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Electronic Presentations

Convention ID: 11
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Sequence Variations in Three Disease-associated Genes Display Potentially Functional role in Major Depression and Suicide Attempts in Chinese

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Keywords:
common and rare variants
case-control association study
re-sequencing analysis
bioinformatics prediction
major depression
suicide attempt

Introduction

Background: A large number of studies suggested that major depression (MDD) and suicidal behavior is heritable in nature. To date almost 200 genes were found to be associated with the diseases, although few genes were reported for their molecular mechanisms.

Objectives

This study aimed to find out whether there were common or rare sequence variations altering the risk for MDD or suicide attempt (SA) in three disease-associated genes.

Methodology

Materials and Methods: Three disease-associated genes (HOMER1, SLC6A4 and TEF) were chosen for case-control association studies and re-sequencing analysis. Following that, bioinformatics prediction was applied on those variants of interest.

Result

Results: HOMER1 polymorphism rs7713917 was found to have a significant association with MDD in recessive model and this polymorphism was also significantly associated with SA in homozygous and recessive models. In addition, some potentially shared functional genetic factors were found in the three genes for MDD and SA. Rs60029191 and a rare variant located in the regulatory region of the HOMER1 gene may affect the gene's promoter activities through interacting with predicted transcription factors (TFs). Two rare missense mutations in SLC6A4 coding regions were firstly reported in our group of Hong Kong Chinese MDD and SA patients, and both of them could affect the transport efficiency of SLC6A4 for serotonin as reported by previous studies. In addition, both of a most studied TEF polymorphism

rs738499 and a rare variant located in the promoter region of the TEF gene were found to be bound by TFs, which may be able to influence the gene's promoter activities.