

Protrudin functions from the endoplasmic reticulum to support axon regeneration in the adult CNS

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Adult mammalian central nervous system axons have intrinsically poor regenerative capacity, so axonal injury has permanent consequences. One approach to enhancing regeneration is to increase the axonal supply of growth molecules and organelles. We achieved this by expressing the adaptor molecule Protrudin which is normally found at low levels in non-regenerative neurons. Elevated Protrudin expression enabled robust central nervous system regeneration both in vitro in primary cortical neurons and in vivo in the injured adult optic nerve. Protrudin overexpression facilitated the accumulation of endoplasmic reticulum, integrins and Rab11 endosomes in the distal axon, whilst removing Protrudin's endoplasmic reticulum localization, kinesin-binding or phosphoinositide-binding properties abrogated the regenerative effects. These results demonstrate that Protrudin promotes regeneration by functioning as a scaffold to link axonal organelles, motors and membranes, establishing important roles for these cellular components in mediating regeneration in the adult central nervous system.

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