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Single Nucleotide Polymorphisms associated with Angle's Class I and III Occlusal Relationship in Thais with Thyrotoxic Hypokalemic Periodic Paralysis

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Abstract

Objective: To identify single nucleotide polymorphisms (SNPs) that associated with different occlusal relationship in a group of Thai population.

Materials and Method: One hundred and sixty unrelated Thai subjects who participated in Ramathibodi GWAS study for thyrotoxic hypokalemic periodic paralysis (TTPP) (Jongjaroenprasert, 2012) were selected. The subjects that were 20 years old and above with at least a pair of untilted permanent first molars or canines were selected from these subjects. Seventeen subjects met these criteria in our study. Angle's/canine classification of subjects were observed both intraorally and from diagnostic models. Eight hundred and sixty four human active SNPs from 28 related genes were selected from previous craniofacial studies. PERL software with Fisher exact test was used to identify the SNPs that correlated with subjects' occlusal relationship.

Results: There were 17 SNPs from 6 genes including IGF1, HSPG2, MATN1, TGFB2, VEGF and EVC that significantly correlated with Angle's/canine class I occlusal relationship and 27 SNPs from 5 genes including IGF1, HSPG2, MATN1, TGFB1 and LTBP2 that significantly correlated with Angle's/canine class III occlusal relationship (P value < 0.05). These findings show that there are specific SNPs in the marker genes that correlated with Angle's/canine class l and class III occlusal relationship.

Conclusion: There are significant correlations between SNPs and occlusal relationship in a Thai population subgroup. This finding leads to a further understanding in genetic basis of occlusal relationship.

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Key words: *Angle's classification; GWAS study; Genome, Occlusion; Single Nucleotide Polymorphism; Thai population*

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Introduction

Abnormal skeletal and occlusal relationships affect masticatory system and facial profile esthetics, resulting in malfunctions of chewing, swallowing and speech. The prevalence of abnormal skeletal relationship varies among populations and races. The prevalence of mandibular prognathism in Asian population is approximately 15%, while mandibular retrognathism is rarely found. In Caucasians, there were 21.6% mandibular retrognathism and 3.4% mandibular prognathism. Angle's classification has been widely used to classify occlusal relationships by using the position of maxillary and mandibular first molars (Angel, 1907). It was found that there are some correlations between skeletal, occlusal plane, and occlusal relationship (Kim et al., 2014; Wasserstein et al., 2015).

In a number of previous studies, genetic inheritance and environmental factors play important roles in the etiology of skeletal relationship (Jena et al., 2005). Environmental factors, hormones, enlarged tonsils and imbalances in the endocrine system have been reported to affect skeletal growth pattern of the mandible (Chang et al., 2006). Because of advances in genetic studies, Genome-wide association (GWAS) was used to explore the association between genetic components and the skeletal relationship in some population, for example, Korean and Japanese (Yamaguchi et al., 2005) and Brazil (Cruz et al., 2011). Among these studies there were different and overlapping genes. A linkage analysis study for an Asian population investigated possible genes for mandibular prognathism, such as Matrilin-1 (cartilage matrix protein) (Deak et al., 1999). A further study also proposed the association between the single-nucleotide polymorphisms (SNPs) in Matrilin-1 and mandibular prognathism and found that the haplotype TGC of Matrilin-1 polymorphism had pronounced risk effect for mandibular prognathism compared to controls (Jang et al., 2010). Another study showed the region linked tomandibular prognathism phenotype in four Hispanic families by performing a genome-wide scan and linkage analysis (Frazier-Bowers et al., 2009). They showed thatthis phenotype segregated inan autosomal-dominant manner, and 5 loci (1p22.1, 3q26.2, 11q22, 12q13.13, and 12q23) are indicative of linkage. The results in chromosome 1 were similar to those reported previously in an Asian cohort with mandibular prognathism (Li et al., 2010). Recently, next-generation sequencing was used to study a single European family with a large number of mandibular prognathism members and identifed mandibular prognathism-related candidate genes including BMP3, ANXA2, FLNB, HOXA2, and ARHGAP21 (Perillo et al., 2015). This project studied the genes previously reported as markers that are associated with skeletal relationship.

