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Smoking modifies the genetic risk for early-onset periodontitis

Periodontitis has low-prevalence, highly severe disease manifestations with an early onset and rapid progression. The diagnosis is based on severe destruction of the alveolar bone in adolescents and young adults. Genetic susceptibility variants and smoking are well-established risk factors, but their interactions in modifying disease susceptibility have not been studied. We aimed to identify genetic risk variants of early-onset periodontitis that unmask their effects on tobacco smoke exposure. To this end, we analyzed 79,780,573 common variants in 741 northwest Europeans diagnosed to have >30% bone loss at >2 teeth before 35 y of age, using imputed genotypes of the OmniExpress BeadChip. Never versus ever smokers were compared in a logistic regression analysis via a case-only approach. To explore the effect of tobacco smoke on the expression of the G×S-associated genes, cultures of primary gingival fibroblasts (n = 9) were exposed to cigarette smoke extract, and transcripts were quantified by reverse transcription polymerase chain reaction. We identified 16 loci for which our analysis suggested an association with G×S increased disease risk ($P < 5 \times 10^{-5}$). Nine loci had previously been reported to be associated with spirometric measures of pulmonary function by an earlier G×S genome-wide association study. Genome-wide significant cis expression quantitative trait loci were reported for G×S-associated single-nucleotide polymorphisms at ST8SIA1 and SOST, indicating a causal role of these genes in tobacco-related etiopathology. Notably, SOST is a negative regulator of bone growth, and ST8SIA1 has a role in tissue remodeling. Cigarette smoke extract significantly altered the expression of 2 associated genes: SSH1 ($P = 5 \times 10^{-07}$), which is required for NF- κ B activation and innate immune responses to bacterial invasion, and ST8SIA1 ($P = 0.0048$). We conclude that the genetic predisposition to early-onset periodontitis is in part triggered by smoking and that tobacco smoke directly affects the expression of genes involved in bone homeostasis, tissue repair, and immune response.

Biography

Gurmukh Singh is Dental at Baba Farid University of Health Science. He is Research Focus on Bad impacts of Smoking on tooth and can lead to gum disease. His Student Level has a Bachelor of Dental Surgery.



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