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# Perinatal or Adult *Nf1* Inactivation using Tamoxifen-inducible PlpCre Each Cause Neurofibroma Formation

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## OBJECTIVES

Neurofibromas are tumors initiated by biallelic mutation of the *NF1* tumor suppressor gene in the Schwann cell lineage. One idea within the field suggests that *Nf1* loss must occur within progenitor cells present within a critical window during Schwann cell development in order for neurofibromas to form. To test this hypothesis and to examine whether myelinating Schwann cells can serve as a neurofibroma cell of origin, *Nf1* loss was induced at perinatal or adult timepoints using a tamoxifen-inducible Plp-CreERT driver.

## RESULTS

Perinatal loss of *Nf1* resulted in small neurofibromas late in life, while adult loss caused large neurofibromas and morbidity beginning 4 months after onset of *Nf1* loss. PLP-CreERT recombination (EGFP+ cells) occurred in: satellite cells, S100+ myelinating Schwann cells, and p75+ cells. Plp-CreERT nerves and neurofibromas contained cells with Remak bundle disruption; however, no recombination within GFAP+ non-myelinating Schwann cells was identified. Extramedullary lympho-hematopoietic expansion that contained EGFP+/Sca-1+ stromal cells amongst EGFP-negative lympho-hematopoietic cells was also observed.

## CONCLUSIONS/SIGNIFICANCE

Neurofibroma formation is not restricted to loss of *Nf1* in embryonic life, but can be triggered by *Nf1* loss throughout life. Although all neurofibroma models and human samples have Remak bundle disruption (leading to the assumption that *Nf1* loss within the non-myelinating Schwann cell may be vital for tumor formation), there was no EGFP+ recombination within GFAP+ non-myelinating Schwann cells ? eliminating the GFAP+ non-myelinating Schwann cell as the cell of origin for neurofibroma formation.

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