The objective of this study was to further understand the genetic roles in malocclusion and to find the SNPs that are associated with different occlusal relationships in Thai population, which could be developed as a diagnostic tool for individual patients.

Materials and Methods

Subject selection

The total 160 subjects were unrelated Thai patients in the thyrotoxic hypokalemic periodic paralysis (TTPP) Ramathibodi GWAS study by Jongjaroenprasert et al.,. in 2012 that was reviewed and approved by the Ethics Committee of Ramathibodi Hospital, Mahidol University. All subjects were healthy and were in follow up protocol of Ramathibodi Hospital TTPP treatment. None of the subjects had bone and joints diseases. The subjects who were 20 years old and above with at least a pair of untilted permanent first molars or canines were selected. The subjects who have history of orthodontic treatment or oral and maxillofacial surgical treatment were

excluded. After having intra-and extraoral examination of all subjects, seventeen subjects met our inclusion criteria. Informed consent was obtained from every subject. The project protocol was approved by Faculty of Dentistry, Chulalongkorn University Human Research Ethic Committee (approval number 057/2012).

DNA isolation and Genome wide genotyping

Collection of blood samples was done by TTPP study Ramathibodi GWAS study with informed consent and approved by the institutional review boards. Genomic DNA was isolated using the QIAamp DNA Blood Mini Kit (Qiagen, Hilden, Germany) according to the manufacture protocol and resuspended in Tris-HCl buffer (pH, 8.5). The concentration was quantified using a UV spectrophotometer ND-1000 (NanoDrop Technologies). The purity was determined by calculating the ratio of absorbance at 260-280 nm.

For the genome-wide genotyping, the Illumina HumanHap550v3 Genotyping BeadChip which contains >500000 haplotype tagging SNPs derived from phase 1 of the International HapMap project was used for all DNA samples. The overall call rates of all samples were 98%. More information for SNP genotyping can be found in the original paper (Jongjaroenprasert et al., 2012)

Genes and SNPs selections

Twenty eight candidate genes, which have been reported as related to skeletal relationship were selected from previous craniofacial studies (Woods et al., 1996; Arikawa-Hirasawa Watanabe et al., 1999; Deak et al., 1999; Ohno et al., 2001; Hansson et al., 2001; Prescott et al., 2001; Zeiger et al., 2002; Rabie et al., 2002; Edison et al., 2003; Jena et al., 2005; Yamaguchi et al., 2005; Chang et al., 2006; Rodger et al., 2007; Jelenkovic et al., 2008; Pei et al., 2008; Frazier-Bowers et al., 2009; Jang et al., 2010; Li et al., 2010; Cruz et al., 2011; Li et al., 2011). The races in those craniofacial studies include Hispanic, Chinese, Korean, Japanese, and Brazilian. We then analyzed 864 human active SNPs from 28 genes, which were cited in NCBI SNPs database.

Clinical assessment

We performed the history taking (medical and dental history, family history, social history), extra and intra oral examination. Facial profile was observed during extraoral examination. The Angle's and canine classification of the subjects were recorded. The Angle's classifications were observed first based on the relationship of the mesiobuccal cusp of the maxillary first molar and the buccal groove of the mandibular first molar. If the mesiobuccal cusp of the maxillary first molar is aligned with the buccal groove of the mandibular first molar, it was called Angle's class I relationship. Angle's class II relationship and Angle's class III relationship were recorded if the mesiobuccal cusp of the maxillary first molar mesially and distally positioned when occluded with the buccal groove of the mandibular first molar, respectively. The canine classifications were observed if the subject does not have molars based on the relationship of the mesial cusp ridge of the maxillary canine and the distal cusp ridge of the mandibular canine. If the mesial cusp ridge of the maxillary canine is aligned with the distal cusp ridge of the mandibular canine, it was called canine class I relationship. Canine class II relationship and Canine class III relationship were recorded if the mesial cusp ridge of the maxillary canine mesially and distally positioned to the distal cusp ridge of the mandibular canine, respectively. Dental impression were made by using alginate and stock trays and diagnostic models were made from dental plaster (gypsum product type II). Data from charting record, oral examination and diagnostic models were used to classify the occlusal relationship by using Angle's and canine classification. All clinical procedures were done by one observer.

