

A Proposed New Definition for the Concept of Precancerous Conditions

There is a general consensus that precancerous lesions represent a morphologically recognizable entity in which carcinoma is significantly more likely to occur than in their apparently normal counterpart tissues, and that precancerous conditions represent a generalized state associated with a significantly increased risk of cancer. Clinically, it is considered that such lesions and conditions are associated with an increased risk of carcinoma development if they are left untreated. The term “precancerous condition” was first coined in 1875 by the Romanian, Professor Victor Babeş.

Typical examples of precancerous conditions include actinic keratosis, oral leukoplakia, Barrett's esophagus, atrophic gastritis, ulcerative colitis, cervical dysplasia, and chronic hepatitis.

We have conducted systematic studies of telomere length and chromosomal instability in many tissues, both with and without precancerous lesions, and in precancerous conditions and carcinomas (1-9), including actinic keratosis (1), oral leukoplakia (2), and Barrett's esophagus (3), which were always found to have shorter telomeres with associated chromosomal instability, relative to controls. Other groups have also demonstrated telomere shortening and chromosomal instability in ulcerative colitis (10), dysplasia of the uterine cervix (11), and chronic hepatitis (12). It has been suggested that critical shortening of telomeres causes chromosomal instability, during both progression of papillary urothelial neoplasms (4) and normal cellular aging (12).

Actinic keratosis (1) and oral leukoplakia (2), PanIN (9) are all characterized by short telomeres, and arise from histologically normal epithelium with short telomeres. Background tissues without atypical changes, but associated with small squamous cell carcinomas *in situ* of the oral mucosa (5) and esophagus (6), have also been shown to have shorter telomeres and greater chromosomal instability than normal tissues unassociated with carcinoma. Furthermore, normal duct epithelium without atypical changes associated with pancreatic cancer, have also been shown to have shorter telomeres (9).

Therefore, we consider that premalignant conditions including precancerous lesions can be newly defined as tissues with telomere dysfunction and chromosomal instability, with or without morphologic changes, and this concept was defined for the first time in our recent papers (1, 2).

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