eISSN: 09748369, www.biolmedonline.com

Emerging trends in oral health profession: The molecular dentistry

Sandhya Maheshwari, **Sanjeev K Verma, Mohd. Tariq, *Prabhat KC, Shailendra Kumar[1]**
Department of Orthodontics and Dental Anatomy, Aligarh Muslim University, Aligarh, India.
[1]Research Cell, C.S.M. Medical University (KGMC), Lucknow, India.

***Corresponding Author:** dr.prabhatkc@gmail.com

Abstract
Oral health practice has now entered the era of "evidence based dentistry," characterized by an increasing societal belief around the world that clinical practice should be based on scientific information. Molecular dentistry, the human genome project, transcriptomes and proteomes have recently opened vast opportunities for translation of basic science discoveries to oral health care at the chairside and bedside through the intermediary process of clinical research. Multiple factors and processes contribute to the response of dental treatment. Understanding of the interaction between genetic and environmental factors (including treatment) that influence the treatment response of our patient will be fundamental to the practice of personalized Orthodontics. Curiosity and innovations have been known and appreciated for thousands of years, from basic discovery through clinical applications influencing and improving standards of oral health care, but these have not received sufficient emphasis until recently.

Keywords: Molecular Dentistry; Human Genome; Personalized Orthodontics.

Introduction

Science is the fuel of the engine of technology. Science is the fuel of progress in the clinical fields of dentistry, medicine, pharmacy and nursing. Science has made a profound difference in the quality of life for billions of people. These benefits coupled to scientific advances are especially evident in modern dentistry and medicine. What are some of the highlights? At the end of the 17th century, Antonie Philips van Leeuwenhoek invented the light microscope (Egerton, 2006). Through this and other incredible "ways of seeing and knowing," more than 500 species of bacteria have been identified within the biofilms located upon tooth and oral mucosal surfaces (Moore and Moore, 1994). In the 19th century, Gregor Mendel advanced his principles of genetics (Druery and Bateson, 1901) and by 20th century international teams of scientists and clinicians has defined modern human genetics and their efforts led to the completion of the international Human Genome Project by April 2003. Thousands of human genetic diseases are now being identified and tens of thousands of new therapeutics are being developed to provide clinical efficacy, specificity and minimal toxicity in oral health care (Collis et al., 1998; Collis and McKusick, 2001).

Pharmacogenomics and pharmacogenetics provide new insights into how human genetic variations influence individual drug absorption and utilization during therapy (Evans and Relling, 1999). Biomimetics refers to human-made processes, substances, devices, or systems that imitate nature and describes the new scientific opportunities based upon the recently discovered rules of biology. Imagine, this new biomimetic strategy applied through molecular dentistry to improve soft and hard tissue engineering and towards tooth and salivary gland organ regeneration (Center for Nanostructured Biomimetic Interfaces, 2004).

Now oral fluids have become "informative fluids" that can be used for diagnostic purpose (Figure-1), the management of drug therapy, and a number of forensic applications (Reznik, 2008). The science and technology of miniaturization (nanotechnology) now enables a full clinical laboratory to be compressed upon a miniature chip and this "lab-on-a-chip" technology is being applied to rapid and sensitive analysis using saliva as a diagnostic fluid.