Statistical analysis

Deviation of genotype frequencies from Hardy-Weinberg equilibrium expectations was evaluated with a chi-square test (degree of freedom = 1). SNPs that showed a significant distortion from Hardy-Weinberg equilibrium ($p<0.001$) was excluded from the analysis. Of all SNPs in this study, Fisher's exact test was applied to two-by-two contingency table in three genetic models: allele 1 versus allele 2, genotype 11 versus 12+22 and genotype 22 versus 11+12. The P-value was two-tailed with statistical significance at less than 0.05 ($p<0.05$).

Results

From 17 subjects, 7 subjects had Angle's class I relationships, 1 subject had canine class I relationships, 8 subjects had Angle's class III relationships, and only 1 subject had Angle's class II relationships. All subjects with Angle's class III relationship had concave facial profile and subjects with Angle's class I, canine class I, and Angle's class II relationship had straight facial profiles. We found 17 SNPs from 6 genes including IGF1, HSPG2, MATN1, TGFB2, VEGF and EVC that significantly correlated to Angle's/canine class I occlusal relationship (see Table 1) and 27 SNPs from 5 genes including IGF1, HSPG2, MATN1, TGFB1 and LTBP2 that significantly correlated to Angle's/canine class III occlusal relationship (see Table 2) at P value<0.05. The details of SNPs are in table 3 and 4. These findings showed that there were specific SNPs for Angle's/canine class 1 and class III occlusal relationship.

Discussion

The growth pattern of craniofacial structure and occlusal relationship are controlled by multiple factors including genetics and environment. The contribution of genetics and environment are poorly understood because of the developmental and structural complexity of the craniofacial region (Edison et al., 2003; Jelenkovic et al., 2008; Godinho et al., 2008; Wang et al., 2008; Shuhua et al., 2012). Most of the previous studies used loci and genes, while this study used SNPs which were known as one of the most specific biological markers.

Table 1 SNPs and genes associated with Angle's/canine class I relationship

Gene	SNPs
IGF1	rs6219, rs2288378, rs7136446, rs10735380, rs2946833, rs10860856, rs11111254
HSPG2	rs3736360, rs2290501, rs2290500, rs2305562, rs12567548
MATN1	rs10799085
TGFB2	rs3009947
EVC	rs11723498
VEGFC	rs309791, rs309800

Table 2 SNPs and genes associated with Angle's/canine class III relationship

Gene	SNPs
IGF1	rs2946833, rs6219, rs2288378, rs7136446, rs10735380, rs1457596, rs4015690
HSPG2	rs3736360, rs2290501, rs2290500, rs2305562, rs12567548, rs4654771, rs9426785
MATN1	rs6656216, rs686393, rs460911, rs10915065, rs437709, rs437722, rs675696, rs12022741, rs7520877, rs593993, rs665053
LTBP2	rs862037
TGFB1	rs2241715

The genetic backgrounds among populations are different due to the dispersion of settlement. Thai population was formed with the mixture of races and genetics, with contribution of Chinese (Shuhua et al., 2012) while American was formed with the mixture of European, African and Amerindian (Godinho et al., 2008; Wang et al., 2008). The different genes implicated in the etiology of malocclusion related to the different genetic backgrounds. In this study, only Thai population was selected to minimize the heterogeneity. We found only one subject who had Angle's class II relationship. This finding correlated with the low prevalence of mandibular retrognathism in Asian population (Angle et al., 1907). However, only one Angle's class II relationship subject is not adequate to find a relationship between Angle's class II relationship and SNP. More SNPs as well as more Angle's class II subjects need to be recruited.

