SKIN CANCER (OTHER THAN MELANOMA)

A NOVEL MODEL OF CUTANEOUS NEUROFIBROMA THAT DECIPHERS ITS DEVELOPMENTAL ORIGIN AND SUSCEPTIBILITY TO MODIFICATION BY THE HIPPO PATHWAY

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Introduction: Dermal or cutaneous neurofibromas (cNF) affect most adults with Neurofibromatosis Type 1 (NF1) and are a major source of emotional and physical distress as NF1 patients can have thousands of these tumors covering most of their skin. Thus, patients with NF1 often identify these tumors as their greatest burden. To date, there is no available medical treatment for cNF, no known way to prevent them from developing. The major barriers that impede progress in this field are the lack of accurate models of these common cNF tumors for drug evaluation and a limited understanding of their pathogenesis as well as the identity of specific cell of origin that directly gives rise to cNF.

Objective: The aim of this study is to create novel cNF model for elucidating the molecular mechanism and preclinical drug screening.

Methods: We take advantage of genetic labeling for cell lineage tracing to identify mouse neural crest Cre lines that are expressed in the sub-population of Schwann cell lineage that give rise to cNF when NF1 is deleted.

Results: We discovered that Homeobox B transcription factor serve as the lineage marker to trace the developmental origin of cNF, generating novel mouse model that spontaneously develops both cutaneous and plexiform neurofibroma. In addition, we discovered that modulation of the Hippo pathway acts as a modifier to promote neurofibromagenesis, suggesting that dampen the Hippo pathway may serve as part of the comprehensive treatment approach for neurofibroma.

Conclusions: This study provides insights into the developmental origin of cNF, the most common tumor in NF1, and generates the first mouse model that faithfully recapitulates both human cutaneous and plexiform neurofibroma. This novel mouse model has begun to yield

vital clues to neurofibroma pathogenesis and now opens the doors for deciphering the evolution of cNF to identify potential effective therapies.