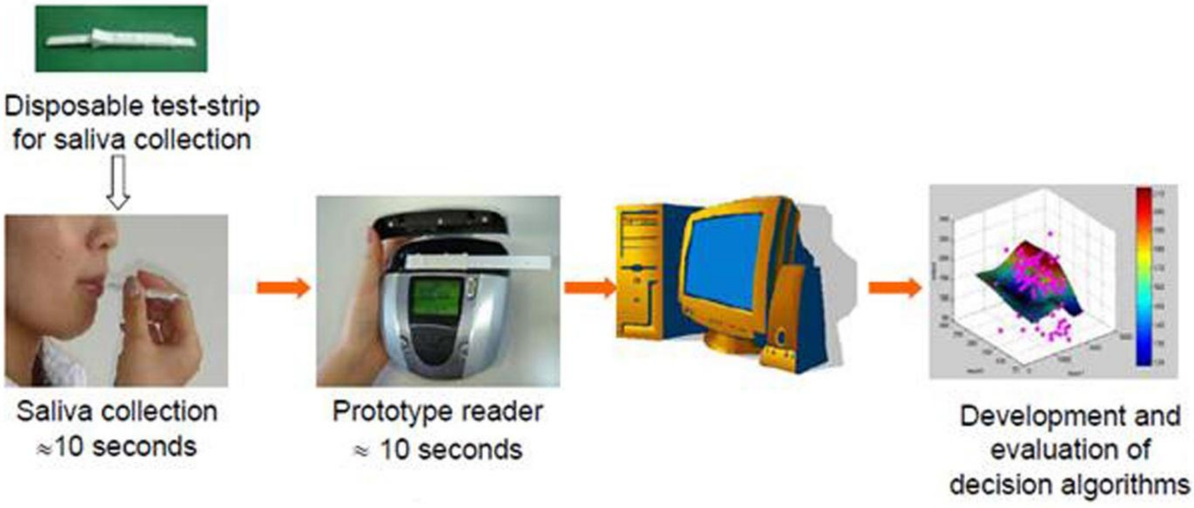

Figure-1: Salivary biosensor used for diagnostic purpose.

Terminology Used

The Genome

Defined as the master blueprint for cellular structures and activities during the lifetime of each cell.

DNA Nucleotide Bases

The Human Genome Project defines a gene as a specific sequence of nucleotide bases whose sequences carry the instructions for construction of proteins. These proteins provide the structural components of cells and tissues, as well as enzymes for essential biochemical reactions. Hundreds of genes reside on each chromosome. The complete human genome is estimated to contain about 30,000 genes. It is astonishing that more than 99.9 percent of DNA sequences are the same across the entire human population. However, these small genetic dissimilarities have a major impact on a person’s physical makeup and response to disease, as well as on the effectiveness of therapies instituted.

Single-Nucleotide Polymorphisms

Our genome varies from one individual to the next, most often in terms of single base changes of the DNA called single nucleotide polymorphisms (SNPs, pronounced “snips”). The main research use of a human SNP map will be to determine the contributions of genes to diseases (or nondisease phenotypes) that have a complex, multifactorial basis. More than 1.4 million SNPs have been identified in the human genome.

The Proteome

The primary function of genes is to direct the manufacture of proteins. Genes contain instructions for the production of proteins.

Where Will Genome Lead Us in Future

The deciphering of the genome, the impending understanding of protein construction and the continuing investigations of cellular function portend momentous changes in the art and practice of the dental sciences. Genetic bioengineering will impact all phases of dental practice. Most significant will be the interaction between dentists and patients as new systems of diagnosis, prevention and treatment are developed.

Alteration of the Pathogenicity of Oro-Dental Infectious Agents

As the sequencing of bacteria is progressing rapidly, the first major impact will likely be the modification of bacteria causing dental disease. More significantly, researchers at the Joint Genome Institute operated by the University of California and the University of Oklahoma Health Science Center announced the completion of the sequencing of the pathogen *Streptococcus pyogenes*, the bacteria responsible for a wide variety of human ailments, including streptococcal sore throat, rheumatic fever, septicemia, and necrotizing fasciitis or flesh-eating disease (Preuss, 2000; Ferretti et al., 2001). Discovery of the specific bacterial SNPs and their products that cause dental disease will lead to the development of measures to counter or mitigate their untoward effects (Figure-2).