From our result, there were different SNPs from 3 genes including Insulin-like growth factor 1 (IGF1), Heparin sulfate proteoglycan 2 (HSPG2) and Matrilin1 cartilage matrix protein (MATN1) that were specific for Angle's and canine class I and Angle's class III relationship patients. HSPG2 encodesa heparin sulfate proteoglycan called perlecan which is present in basement membrane and extracellular matrix. Perlecan is essential for cartilage and cephalic development which related to craniofacial abnormalities (Arikawa-Hirasawa et al., 1999). Reduction of perlecan results in chondro-dysplasia with facial bone anomally in Schwartz-Jampel syndrome (Rodger et al., 2007). *MATN1* encodes protein secreted by chondrocytes. This protein is thought to be involved in the formation of filamentous networks in the extracellular matrices of various tissues (Deak et al., 1999). This gene is considered to be a marker for the formation of cartilage (Pei et al., 2008). MATN1 influences in the development of long bone growth plate in endochondral ossification (Hansson et al., 2001). The increase of MATN1 can also be found in arthritic articular mandibular cartilage (Ohno et al., 2001). HSPG2 and MATN1 which were located in the 1p36 and 1p35 respectively were reported to be significantly related to mandibular prognathism (Yamaguchi et al., 2005). Recently in 2010, Jang and colleagues also found that Matrillin-1 polymorphism haplotype TGC (ht4;158T, 7987G and 8572C alleles) had risk effect for mandibular prognathism (Jang et al., 2010). According to Frazier-Bowers, IGF1 was one of candidate genes within the 12q23 region which related to mandibular prognathism (Frazier-Bowers et al., 2009). IGF1 is also reported to influence the body size in human (Woods et al., 1996).

Table 3 SNPs and genes associated with Angle's/canine class I relationship compared with Angle's/canine class III relationship

				Allele															
SNPs	gene	location	p-value	Angle's/canine class III subjects								Angle's/canine class I subjects							
				1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8
rs6219	IGF1	3UTR	0.003	G/A	G/A	G/A	G/A	G/A	G/G	G/A	G/A	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/A
rs2288378	IGF1	intron	0.003	G/A	G/A	G/A	G/A	G/A	G/G	G/A	G/A	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/A
rs7136446	IGF1	intron	0.003	A/G	A/G	A/G	A/G	A/G	A/A	A/G	A/G	A/A	A/A	A/A	A/A	A/A	A/A	A/A	A/G
rs10735380	IGF1	intron	0.003	A/G	A/G	A/G	A/G	A/G	A/A	A/G	A/G	A/A	A/A	A/A	A/A	A/A	A/A	A/A	A/G
rs3736360	HSPG2	coding	0.009	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/A	G/G	G/G	G/A	G/A	G/A	G/A	G/A
rs2290501	HSPG2	intron	0.009	A/A	A/A	A/A	A/A	A/A	A/A	A/A	A/A	A/C	A/A	A/A	A/C	A/C	A/C	A/C	A/C
rs2290500	HSPG2	intron	0.009	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/A	G/G	G/G	G/A	G/A	G/A	G/A	G/A
rs2946833	IGF1	flanking_3UTR	0.009	C/C	C/C	C/C	C/C	C/C	C/C	C/C	C/C	C/A	C/A	C/A	C/A	C/A	C/C	C/A	C/C
rs10799085	MATN1	flanking_3UTR	0.015	G/G	G/G	G/G	G/G	G/A	G/G	G/G	G/A	G/A	G/A	G/A	G/A	G/A	G/A	G/G	G/A
rs10860856	IGF1	flanking_3UTR	0.015	A/G	A/G	A/G	A/G	A/G	A/A	A/G	A/G	A/A	A/A	A/A	A/A	A/A	A/G	A/A	A/G
rs11111254	IGF1	flanking_3UTR	0.015	A/G	A/G	A/G	A/G	A/G	A/A	A/G	A/G	A/A	A/A	A/A	A/A	A/A	A/G	A/A	A/G
rs3009947	TGFB2	flanking_3UTR	0.029	G/G	A/G	A/G	A/G	A/G	A/G	A/G	A/G	A/G	A/G	G/G	A/A	A/A	A/A	A/A	A/G
rs11723498	EVC	intron	0.029	G/A	G/G	G/A	G/A	G/G	G/G	G/G	A/A	A/A	G/A	A/A	G/A	G/A	G/A	G/A	G/A
rs309791	VEGFC	flanking_3UTR	0.029	C/A	C/C	C/A	C/C	C/C	C/A	C/C	C/A	A/A	A/A	C/C	A/A	C/A	C/C	A/A	C/C
rs309800	VEGFC	flanking_3UTR	0.029	C/A	C/A	C/A	C/A	C/A	C/A	A/A	C/A	C/C	C/C	C/A	C/C	C/A	C/A	C/C	A/A
rs2305562	HSPG2	intron	0.029	G/G	A/G	A/G	G/G	G/G	A/G	A/G	A/G	A/G	A/A	G/G	A/A	G/G	A/A	A/A	A/A
rs12567548	HSPG2	flanking_5UTR	0.029	A/G	A/G	A/G	A/G	A/G	A/G	A/G	A/G	A/G	A/A	A/G	A/A	A/A	A/G	A/A	A/A

