

## Genetic Paradigm in Orthodontics

Satinder Pal Singh, Vinay Kumar\* and Ashok Utreja

Oral Health Sciences Centre, Post Graduate Institution of Medical Education and Research, India

\*Corresponding author: Vinay Kumar, Unit of Orthodontics, Oral Health Sciences Centre, Post Graduate Institution of Medical Education and Research, Chandigarh-160012, India, Tel: 9855618982; E-mail: sonidvinay16@gmail.com

Rec date: Nov 14, 2015; Acc date: Feb 02, 2016; Pub date: Feb 10, 2016

Copyright: © 2016 Singh SP, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### Abstract

Orthodontics, the oldest discipline of dental specialty concerns with the treatment of malocclusion both dental and skeletal. Although etiology of malocclusion is multifactorial, genes do have influence on this condition, beside their role in mechanism of tooth movement and unwanted sequel like external root resorption following orthodontic treatment. This short communication will focus the issue on role of gene in various conditions which have paramount effect either on the etiology of malocclusion or mechanism by which tooth movement occurs. Human genome project and future advancement in genomic medicine will help us in clear identification of conditions causing mutation and the unsolved zigzag puzzle of molecular interaction can be solved.

**Keywords:** Orthodontics; Dental specialty; Malocclusion; Etiology; Genetics

### Introduction

The word orthodontics has evolved from Greek word, "orthos" meaning right or correct, and "dons" meaning tooth. This is the first bonafide dental specialty that concerns with the management and treatment of malocclusion. Malocclusion in strict sense does not represent any disease; rather it is a variation from, what is considered normal/ideal [1]. It was rightly said by Jackson that orthodontics is a "science of infinite variations" [2]. Etiology of malocclusion is multifactorial; having specific causes viz. any disturbances during embryonic period, fetal molding and birth trauma, any childhood fracture of jaw, muscle dysfunction, Acromegaly, hemimandibular hyperplasia and developmental disturbances of dentition [3]. Beside this a strong influence of heredity/gene has been found in the etiology of malocclusion. The famous "habsburgs jaw" (prognathic mandible), which was classical phenotype of European Royal ancestry is the best known example of genetic influence on malocclusion and later on Dr. Stockard's and Johnson experiment on crossbreeding dogs also strengthened this hypothesis [4]. Contemporary knowledge among orthodontic arena reveals that several genes are linked with etiology of malocclusion, tooth movement following orthodontic treatment and side-effects following orthodontic therapy. The purpose of this article is to highlight the role of genetics involved in different clinical conditions leading to severe skeletal and dental malformation and hence poses a great impact on orthodontics as discipline.

### Genetics in Skeletal Malocclusion

Data from the studies conducted by Manfredi, et al. [5] and Savoye, et al. [6] confirms that vertical skeletal malocclusion have more genetic preponderance than sagittal skeletal dysplasias. Apertognathia (skeletal open bite) with dolichofacial pattern was most frequent inherited

dentofacial deformity [3]. Harris conducted a cephalometric investigation in skeletal class II division 1 malocclusion that revealed significant reduction in mandibular body length as compared to skeletal class I patients, thus supporting polygenic inheritance [7]. A clinical and cephalometric study conducted by Markovic on 114 class II division 2 patients showed a strong evidence for gene as main etiological factor [8]. The association of vascular endothelial growth factor (VEGF), parathyroid-hormone like hormone (PTHrP), Indian hedgehog homolog (IHH) and insulin-like growth factor-1 (IGF-1) have been found to cause class III malocclusion (mandibular prognathism) [9]. Recent study conducted by Guan, et al. on Chinese family has shown that ADAMTS1 gene is associated with familial mandibular prognathism [10]. These entire data do confirms the involvement of genes in the causation of skeletal malocclusion.

### Miscellaneous Consequences in Orthodontics

In clidocranial dysplasia, associated gene is RUNX2, presented as hyperdontia and multiple impacted supernumerary teeth [11]. Animal studies have shown that complete lack of RUNX2 gene resulted in the failure of teeth and bone development, whereas mutation in RUNX2 led to arrested tooth development [12]. Cleft lip and palate, several genes have been highlighted viz. 17q12 (RARA), 7p13-15, 2p13 (TGFA), 6p21.3-21.1, 1q22.3-41 (IRF6), 2q35-36, 7q22-qter and 12q24-qter [13]. Crouzon syndrome that has been evidenced to have maxillary hypoplasia, results from mutations in the fibroblast growth factor receptor 2 gene (FGFR2) [14], odonto-oncho-dermal dysplasia (a rare form of ectodermal dysplasia), causative gene is WNT10A [15]. Duplication of chromosome segment 16p13.3 have been reported as cause for non-syndromic Pierre Robin sequence [16], that is characterized with cleft palate, glossoptosis and micrognathia. Association of SOX-9 gene, PTHrP and IHH with orthodontic tooth movement [17], MSX1 and PAX9 genes with hypodontia [18], MSX1, PAX9, AXIN 2 with oligodontia [19], CBFA 1 (RUNX2), TRAF6 and FGFR 1-3 with some of syndromes associated with tooth eruption failure [20]. External apical root resorption, an unwanted sequel of orthodontic treatment believed to have association of decreased level of IL-1 $\beta$  production in the case of IL-1B (+3953) allele 1 [21] and tight linkage of TNFRSF 11A gene loci [22].