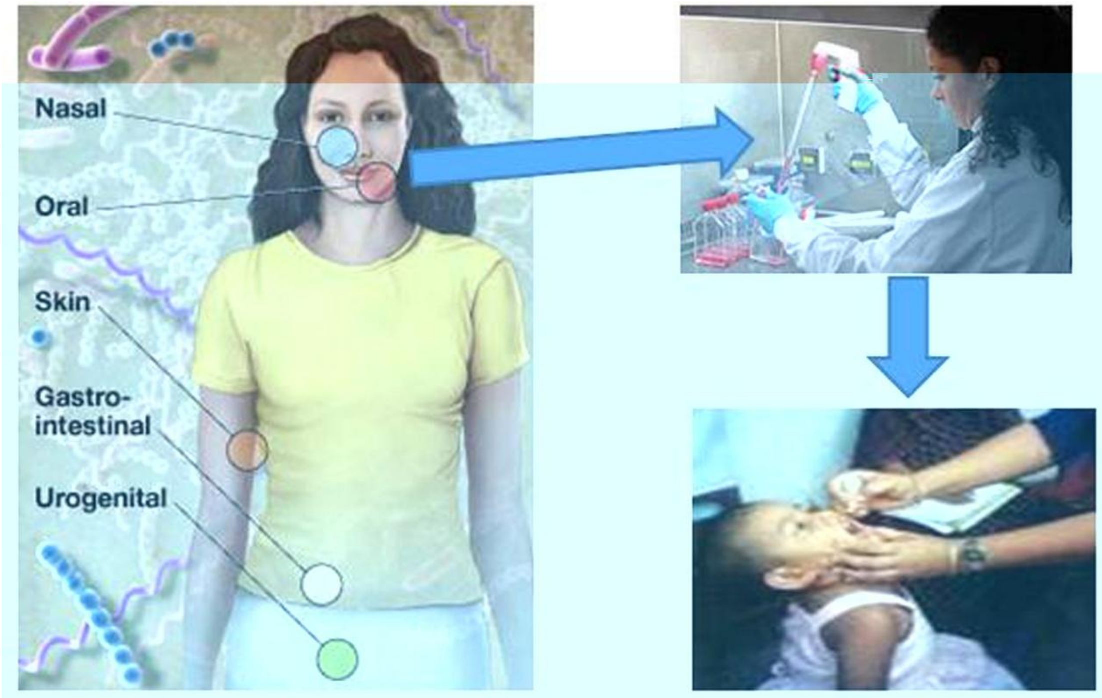

Figure-2: Development of caries vaccine.

Renaturalization of Dental Tissues

Within the next few decades, changes in the methods and materials used to treat dental disease will take place. As genetic researchers continue to study the specific genes that control the development and maintenance of teeth (Figure-3) and their surrounding structures, implementing proteins will be located, and their tissue-building functions defined. Treating dentists then will be able to apply genetic engineering techniques to stimulate the body to repair itself, rather than place extrinsic materials. For example, during endodontic therapy, dentists will be able to seed genetically developed pulpal tissue into the canal to grow and fill the chamber (Figure-4). A layer of epithelial cells then could be triggered to form dentin and enamel to complete the biological restoration of the tooth.

Current Technology

Some of the technology needed to implement such tissue regeneration is currently available. In a report published in The New England Journal of Medicine, Tsai and colleagues presented the results of a study in which they cultured corneal epithelial cells from healthy eyes of patients with severe unilateral corneal disease and subsequently transplanted the cells to the diseased eyes (Figure-5) to restore vision (Tsai et al., 2000).

