Whole exome sequencing of sporadic cerebellar hemangioblastoma

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Introduction

Cerebellar Hemangioblastomas of the CNS can occur sporadically or, frequently, as part of von Hippel-Lindau (VHL) syndrome. To date, genetic evaluation of sporadic hemagioblastomas has been limited to epigenetic and mutational characterization of the VHL gene, located in chromosome 3p. Mutations in the VHL gene are known to be associated with von Hippel-Lindau syndrome in autosomal dominant fashion.

Methods

In an effort to further genetically characterize these lesions, we used whole-exome sequence analysis to study 16 blood matched sporadic hemangioblastomas tumor samples from patients without diagnosed von Hippel-Lindau syndrome.

Results

Germline analysis confirmed the patients had no bloodline VHL gene mutations. Somatic analysis of the blood matched tumor pairs identified nine somatic VHL gene mutations (56%). Furthermore, copy number variant (CNV) analysis and LOH analysis found alterations in chromosome 3 in eleven of the 16 samples (69%). Only 2 of the 16 samples (13%) had neither a sporadic mutation of the VHL gene, CNV alterations or LOH at chromosome 3p.

Conclusions

Our findings further confirm the involvement of the VHL gene and chromosome 3 mutations in this disease process, and underscore the importance of VHL pathway in sporadic hemangioblastomas.

Learning Objectives

By the conclusion of the session, participants should be able to: 1) Better understand the genetic profile of hemangioblastomas. 2) Understand the relationship between sporadic cerebellar hemangioblastomas and mutations in the VHL gene and chromosome 3.

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