GENETIC ASPECTS OF DENTAL CARIES- PART II

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INTRODUCTION:

ROLE OF GENETICS IN CARIES PREVENTION: The use of genetic engineering to prevent caries has led to the down of a new era in caries prevention. Once successfully tested on human models, use of such modalities as genetic manipulation, genetic modification or recombinant technology may have the potential to revolutionize the whole mode of caries prevention. The various approaches that have been taken in this direction are (Fig. 1):-Altering the cariogenic flora:

1. Genetically modified foods.
2. Gene alterations.

ALTERING THE CARIOGENIC FLORA: Microorganisms play a vital role in the causation of dental caries. Among them s. mutans (a spherical bacterium) that thrives on the organic film that coats the tooth surfaces and produces the enzyme lactate dehydrogenase, plays the lead role.

In rat experiments, scientists found that a type of bacteria called lactobacilluszeas, could be genetically modified to produce antibodies to attach the themselves to the surface of s.mutans. Such bacteria are known as **'Genetically modified good Bacteria'**. The antibodies produced by them grab the free floating s. mutans in saliva and give them a 'Kiss of death'.

Hillman [2002] used recombinant DNA technology to create a strain of s. mutans [BCS3-L1] that lacks the lactate dehydrogenase gene. This harmless effector strain is permanently implanted in the host that kills conventional caries producing s.mutans without harming other bacteria. The BCS3-L1 replacement therapy for the prevention of dental caries is an example of biofilm engineering that offers the potential for highly efficient, cost effective augmentations of conventional prevention strategies.

Dr. Lawrence of the National Institute of Dental and craniofacial research prefers the concept of replacing s.mutans with a species engineered to rebuild both surface. Another approach that has been tried is the use of a strain of s.mutans engineered to increase the production of urease, which converts urea to ammonia to create conditions conductive to enamel re mineralization.

Genetically modified Foods: British scientists are genetically engineering fruits to combat tooth decay. A gene for peptide protein (P1025) is added to strawberries and apples. The antagonist peptides work against the specific enzyme system, glycosyl transferase of s.mutans and prevent it from binding to the tooth, thus preventing dental caries for up to 80 days at a time without using antibiotics. If such a gene could make to produce a protein, and were engineered

into fruit, then it could be one of the magic bullets in the form of fruit and vegetables in the armory of health care.

Lactobacillus laden foods and supplements are commonly referred to as probiotics and have grown increasingly popular as they are believed to promote good gastro intestinal health.

GENE ALTERATIONS: Genetically engineered mouse and human cell lines have been used to form the enamel, cementum and dentin of the tooth. The goal of the research is to grow teeth that are lost due to extensive cavities, diseases or accidents.

Exploring the genetic basis of dental disease has become the direction of today's research efforts in dentistry. Ideally, this approach will provide answers to perplexing questions and is the ultimate challenge for today's dentist.

Among the 3 essential interactions – microbes, substrates, host factors – that comprise the model system for dental caries, it is in the host factors, where genetics exerts major influence upon dental caries initiation.

It is clear from many studies that individual variations in susceptibility to dental caries exist even under identical controlled conditions. The evidence of the involvement of hereditary factors in susceptibility or resistance to the development of dental caries is derived from various human observations and animal experimental studies.

Dental caries incidence is affected by host factors that may be related to the structure of dental enamel, immunologic response to cariogenic bacteria, or the composition of saliva. Genetic variation of the host factors may contribute to increased risks for dental caries. Establishing a basis for genetics in future studies utilizing the human genome sequence to improve understanding of the disease process will be extremely use full.

Human Studies: Numerous studies have explored the frequency of dental caries development in related individuals and in all these studies, the existence of familial resemblance in dental caries experience were reported (Klein et al, 1938; Klein, 1946; Klein, 1947, Book et al, 1953). Studies of twins also suggest that there may be genetic contribution to dental development (Fairpo, 1979; Conry et al, 1993).

Animal Studies: Experimental studies conducted on animals can be more strictly controlled than with human observation studies. Hunt and Hoppert did a study where they placed over one hundred albino rats (Mus norvegicus) on a cariogenic diet. The surviving animals developed dental caries in 28 to 209 days. The most susceptible rats from the first generation were crossed to start a caries susceptible strain and the more caries resistant rats were crossed to begin the resistant line. In this fashion, they developed genetically resistant and susceptible strains of rats.

The strains were studied for many generations and included about 9,800 rats altogether.

The average time for inducing the first carious lesion in the lower molars of the susceptible rats decreased from 57 days in the second generation to 35 days in the twenty-fifth generation. The average time to induce carious lesions in the resistant strain increased from 116 days for the second generation to 505 days for the seventeenth generation (Hunt et al, 1944; Hunt et al, 1944; Hunt et al, 1955).

Shaw and Griffiths used the Harvard strains with high and low susceptibility of dental caries development. In the experiment they transferred the newborn of the resistant strain to the mothers of the susceptible strain to be nursed, and vice versa. The characteristic level of dental caries development for particular strain prevailed in spite of cross nursing (Shaw et al, 1960). Rosen, Hunt, and Hoppert (Rosen et al, 1961) experiments are in agreement with those of Shaw and Griffiths. In another cross breeding experiment and study the authors concluded that both parents exert equal influences on the caries activity of the offspring, and that nursing mothers had little, if any, effect (Shaw et al, 1961).

According to Keyes (1960), dental caries cannot be induced in caries inactive animals by exposing them to 'resistant' animals that do not develop dental caries simply because they were not infected with caries producing bacteria. This was further substantiated by experiments of Rosen et al (1961).

Larson and Sims demonstrated that dental caries is appreciably more active in Osborn-Mendel (O-M) strain than in NIH black rats (B-R) when both were exposed to identical diets (Larson et al, 1965). In another experiment the same researchers used (O-M) female rats and mated them with both (O-M) and NIH black rats (B-R). The litters contained both (O-M) white and crossbreed gray to black offspring and both groups developed significantly different dental caries status. The (O-M) and NIH black crossbreeds had significantly lower caries activity than pure (O-M) stain. This phenomenon occurred even though the rats were exposed to identical environmental conditions (Larson et al, 1965).

Since variations may exist in the oral microflora harbored by different strains of rats, it could be concluded that these variations may be the reason for the different in caries level observed in these 2 groups. In order to investigate further, Grenby and Owen set up an experiment under strictly gnotobiotic conditions. Two different strains of rats – Osborne – Mendle (Caries Susceptible) and Wister (much less caries susceptible) were infected with the same oral microorganism. The authors found that Osborne – Mendle rats were consistently more caries active than the Wister rats and the difference was highly significant.

They concluded that heredity, rather than the nature of the oral microflora is the dominant factor in determining the different levels of caries cavity in the 2 strains of rats.

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Figure 1: showing the modes prevention and their interactions in prevention of dental caries.

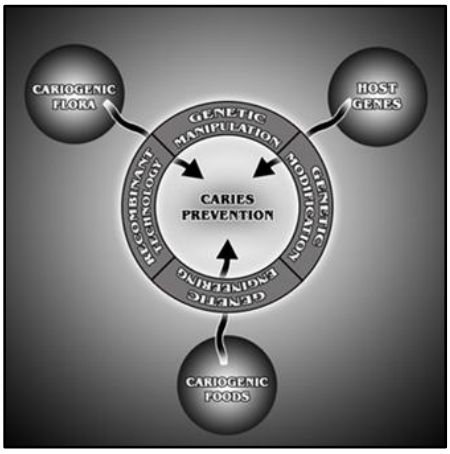

Fig. 1

REVIEW ARTICLE

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