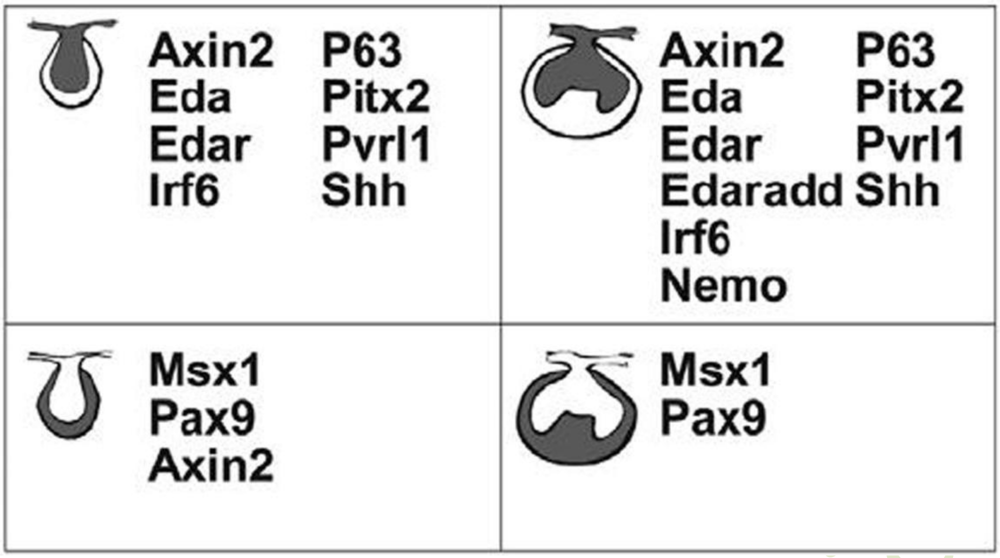

Figure-3: Expression of molecules related to tooth agenesis during early tooth development from the bud to bell stage.

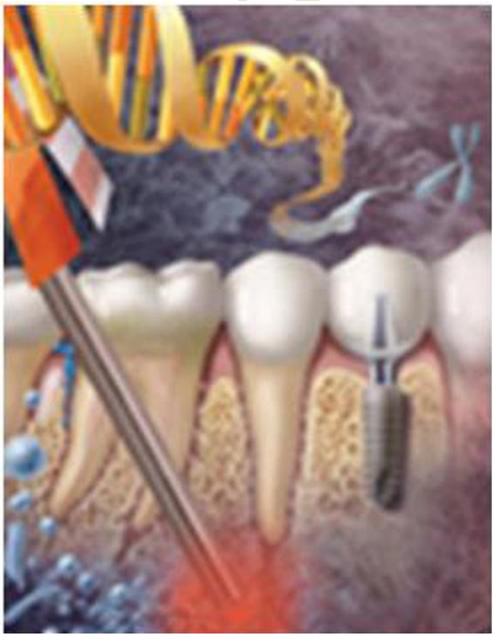

Figure-4: Formation of pulp by genetically engineered developed pulp tissue.

