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Cytochrome Family's & Oral Cancer: A Mini Review

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Abstract

Betel quid (BQ) products have been classified by the International Agency for Research on Cancer (IARC) as group I human carcinogens that are associated with an elevated risk of oral cancers. The human genome encodes fifty-seven cytochrome P45O (P45Oor CYP) proteins. The majority of these are involved in the metabolism of steroids, bile acids, fatty acids and xenobiotic compound which activate carcinogens. The present paper focuses on the relationship of cytochrome families with oral cancer induced by betel quid.

Keywords: *Cytochrome family, CYP2A6 gene, Betel Quid (BQ), Oral Cancer.*

1. INTRODUCTION

The cytochrome P450 (CYP) is a large super family of integral membrane conserved proteins present in animals, plants, and microorganisms [1]. The CYP isoenzyme super family comprises 57 CYP genes and 58 pseudogenes arranged into 18 families and 43 subfamilies in man [2]. They are heme-containing proteins that catalyse the oxidative metabolism of many structurally diverse drugs and chemicals. The polycyclic aromatic hydrocarbons (PAHs) are wide spreading environmental procarcinogens that induce tumorigenesis when they are activated by CYPs 450.

Genetic polymorphisms in CYPs are a major cause of the inter individuals' variation in drug metabolism. They lead to the occurrence of variation in response to the drugs ranging from adverse effects to lack of efficacy [3]. From the 50 identified CYPs isoenzymes that catalyse the drug metabolism, there are more than 20 genes of CYPs are functionally polymorphic, for instance the CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP1B1, and CYP1A2. Therefore, about 40% of drug metabolism is catalysed by the polymorphic CYPs [4].

The CYP2A6 enzyme participates in the biotransformation of several xenobiotics that has been categorized as pharmaceuticals and toxic agents [5]. CYP2A6 gene polymorphism has been associated with smoking behaviour, drug metabolism and lung cancer risk [6]. This polymorphism resulted in a variety of phenotypes of the CYP2A6.

Human CYP2A and CYP2E subfamily members play important roles in the metabolic activation of arecoline related N-nitrosamines. Located on human chromosome 19, CYP2A express at least 13 different isoenzymes, among which CYP2A6metabolically activates the N-alkyl nitrosamines, N-nitrosonornicotine, and4-(methylnitrosamine) - 1 - (3-pyridyl) - 1 - butanone, which have relatively long alkyl chains. Miyazaki et al. first reported that CYP2A subfamilies play important roles in the mutagenic activation of AN-derived N-nitrosamines.

CYP2A6 gene may also affect susceptibility to precarcinogen in the environment. People are classified as EM known as early metabolizers and PM known as poor metabolizers based on genetic variation. Poor metabolizers are less prone to oral cancer than early metabolizers due to CYP2A6 gene polymorphism. The areca nut-specific nitrosamines (ASNA) and betel quid specific nitrosamines (BQSN) are formed due to the interaction of betel quid and CYPs family [7].

We screened total 311 subjects in the Eastern and North Eastern region of India, who had betel quid chewing habit. It has been found more than 50% of eastern region subjects were early metabolizers (EM) according to xenobiotics metabolizing property of CYPs

family. Poor metabolizers (PM) are less prone to oral cancer than early metabolizer due to CYP2A6 gene polymorphism.

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