Table 4 SNPs and genes associated with Angle's/canine class III relationship compared with Angle's/canine class I relationship

				Allele															
SNPs	gene	location	p-value	Angle's/canine class III subjects								Angle's/canine class I subjects							
				1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8
rs3736360	HSPG2	coding	0.002	G/A	G/G	G/G	G/A	G/A	G/A	A/A	G/A	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G
rs2290501	HSPG2	intron	0.002	A/C	A/A	A/A	A/C	A/C	A/C	C/C	A/C	A/A	A/A	A/A	A/A	A/A	A/A	A/A	A/A
rs2290500	HSPG2	intron	0.002	G/A	G/G	G/G	G/A	G/A	G/A	A/A	G/A	C/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G
rs2946833	IGF1	flanking_3UTR	0.002	C/A	C/A	C/A	C/A	C/A	C/C	C/A	C/C	C/C	C/C	C/C	C/C	C/C	C/C	C/C	C/C
rs6656216	MATN1	flanking_3UTR	0.009	G/G	G/A	G/A	G/A	G/G	G/A	G/G	G/G	G/G	A/A	A/A	G/A	G/G	A/A	A/A	A/A
rs2305562	HSPG2	intron	0.009	A/G	A/A	G/G	A/A	G/G	A/A	A/A	A/A	G/G	A/G	A/G	G/G	G/G	A/G	A/G	A/G
rs12567548	HSPG2	flanking_5UTR	0.009	A/G	A/A	A/G	A/A	A/A	A/G	A/A	A/A	A/G	A/G	A/G	A/G	A/G	A/G	A/G	A/G
rs686393	MATN1	flanking_3UTR	0.015	G/A	G/A	G/G	G/A	G/G	G/A	G/A	G/A	G/G	G/G	G/G	G/G	G/A	G/G	G/G	G/G
rs4654771	HSPG2	intron	0.015	G/G	G/G	A/A	G/G	G/A	G/G	G/G	G/G	A/A	G/A	G/A	A/A	A/A	G/A	G/A	G/G
rs6219	IGF1	3UTR	0.015	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/A	G/A	G/A	G/A	G/A	G/A	G/G	G/A	G/A
rs2288378	IGF1	intron	0.015	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/A	G/A	G/A	G/A	G/A	G/A	G/G	G/A	G/A
rs7136446	IGF1	intron	0.015	A/A	A/A	A/A	A/A	A/A	A/A	A/A	A/G	A/G	A/G	A/G	A/G	A/G	A/A	A/G	A/G
rs10735380	IGF1	intron	0.015	A/A	A/A	A/A	A/A	A/A	A/A	A/A	A/G	A/G	A/G	A/G	A/G	A/G	A/A	A/G	A/G
rs1457596	IGF1	flanking_5UTR	0.015	G/A	G/A	G/G	G/A	G/A	G/A	G/G	G/A	G/G	G/A	G/G	G/G	G/G	G/G	G/G	G/G
rs460911	MATN1	flanking_3UTR	0.029	G/G	G/A	G/G	G/A	G/G	G/A	G/A	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G
rs10915065	MATN1	flanking_3UTR	0.029	G/G	G/A	G/G	G/A	G/G	G/A	G/A	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G
rs437709	MATN1	flanking_3UTR	0.029	G/G	G/A	G/G	G/A	G/G	G/A	G/A	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G
rs437722	MATN1	flanking_3UTR	0.029	G/G	G/A	G/G	G/A	G/G	G/A	G/A	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G
rs675696	MATN1	flanking_3UTR	0.029	G/G	G/G	G/A	G/G	A/A	G/G	G/A	G/A	G/G	G/G	G/G	G/G	G/G	G/G	G/G	G/G
rs12022741	MATN1	flanking_3UTR	0.029	A/A	A/A	A/G	A/A	G/G	A/A	A/G	A/G	A/A	A/A	A/A	A/A	A/A	A/A	A/A	A/A
rs7520877	MATN1	flanking_3UTR	0.029	A/A	A/A	A/G	A/A	G/G	A/A	A/G	A/G	A/A	A/A	A/A	A/A	A/A	A/A	A/A	A/A
rs593993	MATN1	flanking_3UTR	0.029	C/C	C/C	C/A	C/C	A/A	C/C	C/A	C/A	C/C	C/C	C/C	C/C	C/C	C/C	C/C	C/C
rs665053	MATN1	flanking_3UTR	0.029	A/A	A/A	A/A	G/G	G/A	G/G	A/A	G/G	G/G	G/A	G/G	G/G	G/G	G/G	G/G	G/G
rs9426785	HSPG2	flanking_3UTR	0.029	A/G	A/A	A/G	A/A	A/A	A/G	A/G	A/A	A/G	A/G	A/G	A/G	A/G	A/G	A/G	A/G
rs4015690	IGF1	flanking_5UTR	0.029	C/A	C/A	C/A	C/C	C/C	C/A	C/C	C/C	C/C	C/C	C/C	C/C	C/C	C/C	C/C	C/C
rs862037	LTBP2	intron	0.029	A/A	A/G	G/G	A/A	A/A	A/A	A/G	A/G	G/G	A/G	A/G	A/G	G/G	A/G	G/G	A/G
rs2241715	LGBF1	intron	0.029	C/C	C/C	A/C	A/C	C/C	C/C	A/C	A/C	A/C	C/C	A/A	A/A	C/C	A/C	A/A	A/A