### Conclusion

Malocclusion is the result of various combinations and permutation of genetic as well as environmental influences. Although there is tremendous advancement in the science of genetics, but the underlined cause of malocclusion is still unclear. Refinements in the knowledge of genetics in the field orthodontics will pave the way for genetic correction of some traits of malocclusions through human genome project. Future advancements in genomic medicine will help us in the

identification of disease causing mutations and zig-zag puzzled network of molecular interaction.

## References

1. Cobourne MT, DiBiase AT (2009) Handbook of orthodontics (1stedn), Elsevier, Edinburgh, London, Newyork, Oxford, Philadelphia, St Louis, Sydney, Toronto.
2. Jackson AF (1948) The art of orthodontic practice. Am J Orthod 34: 383-413.
3. Proffit WR, Fields HW, Sarver DM (2007) Contemporary orthodontics (4thedn), Elsevier, St. Louis.
4. Stockard CR, Johnson AL (1941) Genetic and endocrinic basis for differences in form and behavior. Philadephia: The Wistar Institute of anatomy and biology.
5. Manfredi C, Martina R, Grossi GB, Giuliani M (1997) Heritability of 39 orthodontic cephalometric parameters on MZ, DZ twins and MN-paired singletons. Am J Orthod Dentofacial Orthop 111: 44-51.
6. Savoye I, Loos R, Carels C, Derom C, Vlietinck R (1998) A genetic study of anteroposterior and vertical facial proportions using model-fitting. Angle Orthod 68: 467-470.
7. Harris JE (1975) Genetic factors in the growth of the head. Inheritance of the craniofacial complex and malocclusion. Dent Clin North Am 19: 151-160.
8. Markovic MD (1992) At the crossroads of oral facial genetics. Eur J Orthod 14: 469-481.
9. Xue F, Wong RW, Rabie AB (2010) Genes, genetics, and Class III malocclusion. Orthod Craniofac Res 13: 69-74.
10. Guan X, Song Y, Ott J, Zhang Y, Li C, et al. (2015) The ADAMTS1 Gene Is Associated with Familial Mandibular Prognathism. J Dent Res 94: 1196-1201.
11. Roberts T, Stephen L, Beighton P (2013) Cleidocranial dysplasia: a review of the dental, historical, and practical implications with an overview of the South African experience. Oral Surg Oral Med Oral Pathol Oral Radiol 115: 46-55.
12. Aberg T, Cavender A, Gaikwad JS, Bronckers AL, Wang X, et al. (2004) Phenotypic changes in dentition of Runx2 homozygote-null mutant mice. J Histochem Cytochem 52: 131-139.
13. Stanier P, Moore GE (2004) Genetics of cleft lip and palate: syndromic genes contribute to the incidence of non-syndromic clefts. Hum Mol Genet 13 Spec No 1: R73-81.
14. Reardon W, Winter RM, Rutland P, Pulleyn LJ, Jones BM, et al. (1994) Mutations in the fibroblast growth factor receptor 2 gene cause Crouzon syndrome. Nat Genet 8: 98-103.
15. Adaimy L, Chouery E, Megarbane H, Mroueh S, Delague V, et al. (2007) Mutation in WNT10A is associated with an autosomal recessive ectodermal dysplasia: the odonto-onycho-dermal dysplasia. Am J Hum Genet 81: 821-828.
16. Sun M, Zhang H, Li G, Wang X, Lu X, et al. (2014) 16p13.3 duplication associated with non-syndromic pierre robin sequence with incomplete penetrance. Mol Cytogenet 7: 76.
17. Nayak BN, Galil KA, Wiltshire W, Lekic PC (2013). Molecular Biology of Orthodontic Tooth Movement. J Dent Oral Health 1: 101.
18. Pemberton TJ, Das P, Pate PI (2005). Hypodontia: genetics and future Perspectives. Braz J Oral Sci 4: 695-706.
19. Matalova E, Fleischmannova J, Sharpe PT, Tucker AS (2008) Tooth agenesis: from molecular genetics to molecular dentistry. J Dent Res 87: 617-623.
20. Ahmad S, Bister D, Cobourne MT (2006) The clinical features and aetiological basis of primary eruption failure. Eur J Orthod 28: 535-540.
21. Hartsfield JK Jr, Everett ET, Al-Qawasmi RA (2004) Genetic Factors In External Apical Root Resorption And Orthodontic Treatment. Crit Rev Oral Biol Med 15: 115-122.
22. Al-Qawasmi RA, Hartsfield JK Jr, Everett ET, Flury L, Liu L, et al. (2003) Genetic predisposition to external apical root resorption in orthodontic patients: linkage of chromosome-18 marker. J Dent Res 82: 356-360.