1. Relationship: (Author of)
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3. Title: The regulation of peripheral nerve homeostasis, regeneration and tumourigenesis
4. Abstract:

Peripheral nerves are regenerative, with Schwann cells (SCs), the main glial cells of the peripheral nervous system, orchestrating multiple aspects of the multicellular regenerative process. A regenerating nerve resembles tumours that form in this tissue in patients with Neurofibromatosis Type 1 (NF1) and in a mouse model we have developed, we have identified a key role for the injured microenvironment in stimulating tumour formation derived from adult Nf1$^{-/-}$ myelinating Schwann cells (mSCs).

Here, we have investigated the homeostatic turnover of peripheral nerve and how this changes following injury in order to understand how the injured microenvironment could contribute to tumour formation. We find that mSCs do not turnover in adulthood. Following injury however, all mSCs proliferate and dedifferentiate to progenitor-like SCs, which contribute to the nerve regeneration process without the requirement for a distinct SC stem cell population. Moreover, lineage analysis, demonstrated that mSC derived cells retain the SC lineage but can switch from a mSC to a non-myelinating SC fate during nerve regeneration. In contrast, during tumourigenesis, Nf1$^{-/-}$ mSCs lose this lineage restriction.

To identify the microenvironmental pro- and anti- tumourigenic signals involved in the early stages of tumourigenesis, we have characterised the early stages of tumour formation in our mouse model to identify the point of divergence between tissue regeneration and tumour formation. We subsequently performed a molecular analysis at this time-point that identified several potential pro- tumourigenic signals at the injury site. This work provides a further illustration of the distinct mechanisms that tissues use to maintain and repair themselves. Moreover, it provides insight into links between tissue repair and tumourigenesis and how studying these processes may provide new approaches for the treatment of this disease.

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