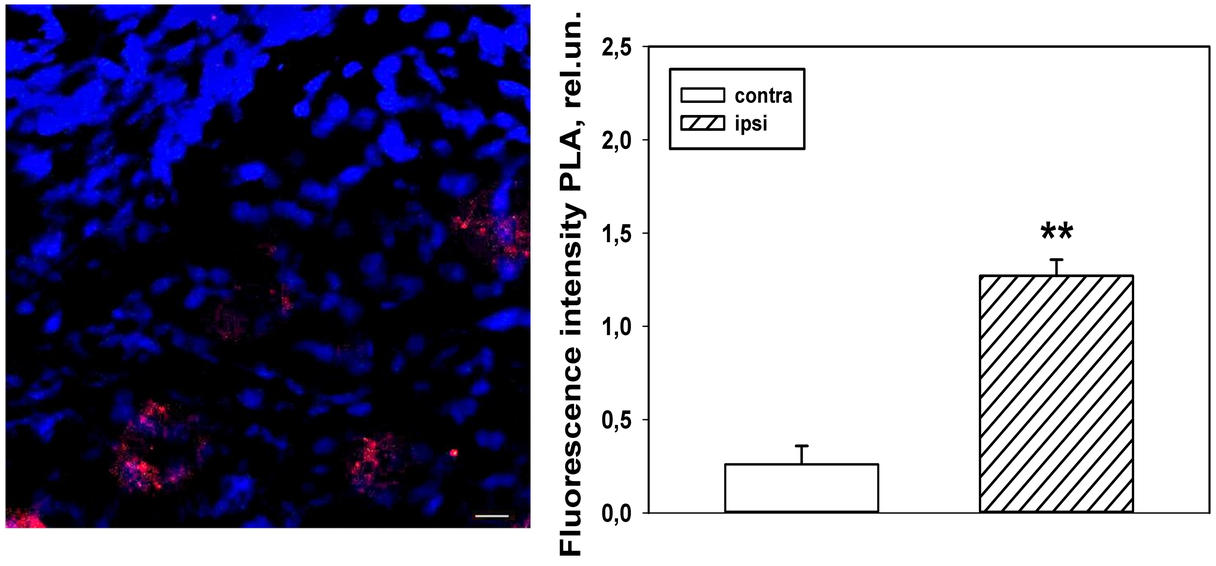


Schematic diagram of dorsal root ganglion (DRG) structure and cell types composition. **(A)** A diagram of a DRG. The sensory neurons cell body is located within the DRG, with central and peripheral axon extensions. The motor neurons project out from the ventral horn of the spinal cord and combine with the peripheral sensory neurons to form the sciatic nerve. **(B)** An illustration of the prominent cells within the DRG. The satellite glial cells (SGCs) surround the neuronal cell bodies, whilst the Schwann cells (SCs) ensheath and myelinate single or multiple axon fibres, and finally the macrophages are present for the immune response.



The result of immunoblotting for coimmunoprecipitation of endogenous Acp53 and HDAC1 in the cytoplasmic fraction of DRG 24 hours after axotomy.

Results. Co-IP and PLA data indicated that HDAC1, but not HDAC2 and p53, do interact. Thus, HDAC1 mediates p53 deacetylation in cytoplasm fraction DRG after axotomy and so is involved in the axotomy-induced injury of DRG neurons and glial cells. HDAC1 and downstream target factors, for example p53, may be considered promising molecular targets for the development of potential neuroprotective agents.



Representative images of Duo link in situ PLA showing that there is a direct physical interaction between Asp53 (K373)/HDAC1

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