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HMG2 and PLAG1 protein expression in Pleomorphic Adenoma Tumorigenesis and its recurrence and in the progression to Carcinoma ex-Pleomorphic Adenoma

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Abstract

The Pleomorphic Adenoma (PA) is the most common neoplasm of salivary glands. Recurrences of APs are common and increase the probability of the malignant transformation giving rise to the Carcinoma Ex Pleomorphic Adenoma (CXPA), which, although rare, is an aggressive tumor with frequent metastasis and death related to the disease. As previously reported in the literature, the Pleomorphic Adenoma Gene 1 (PLAG1) and High Mobility Group AT-hook 2 (HMGA2) genes are associated with the onset and progression of PAs and CXPAs. HMGA2 plays a role in the architectural transcription factor, modulating the threedimensional conformation of the DNA and consequently modulating the expression of several genes. The PLAG1 gene is involved in cell proliferation through the control of various target genes. In normal tissues, its activity is high during embryonic and fetal development, but in adult life, however, its participation is low or absent. The protein expression of PLAG1 and HMGA2 in 38 cases of PA, 36 cases of Recurrent PA (RPA) and 41 cases of CXAP was analyzed.

The histological subtype and degree of tumor progression were considered. A significant association of PLAG1 with PAs was found (89.5%), while the HMGA2 gene protein was presented with a relevant association with the malignant counterpart of the disease (48.78%). A higher prevalence of HMGA2 protein expression in high grade and aggressive tumors considering the histological subtype and degree of tumor progression was observed. PLAG1 protein expression was lower when PA underwent malignant transformation, possibly due to other pathway activation and different clone cells.

In addition, PLAG1 protein expression was present mainly in low-grade carcinomas and in cases with the early phase of invasion probably due to its property of regulation of oncogene-induced cell senescence.

Cupriavidus necator H16 (also known as Ralstonia eutropha H16) is a Gram-negative bacterium that belongs to the order Burkholderiales, class Betaproteobacteria. H16 has been isolated from a soil near Goettingen, Germany, almost 60 years ago (Schlegel et al. 1961a, b; Wilde 1962). Since then, it has become the most-studied hydrogen-oxidising 'Knallgas' bacterium with best-characterised poly(3-hydroxybutyrate) (PHB) metabolism.

Cupriavidus necator H16 is a facultative anaerobe, which can switch to anaerobic respiration by using NO3 and NO2 as electron acceptors. It grows utilizing a variety of organic substrates ranging from sugars, fatty acids, amino acids and citric acid cycle intermediates. It is also capable to fix directly a carbon dioxide (CO2) through the CBB cycle using hydrogen as the energy source (Bowien and Kusian 2002), making it a useful organism for studying mixotrophic and autotrophic metabolism.

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