

## The Paper Explained

### PROBLEM:

Neurofibromatosis type 1 (NF1) is one of the most common inherited human diseases worldwide. Effective therapies are lacking. Peripheral nerve sheath tumors (neurofibromas) are the hallmark of NF1. They consist of benign dermal and plexiform subtypes, but plexiform neurofibroma can transform to malignant peripheral nerve sheath tumor (MPNST), a highly aggressive, life threatening sarcoma. Neurofibromas are composed of multiple cell types, including Schwann cells, the pathogenic cell type of NF1. The molecular changes that drive tumorigenesis are largely unknown.

### RESULTS:

The authors used DNA microarrays to profile gene expression in normal Schwann cells, Schwann cells cultured from primary benign neurofibromas (dermal and plexiform subtypes), MPNST cell lines, and solid tumors. They find that neurofibromas repress gene programmes normally expressed in late-developing immature Schwann cells, while MPNSTs activate gene programmes normally expressed earlier in development at the neural crest stage. Strong expression of the transcription factor SOX9 is seen in neurofibroma and MPNST tissue sections, while schwannomas show weak or absent expression. Synovial sarcomas, which may histologically mimic MPNST, are mainly negative. Reduction of SOX9 expression in MPNST cell lines causes cell death.

### IMPACT:

SOX9 expression provides a biomarker of neurofibroma and MPNST. Therapeutics aimed at decreasing SOX9 expression or SOX9 transcriptional targets represents a strategy for killing MPNST cells.