Telomerase activity and expression of human telomerase catalytic subunit gene in esophageal tissues

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Background. Telomerase, the ribonucleoprotein enzyme that synthesizes telomeric DNA, is thought to be necessary for cellular immortality and carcinogenesis. Telomerase activity is associated with the majority of malignant human cancers. The mRNA that encodes the telomerase catalytic subunit (human telomerase repeat transcriptase; hTERT) has recently been identified, and the expression of the hTERT gene is thought to regulate the activation of telomerase. However, the expression of hTERT mRNA in esophageal tissues has not been reported. We investigated hTERT gene expression in cancerous and noncancerous esophageal tissues, and determined the relationship between hTERT mRNA expression and telomerase activity.

Methods. Tissues from esophageal carcinomas in 14 patients, reflux esophagitis in 12 patients, esophageal acanthosis in 2 patients, esophageal papilloma in 1 patient, radiation esophagitis in 1 patient, and normal esophageal epithelium in 11 patients (including 3 specimens of normal epithelium from patients with esophageal carcinoma) were examined. All specimens were taken endoscopically. hTERT gene expression was investigated using reverse transcription-polymerase chain reaction (RT-PCR). Quantitative analysis of telomerase activity was analyzed by fluorescence telomeric repeat amplification protocol (F-TRAP) assay.

Results. Thirteen of the 14 (93%) esophageal carcinoma specimens expressed hTERT mRNA and revealed detectable telomerase activity. Noncancerous esophageal lesions had not only hTERT mRNA expression with a high frequency (14 of 16 cases; 88%) but also detectable telomerase activity (12 of 13 cases; 92%). Normal esophageal epithelium also highly expressed hTERT mRNA (10 of 11 cases; 91%) and revealed detectable telomerase activity (all 9 cases; 100%). In 32 of the 35 specimens analyzed for both hTERT mRNA and telomerase activity (91%), the expression of hTERT mRNA was consistent with detectable telomerase activity.

Conclusions. The expression of hTERT mRNA was detected not only in cancerous but also in noncancerous esophageal tissues at a high frequency. This result was different from that reported for other gastrointestinal epithelium. Moreover, telomerase activity in esophageal carcinoma was significantly stronger than that in reflux esophagitis and normal epithelium. In addition, there was a strong relationship between the detection of telomerase activity and the expression of hTERT mRNA in cancerous and noncancerous esophageal tissues. Thus, the qualitative analysis of hTERT mRNA expression may not be useful as a biomarker of carcinoma in esophageal tissues. Nevertheless, the quantitative analysis of telomerase activity may be somewhat useful.

Key words: telomerase activity, human telomerase reverse transcriptase (hTERT), esophageal carcinoma, normal esophageal epithelium

Introduction

Esophageal squamous cell carcinoma is a frequent malignancy in Japan and in certain areas of China. Several studies have shown that the pathogenesis of esophageal squamous carcinomas involves the functional loss of a tumor-suppressor gene, such as the p53 gene mutation, and allele loss of chromosomal loci, such as 17p. Recently, cell immortalization has been found to be a very important event in carcinogenesis. Cell immortalization requires the activation of telomerase, an enzyme essential for stabilizing telomere length. Telomerase is...
This is a text document discussing the expression of hTERT in esophageal tissues. It mentions the enzyme's role in maintaining telomere length and its activation in reproductive and cancer cells. The document describes the development of the TRAP assay and references the work of Kim et al. in 1994. It also refers to the identification of hTERT mRNA by Nakamura et al. in 1997 and Bodnar et al.'s report of increased telomerase activity and lifespan extension with hTERT gene transfection in normal cells. The text then details the investigation of hTERT expression and telomerase activity in cancerous and noncancerous esophageal tissues, with a table summarizing patient characteristics and the results of the study.