The genes including transforming growth factor beta2 (TGFB2), vascular endothelial growth factor (VEGF) and Ellis-van Creveld (EVC) were found related to Angle's and canine class I relationship. TGFB2 is one of the transforming growth factor beta superfamily, plays important role in bone formation and homeostasis (Li et al., 2011). VEGF is involved with bone formation and was found in highest level at the posterior region of glenoid fossa during growth (Rabie et al., 2002). EVC encodes proteins that function in bone formation and skeletal development (Li et al., 2010).

The gene transforming growth factor beta1 (TGFB1) and latent transforming growth factor beta binding protein2 (LTBP2) were found related to Angle's/canine class III relationship (Jena et al., 2011). TGFB1 has similar structures and function as TGFB2. LTBP2 was known to assist in chondrogenic differentiation of mesenchymal stem cells and chondrocytes (Li et al., 2011).

From our review, this is the first report suggesting the marker genes and SNPs that are associated with different occlusal relationships in Thai population. We found some of our result related with previous studies in Asian population. For example, the relationship of HSPG2 and MATN1 and mandibular prognathism are found in Yamaguchi's study and also in our study.

The advantage of using genome association in this study was that the whole genotyping data could be used to scope down to the specific number of genes or SNPs. Comparing to the previous studies that only investigated genes or SNPs in specific loci, using specific SNPs from the genome wide study would give more information for investigating the relationship between Angels' classifications and SNPs of the marker genes. However, different SNP loci in the same gene may have different functions. Also, there are interactions between SNPs. Network analysis of the whole genotyping data and gene expression data would reveal more about their functions and interactions. The results from this study can be used to further develop a gene diagnostic tool for craniofacial patients. Identifying these polymorphisms in more patients would help clinicians to make an "individualized" diagnosis for their patients, which may result in better treatment plans and treatment outcomes.

Conclusions

In conclusion, there are SNPs related to specific occlusal relationships in a Thai population subgroup. These data lead to a further understanding of the genetic basis of occlusal relationships.

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การศึกษาความแตกต่างทางพันธุกรรมที่เกิดจากการเปลี่ยนแปลงลำดับเบสบนสายนิวคลีโอไทด์เพียงตำแหน่งเดียวของความสัมพันธ์ของการสบฟันในแนวหน้าหลังในประชากรไทยกลุ่มหนึ่ง

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บทคัดย่อ

วัตถุประสงค์ เพื่อระบุตำแหน่งของความแตกต่างทางพันธุกรรมที่เกิดจากการเปลี่ยนแปลงลำดับเบสบนสายนิวคลีโอไทด์เพียงตำแหน่งเดียว (สนิปส์) ที่สัมพันธ์ของการสบฟันที่ผิดปกติในแนวหน้าหลังในประชากรไทยกลุ่มหนึ่ง

