ABSTRACT

MATERIALS AND METHODS FOR SUPPRESSING AND/OR TREATING NEUROFIBROMA AND RELATED TUMORS

Germline mutations in the NF1 tumor suppressor gene cause Von Recklinghausen's neurofibromatosis type 1 (NF1), a common genetic disorder of the nervous system characterized by plexiform neurofibroma development. Using adoptive transfer of hematopoietic cells, we establish that NF1 heterozygosity of bone marrow derived cells in the tumor microenvironment is sufficient to allow neurofibroma progression in the context of Schwann cell nullizygosity. Further, genetic or pharmacologic attenuation of the c-kit signaling pathway in hematopoietic cells greatly diminishes neurofibroma initiation and progression. These studies identify haploinsufficient hematopoietic cells and the c-kit receptor as therapeutic targets for preventing plexiform neurofibromas and implicate mast cells as critical mediators of tumor initiation. Administering therapeutically effective doses of a tyrosine kinase inhibitor such as the compound imatinib mesylate to a patient in need thereof to treat tumors in a human patient afflicted with plexiform neurofibroma.

Figure 6