

Molecular Biology Applications in Oral and Maxillofacial Surgery

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ABSTRACT

Genetics is now considered the most acknowledged field in studying human disease causes and considered a rich field in medical researchers. Pharmacogenomics is a product of that researches and getting attention to personalize medicine to individuals through investing in the DNA based drug therapy. Of all malignancies 1% is mainly caused by single-gene inheritance. Single gene, chromosomal, and multifactorial were used to describe hereditary conditions until the understanding of the interaction between different genes (polygenic inheritance) and including acquired somatic genetic disease category. About 5% of population after age of 25 years will have a disorder with a genetic basis.

DNA is a long polymer forming a chain of series of nucleotide molecules. Each nucleotide molecule has one molecule of deoxyribose sugar, one molecule of phosphoric acid and one nitrogenous base on the side of the sugar. Here are four types of nucleotides in the DNA following the types of nitrogenous bases: Adenine (A), Thymine (T), Cytosine (C) and Guanine (G). The DNA helix model was first suggested by Watson and Crick in which the two polynucleotide chains run besides and opposite to each other. They are attached together by the nitrogen bases through hydrogen bonds with two types. The nitrogen base of the two attached stands of the DNA are paired in a constant arrangement in which Adenine always binds with Thymine and Cytosine always binds with Guanine. This will leads to stable hydrogen bonds between the pairs. The two DNA's stands are complementary twist around forming the double helix. A single turn of the helix is 3.4 nm in length with 10 base pairs and the helix diameter is 2 nm. Odontogenic Keratocyst (OKC) is a developmental odontogenic cyst originated from cell rest of dental lamina and characterized by an aggressive behavior. It is lined by a thin epithelium that has great growth

potential, satellite cysts, cords and islands of odontogenic epithelium are usually present in the wall and may contribute to its high recurrence rate. Multiple OKC can be part of a syndrome known as Nevoid basal cell carcinoma syndrome (NBCCS) or Gorlin syndrome. It is an autosomal dominant inherited syndrome consists chiefly of OKCs, multiple basal cell carcinomas of the skin, frontal and temporoparietal bossing, hypertelorism, mandibular prognathism, rib and vertebral defects and intracranial calcifications. It is caused by mutations in protein patched homolog 1 gene (PTCH1) which is a tumor suppressor gene that is mapped to chromosome 9q22.3-31. PTCH1 is considered a receptor for the Drosophila Hedgehog protein thus it controls the Hedgehog signaling pathway that is essential in embryonic cell differentiation and development for the embryo but in adult life it is involved in tumorigenesis such as NBCCS.

Etiology could be genetic and environmental factors. Environmental factors include radiation, chemicals such as arsenic, viruses such as human papilloma virus, and other microorganisms such as Helicobacter pylori. Genes control cells proliferation and those which are related to cancer development called oncogenes which are around 100 in number. Here are genes that inhibit tumor growth called tumor suppressor genes. Cancer might occur as a result of mutation on those genes. The cell growth is controlled by signal transduction of the growth factors. Any mutation to the genes that encodes growth factors and growth factor receptors might result in cancer. An example of those oncogenes is mutated ras gene and mutated myc gene. The cell cycle is four phases G1, S, G2 and M. The movement between the phases is controlled by checkpoints and the cell cycle is regulated by cdk/cyclin. The control of checkpoint will identify any damaged DNA which might be

from chemicals or x-rays. One of the monitors at checkpoint in G/S is tumor suppressor gene TP 53 which encodes P 53 protein. P 53 level in the cells is normally maintained low. P 53 produced when DNA is damaged and P 53 secreted outside the nucleus to cytoplasm by Mdm2 and then degraded after repair of the DNA. If DNA not repaired the P 53 modified remains in the nucleus leading normally to activation of cell cycle arrest and apoptosis. In case of loss of P 53 no identifier of DNA damage in the cells and cell cycle will escape the checkpoints and leads to tumor formation. From this role P 53 got the name of "guardian of genome". P 53 gene is located in chromosome 17 P13.1 and mutation in TP 53 gene is responsible of 50% of human cancer. Many carcinomas including oral cancers are largely associated with accumulation of genetic mutations. Oral squamous cell carcinoma (OSCC) is related to multiple molecular genetic aberrations, the most important are DNA copy number aberrations (DCNAs), oncogenes, tumor suppressor genes, mitochondrial mutations, epigenetic changes, microRNAs, genomic instability, and loss of heterozygosity. Using microarray methods the array-based comparative genomic hybridization (A-CGH) provided high-resolution and genome-wide screening of DCNAs. Consequently an extensive analysis of DCNAs in OSCCs became possible by applying A-CGH.

Drugs are shown to be more effective in some individuals than others, in addition, some individuals developed drug side effects more than others. Pharmacogenomics is the study of the interaction between people's genetic and drug response. By the use of genome sequencing, it will be possible to provide personalized pharmacogenomics making optimum drug choice, dose, and estimating side effects. Personalized medicine or precision medicine is aiming to provide treatment of a specific disease according to the individual genetic subtype. An example of a drug response is malignant hyperthermia with muscle rigidity and raised body temperature occurred rarely as a complication of using halothane anesthesia and succinylcholine for muscle relaxant. It requires muscle biopsy to test

the reaction with the anesthesia. He most likely cause is mutation in ryanodine receptor gene.

Keywords: Cystic fibrosis Pharmacogenomics; Maxillofacial surgery; Northern blotting; Periplasmic glucans