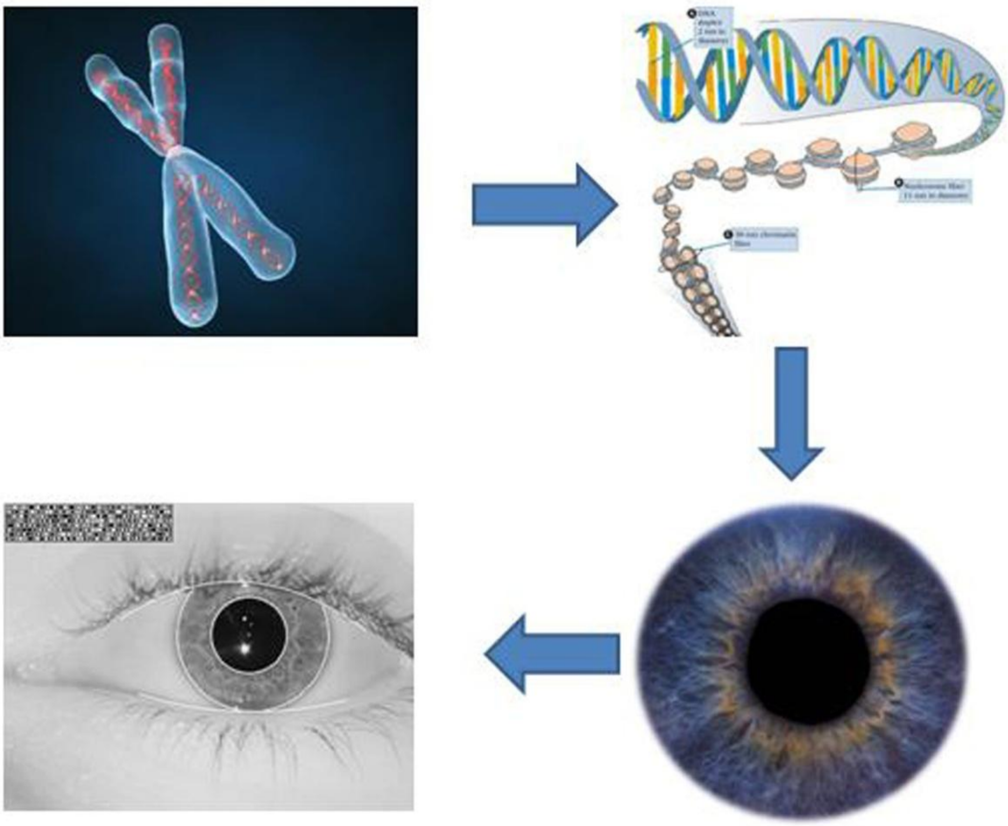

Figure-5: Development of cornea by cell culture.

In an editorial about this study, published in the same issue, Schwab and Isseroff commented, "The promise of bioengineered replacements for diseased or damaged tissue has become a reality". Bioengineered or cultured tissue products to replace other tissues "indicates that such products are likely to revolutionize the treatment of many epithelial diseases" (Schwab and Isseroff, 2000) and replacement of mineralized tissues (Baum and Monney, 2000). Research scientist Robert Freitas explained that nanotechnology, which involves the use of precise, molecular-sized robotic devices to control matter at the atomic and molecular level, could result in the manufacturing of instruments that are able to build and install "a biologically autologous whole-replacement tooth (Figure-6) that includes both mineral and cellular components" (Freitas, 2000).

Construction of Disease Resistant Oro-Dental Tissue

Further in the future—probably by the middle of the century—lies the specter of human germline alteration, or what is often referred to as "designer babies." Different from interference with the pathogenicity of caries- or periodontal disease–producing organisms, or from genetically engineered tissue replacement, alteration of the germline affects the embryonic formation of the dental complex and creates disease resistance in people, who then pass this immunity on to their children and to all succeeding generations. Intercession in the dental formative process would become feasible, leading to infants who are free of caries and periodontal disease for a lifetime.

