Letter to the editor:

NON-RANDOM DISTRIBUTION OF GASTRIC CANCER SUSCEPTIBLE LOCI ON HUMAN CHROMOSOMES

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Dear Editor,

It has been well established that many molecular alterations are involved in the etiology of cancers. Genetic studies indicated that gastric cancer (GC) has significant heritability in human populations (Graham et al., 1994; Drăghicescu et al., 1998; Gao et al., 2011) through different molecular and genetics features (Gigek et al., 2017). In order to find the genetic elements involved, many studies investigated the association of genetic variations of a wide range of candidate genes. Meta-analyses studies have shown significant associations of many polymorphisms of candidate loci with the risk of GC at least in a specific ethnic group.

Numerous data revealed the non-randomness distribution of genes on human chromosomes (Hecht 1988; Lima-de-Faria et al., 1991; Mouchiroud et al., 1991; Saccone et al., 1996; Musio et al., 2002; Rafiee et al., 2008). Previously our study group has reported that polymorphic loci which were associated with the risk of breast cancer (Saify and Saadat, 2012), Alzheimer's disease (Saadat, 2016), schizophrenia (Saadat, 2013), Parkinson's disease and multiple sclerosis (Saadat, 2014) are non-randomly dispersed on human chromosomes. Based on our knowledge, there is no published data about randomness of distribution of the GC susceptible loci on human chromosomes. Therefore the present study was carried out.

A literature database (PubMed) was searched for relevant studies (the last search was updated in February 2018). The following search terms were used: Gastric cancer, meta-analysis, and genetic polymorphism. The search was limited to articles published in English. There were significant associations between genetic polymorphisms of 64 genes and the risk of GC in at least one human ethnic groups. Table 1 summarized these studies.

To evaluate the randomness/non-randomness distribution of GC susceptible loci on chromosomes, the statistical method of Tai and his colleagues (1993) was used. The relative width of human chromosomal band was determined using the diagram of the International System for Chromosome Nomenclature (ISCN, 1981). P-values less than 0.05 were considered as significant differences.
Table 1: List of polymorphic loci associated with susceptibility to gastric cancer

<table>
<thead>
<tr>
<th>Symbol</th>
<th>OMIM</th>
<th>Location</th>
<th>Reference</th>
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<th>OMIM</th>
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Table 1 (cont.): List of polymorphic loci associated with susceptibility to gastric cancer

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Analysis revealed that the 64 susceptible loci were distributed non-randomly on chromosome segments. The 1q22 (P<0.001), 2q14.1 (P<0.001), 5q31-q33 (P<0.001), 6p12-p21 (P<0.001), 10q23 (P<0.001), 11q13-q22 (P=0.025), 12q13.13 (P<0.001), 16q22.1 (P<0.001), 17q21-q25 (P<0.001), 19p13 (P=0.025) and 19q13 (P=0.025) were bearing higher numbers of GC susceptible loci. The human chromosome segments 6p12-p21, 17q21-q25, and 11q13-q22 were bearing seven (IL-17A, IL-17F, VEGFA, CDKN1A, TNF-α, LTA, and HspA1B), five (TP53, BRCAl, NME1, ACE, TIMP-2, and BIRC5) and four (GSTP1, CCND1, MMP7, and MMP1) GC susceptible genes, respectively.

The current findings have two significant aspects:
1) Distribution of the susceptible genes is not random throughout the human chromosomes.
2) The present findings help investigators to design a mass screening test tool for finding high risk persons to GC using the genetic polymorphisms in above-mentioned segments.

Previously it has been reported that human chromosome segments 10q23.3-q24.3, 16q13-q22.1, 17q12-q23, 19q13.1-q13.4, 22q11.2-q13.2 were significantly bearing breast cancer susceptible loci (Saify and Saadat, 2012). Comparing with the present findings, the segments 10q23, 16q22.1, 17q12-q23, and 19q13 revealed significant associations with both gastric and breast cancers.

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Conflict of interest
None.

REFERENCES