วัสดุและวิธีการ นำกลุ่มตัวอย่างประชากรไทยจำนวน 160 คน ซึ่งเป็นกลุ่มผู้ป่วยที่เข้าร่วมในการศึกษาโรคภาวะโพแทสเซียมต่ำและอัมพาตเป็นระยะจากไทรอยด์เป็นพิษ และเข้าร่วมการในศึกษาลักษณะพันธุกรรมที่เกิดจากการเปลี่ยนแปลงลำดับเบสบนสายนิวคลีโอไทด์เพียงตำแหน่งเดียว (สนิปส์) แบบทั่วจีโนม ของโรงพยาบาลรามาธิบดี (จงเจริญประเสริฐ, 2012) มาคัดเลือกตามเกณฑ์ของงานวิจัย โดยผู้เข้าร่วมวิจัยจะต้องมีอายุมากกว่าหรือเท่ากับ 20 ปีบริบูรณ์และมีฟันคู่สบบริเวณฟันกรามแท้ซี่ที่หนึ่งหรือฟันเขี้ยวอย่างน้อยหนึ่งคู่ ได้จำนวนผู้เข้าร่วมงานวิจัย 17 คน ทำการตรวจในช่องปากและพิมพ์ปากทำแบบจำลองฟันเพื่อหาลักษณะความสัมพันธ์ของการสบฟัน โดยใช้การจำแนกการสบฟันแบบแองเกิล และ/หรือการจำแนกการสบฟันโดยใช้ฟันเขี้ยว ทำการคัดเลือกสนิปส์จำนวน 864 สนิปส์จากยีนจำนวน 28 ยีน ซึ่งเคยมีการศึกษาว่ามีหน้าที่ควบคุมการถ่ายทอดลักษณะความสัมพันธ์โครงสร้างขากรรไกร นำสนิปส์ของกลุ่มตัวอย่างมาวิเคราะห์กับลักษณะความสัมพันธ์ของการสบฟัน ทำการวิเคราะห์ผลโดยใช้วิธีทางสถิติฟิชเชอร์ผ่านโปรแกรมเพิร์ล

ผลการศึกษา สนิปส์ 17 สนิปส์ จาก 6 ยีน ได้แก่ ไอจีเอฟ 1, เอซเอสพีจี, เอ็มเอทีเอนท์ 1, ทีจีเอฟบี 2, วีอีจีเอฟและอีวีซี มีความเกี่ยวข้องกับการสบฟันแบบแองเกิลแบบที่ 1 อย่างมีนัยสำคัญ และมีสนิปส์ 27 รายการ จาก 5 ยีน ได้แก่ ไอจีเอฟ 1, เอซเอสพีจี, เอ็มเอทีเอนท์ 1, ทีจีเอฟบี 1 และแอลทีบีพี 2 ซึ่งเกี่ยวข้องกับการสบฟันแบบแองเกิลแบบที่ 3 อย่างมีนัยสำคัญ (P value<0.05) จากผลการศึกษาแสดงให้เห็นว่ามียีนและสนิปส์ที่สัมพันธ์กับการสบฟันแบบแองเกิลแบบที่ 1 และ 3

สรุป มีสนิปส์ที่สัมพันธ์อย่างมีนัยสำคัญกับการสบฟันในแนวหน้าหลังของประชากรไทยกลุ่มหนึ่ง ผลจากการศึกษาในครั้งนี้เป็นผลการวิจัยนำร่องเพื่อทำให้เกิดความเข้าใจที่มากขึ้นเกี่ยวกับความสัมพันธ์ของการเปลี่ยนแปลงลำดับเบสบนสายนิวคลีโอไทด์กับลักษณะความสัมพันธ์ของการสบฟันแบบต่าง ๆ

(ว ทันต จุฬาฯ 2558;38:185-196)

คำสำคัญ: *การจำแนกการสบฟันแบบแองเกิล; การศึกษาพันธุกรรมแบบทั่วจีโนม; การสบฟัน; ความแตกต่างทางพันธุกรรมที่เกิดจากการเปลี่ยนแปลงลำดับเบสบนสายนิวคลีโอไทด์เพียงตำแหน่งเดียว (สนิปส์); จีโนม; ประชากรไทย*

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