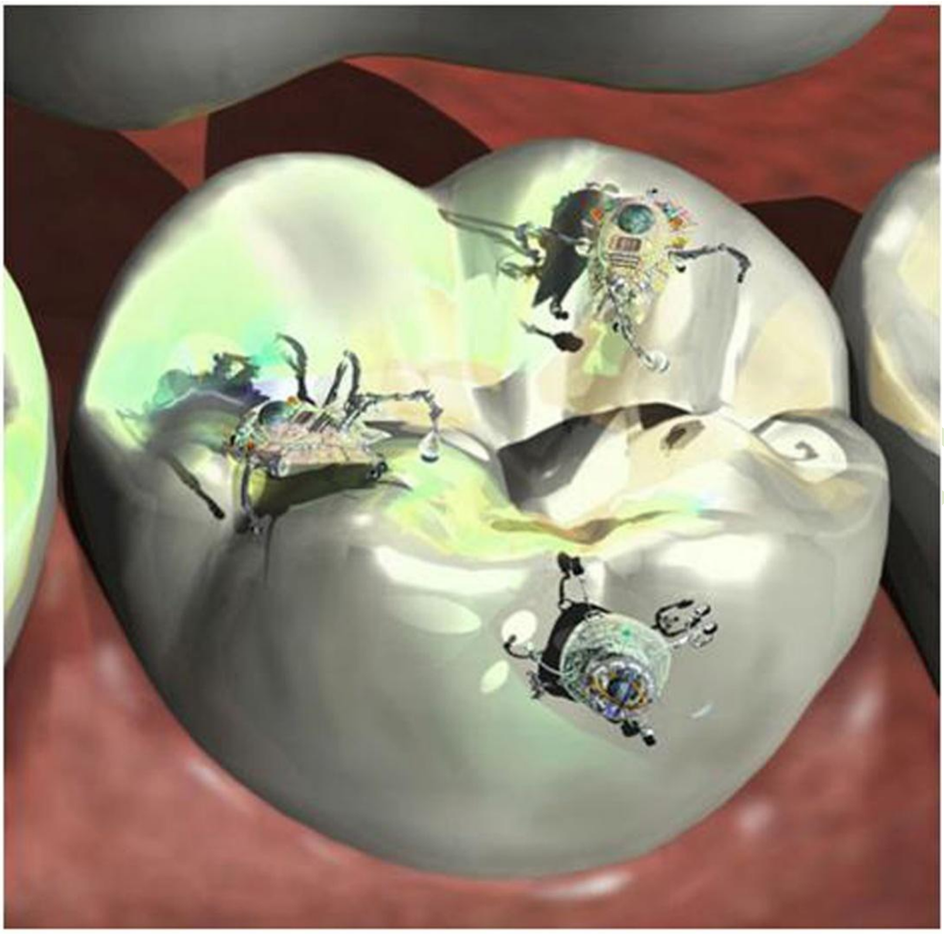

Figure-6: Biologically autologous whole replacement of tooth by orthodontic nanorobots.

Personalized Orthodontics: The Future of Genetics in Practice

"Personalized medicine" is a new buzz phrase, based initially on pharmacogenetics and now exploding, as genome-wide association studies are undertaken. However, it remains to be seen how much this will really affect daily practice. The same may be projected for the future of orthodontics. What would personalized orthodontics be based on, how would the studies be undertaken and then validated in practice? How will this be funded? The understanding of the combination and interaction of genetic and environmental (including treatment) factors (nature and nurture together) that influence the treatment response of our patients is fundamental to the evidence-based practice (Figure-7) of orthodontics (Hartsfield, 2008).

Dental and medical care is generally based on an examination and assessment of the patient's status, diagnosis, and prescription of treatment. The treatment is typically based on a positive response in the majority of individuals with the diagnosis. This approach will work for most patients most of the time. However, what will be effective for most of the population may not be the optimum treatment for others. Recently, the analysis of an individual's response to treatment, largely determined by intrinsic genetic factors and individual behavior, has become more comprehensive, resulting in what has been termed "personalized medicine".

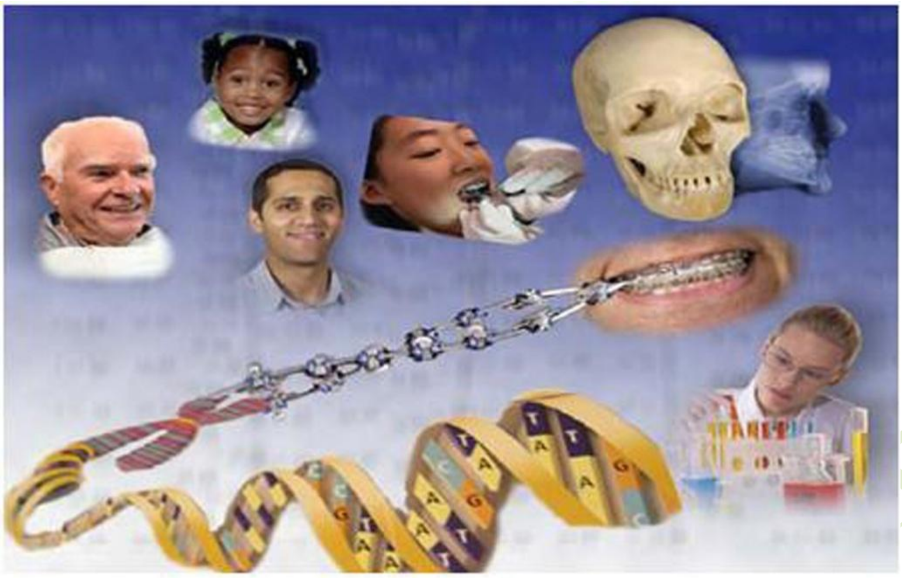

Figure-7: Showing future practice of personalized orthodontics.

