Aurora kinase A in Barrett's carcinogenesis.


Source

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Abstract

In Barrett's mucosa, both aneuploidy and TP53 mutations are consistently recognized as markers of an increased risk of Barrett's adenocarcinoma. Overexpression of the mitotic kinase encoding gene (AURKA) results in chromosome instability (assessed from the micronuclei count) and ultimately in aneuploidy. Eighty-seven esophageal biopsy samples representative of all the phenotypic lesions occurring in the multistep process of Barrett's carcinogenesis (gastric metaplasia in 25, intestinal metaplasia in 25, low-grade intraepithelial neoplasia in 16, high-grade intraepithelial neoplasia in 11, and Barrett's adenocarcinoma in 10) were obtained from long segments of Barrett's mucosa. Twenty-five additional biopsy samples of native esophageal mucosa were used for control purposes. In all tissue samples, the immunohistochemical expression of both AURKA and TP53 gene products was scored; and the micronuclei index was calculated. AURKA immunostaining increased progressively and significantly along with dedifferentiation of the histologic phenotype (P < .001). Nine of 10 Barrett's adenocarcinomas showed AURKA immunostaining. AURKA expression correlated significantly with p53 expression and the micronuclei index (both Ps < .001). AURKA overexpression is significantly associated with Barrett's mucosa progressing to Barrett's adenocarcinoma and contributes to esophageal carcinogenesis via chromosome instability. The identification of AURKA as a novel molecular target of cancer progression in Barrett's mucosa provides a lead for the development of new therapeutic approaches in Barrett's mucosa patients.