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Changes on Chromosome 18 are Involved in Both Sporadic and Familial Ileal Carcinoid Tumor Development

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Background: The small intestine endocrine carcinoma (ileal carcinoid) is a clinically distinct endocrine tumor which produces and secretes serotonin. It is generally considered as a sporadic disease and its molecular etiology is poorly understood. We have identified nine families with an ileal carcinoid tumor diagnosed in two or more individuals. This investigation was performed to compare genetic changes detected in familial cases to those found in sporadic tumors with an aim to reveal genetic aberrations behind carcinoid tumor development.

Methods: Clinical and molecular studies of 55 sporadic and familial patients diagnosed with ileal carcinoids were performed. Molecular analyses of 61 tumors from 45 individuals, including eight familial and 37 sporadic patients, aimed at determination of global copy number aberrations using BAC and Illumina SNP arrays.

Results: Nine pedigrees encompassing 23 affected subjects were established, showing a picture consistent with an autosomal dominant mode of inheritance. Familial and sporadic patients demonstrated an indistinguishable clinical picture concerning tumor spread and hormone levels. Chromosome 18 aberrations were identified in both sporadic (100 %) and in familial tumors (38%). Other, less frequent aberrations were also common for both groups. Frequent gain of chromosome 7 was exclusively observed in metastases, when patient matched primary tumors and metastases were compared.

Conclusion: The clinical and molecular similarities identified between sporadic and familial cases indicate a common pathogenetic mechanism involved in tumor initiation. We suggest that the familial variant of ileal carcinoid represents a previously unrecognized autosomal dominant inherited tumor disease. Based

on our clinical findings we propose that patients presenting with abdominal pain or hormone-related symptoms and a positive family history of ileal carcinoid should be investigated on a wide indication for biochemical and radiological signs of such tumors.