Multiple factors and processes contribute to the response to orthodontic treatment. Some patients will exhibit unusual outcomes linked to polymorphic genes. Analysis of overall treatment response requires a systems analysis using informatics for integration of all relevant information. Genome-wide association studies are necessary to further the evidence base for the practice of orthodontics. Only then will we begin to truly understand how nature (genetic factors) and nurture (environment factors, including treatment) together affect our treatment of our patient (Hartsfield, 2008). These and hundreds of other "highlights" reflect a "tipping point" or that time in human history when scientific discoveries are rapidly translated into improved oral health care for people around the world.

Conclusion

Just as harnessing steam in the 19th century fueled industrial growth, and controlling electrical energy heralded the modern world of the 20th century, deciphering and interpreting the genome of humans and all other living organisms will be seminal event of the 21st century. Armed with this knowledge, molecular biologists will be able to understand and adjust chromosomal function to create optimal cellular performance. As dentistry relies with great gusto on the technology, it will be affected profoundly. In short "Future is coming, it will be amazing".

References

Baum BJ, Mooney DJ, 2000. The impact of tissue engineering on dentistry. Journal of the American Dental Association, 131: 309-18.

Center for Nanostructured Biomimetic Interfaces, 2004. Available at: www.biomimetic.org/participant_wang.html; What is biomimetics - Available at: http://whatis.techtarget.com/definition/0,,sid9_gci517747,00.html

Collins FS, Patrinos A, Jordan E, Chakravarti A, Gesteland R, Walters L, 1998. New goal for US: The Human Genome Project, 282: 682-9.

Collis FS, McKusick VA, 2001. Implication of the Human Genome Project for medical science. Journal of the American Medical Association, 285: 540-4.

Druery CT, Bateson W, 1901. Experiments in plant hybridization. Journal of the Royal Horticultural Society, 26: 1–32.

Egerton FN, 2006. A History of the Ecological Sciences, Part 19: Leeuwenhoek's Microscopic Natural History. Bulletin of the Ecological Society of America, 87 (1): 47-58.

Evans WE, Relling MV, 1999. Pharmacogenomics: Translating functional genomics into rational therapeutics. Science, 286: 487-491.

Ferretti JJ, McShan WM, Ajdic D, Savic DJ, Savic G, Lyon K, Primeaux C, Sezate S, Suvorov AN, Kenton S, Lai HS, Lin SP, Qian Y, Jia HG, Najar FZ, Ren Q, Zhu H, Song L, White J, Yuan X, Clifton SW, Roe BA, McLaughlin R, 2001. Complete genome sequence of an M1 strain of *Streptococcus pyogenes.* Proceedings of National Academy of Sciences USA, 98: 4658-63.

Freitas RA, 2000. Nanodentistry. Journal of the American Dental Association, 131: 1559-65.

Hartsfield JK, 2008. Personalized Orthodontics, The Future of Genetics in Practice. Seminars in Orthodontics, 14: 166-171.

iScreen, Saliva Oral Fluid Drug Tests. Available at: http://www.usscreeningsource.com/iScreen_oral_saliva_drug_test.htm

Moore WE, Moore LV, 2000. The bacteria of periodontal disease. Periodontology, 5: 66.

Preuss P, 2000. Microbial marathon at Joint Genome Institute: fifteen organisms sequenced in one month. DOE Joint Genome Institute News Nov. 2, 2000. Available at: www.jgi.doe.gov/tempweb/News/news_11_2_00.htm

Reznik DA, 2008. Oral Fluid Rapid HIV Testing – A Quick, Painless, and Effective Approach to Increasing Awareness of HIV Status. Available at: http://www.hivdent.org/_Main_/main_OFRH0608.htm

Schwab IR, Isseroff RR, 2000. Bioengineered corneas: the promise and the challenge. New England Journal of Medicine, 343 (2): 136-8.

Tsai RJ, Li L, Chen J, 2000. Reconstruction of damaged corneas by transplantation of autologous limbal epithelial cells. New England Journal of Medicine, 343 (2): 86-93.