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Mutations of the TGF-β RI gene are uncommon

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Introduction

The molecular basis of metastasis is poorly understood. No single metastasis gene or specific genetic alteration that may be responsible for metastases has yet been identified. A recent paper (Chen T *et al*, *Cancer Res* 1999, **58**:4805-4810) reported for the first time that mutations in the TGFβ receptor type I (RI) gene were associated with human cancer. Specifically, a C to A transversion at nucleotide 1160 of the gene, which would result in a serine to tyrosine substitution at codon 387 (S387Y), was described. In that study, 2 of 31 primary breast cancers and 5 of 12 lymph node metastases showed the mutation, leaving the authors to infer an association with metastatic progression.

Aims

To screen a variety of adenocarcinoma metastases for possible mutations of the TGF-β RI gene.

Comments

Genes such as nm23 have been shown to play an important role in metastatic progression; however, there is a lack of compelling data regarding genetic alterations associated with this critical stage of pathogenesis. The earlier report of specific mutations in the TGF-β RI gene in metastatic tissue opened a new avenue for investigation. There is a clear discrepancy, however, between this paper and the earlier report of a high frequency of S387Y mutations in the TGF-β RI gene in breast cancer metastases. The reasons for this remain a matter for conjecture, and further work is required to clarify the role of the TGF-β RI gene in the pathogenesis of cancer.

Methods

Lymph node metastases from 20 breast cancers, 15 pulmonary adenocarcinomas and 13 colorectal adenocarcinomas were collected and tumor cells microdissected from formalin-fixed, paraffin-embedded archival material. Lysates were used directly in a PCR reaction specifically designed to flank nucleotide 1160 of the TGF-β RI gene, where the S387Y mutation was reported. Single-stranded conformational polymorphism (SSCP) and sequencing were used to screen for the mutation.

Results

No mutations in any of the breast, lung or colon cancer metastases were detected by SSCP. Subsequent sequencing confirmed that, for the specific fragment amplified to include nucleotide 1160, only the wild-type sequence was present in all the samples tested.

Discussion

The data presented here conflict with those published in the earlier paper by Chen and co-workers. There is substantial evidence that disruption of the TGFβ signalling pathway can play a role in the pathogenesis of human cancers, including breast cancer, and the RI gene would seem to be a reasonable target for mutations that contribute to the cancer phenotype. This paper suggests, however, that contrary to the previous study, the S387Y mutation in the RI gene is uncommon in adenocarcinomas, including breast cancer.

References

1. Anbazhagan R, Bornman DM, Johnston JC, Westra WH, Gabrielson E: The S387Y mutation of the transforming growth factor-β receptor type I gene is uncommon in metastases of breast cancer and other common types of adenocarcinoma. Cancer Res. 1999, 59: 3363-3364.