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Double somatic SMARCB1 and NF2 mutations in sporadic spinal schwannoma.

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In sporadic schwannomas, inactivation of both copies of the NF2 tumor suppressor gene on 22q is common. Constitutional mutations of SMARCB1 are responsible of schwannomatosis, an inherited tumor predisposition syndrome, characterized by the development of multiple schwannomas. We analysed the frequency of copy number changes on chromosome 22 and the mutation of NF2 and SMARCB1 in 26 sporadic schwannomas. We found two spinal schwannomas with an identical somatic missense mutation in SMARCB1 exon 9: p.(Arg377His). Both SMARCB1 mutated schwannomas had LOH of 22q and one of them harbored an inactivating mutation of NF2. The p.(Arg377His) change was not found in a series of 28 vestibular schwannomas. Our data indicate that mutations affecting SMARCB1 play a role in the development or progression of a small subset of spinal schwannomas and that biallelic inactivation of SMARCB1 may cooperate with deficiency of NF2 function in schwannoma tumorigenesis according to the "four-hit/three events" mechanism of tumorigenesis that we demonstrated in schwannomatosis-associated schwannomas.

KEYWORDS: NF2; **Neurofibromatosis type 2**; SMARCB1; Schwannomatosis

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