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ARMENIANS ON THE GENETIC MAP OF SOUTH-WEST ASIA BASED ON GENOME-WIDE AUTOSOMAL DATA

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Armenians are an indigenous ethnic group historically inhabited the region in the southern Caucasus. The genetic structure of the population has been mostly tested for haploid (mitochondrial DNA and Y-chromosome) markers. Here the genetic relationships between Armenians and neighboring populations were analyzed based on genome-wide autosomal SNP typing data. Congruence between the results based on the Y-chromosomal and autosomal data was revealed, which point to the genetic isolation of Armenians from external influences during last several millennia.

Armenians – Y chromosome – SNP – population genetics

Հայերը հարավկովկասյան տարածաշրջանում պատմականորեն բնակվող տեղաբնիկ էթնիկ խումբ են: Մինչ այժմ պոպուլյացիայի գենետիկական կառուցվածքը հիմնականում հետազոտվել է հապլոիդ (միտոքոնդրիումային և Y-քրոմոսոմային) ժառանգական համակարգերի հիման վրա: Ներկա աշխատանքում ուսումնասիրվել են հայերի և հարակից պոպուլյացիաների միջև գենետիկական կապերը՝ օգտագործելով աուտոսոմային սփրինկլիկ լայնազենոմային տվյալներ: Ստացված արդյունքները վկայում են հայերի գենետիկական մեկուսացման մասին վերջին մի քանի հազարամյակների ընթացքում, ինչը միանգամայն համահունչ է Y-քրոմոսոմային և աուտոսոմային հետազոտությունների արդյունքներին:

Հայեր – Y քրոմոսոմ – SNP – պոպուլյացիոն գենետիկա

Армяне являются автохтонной этнической группой, населяющей Южно-Кавказский регион. До настоящего времени генетическая структура популяции была проанализирована в основном на основе гаплоидных (митохондриальной и Y-хромосомальной) генетических систем. В работе мы исследовали генетические связи между армянами и соседними популяциями, используя данные широкогеномного аутосомального скрининга. Выявлено соответствие результатов, полученных на основе Y-хромосомальных и аутосомальных маркеров, которые указывают на генетическую изоляцию армян на протяжении последних нескольких тысячелетий.

Армяне – Y хромосома – SNP – популяционная генетика

The Armenians represent an isolated ethno-national group that speaks Armenian language, a separate branch within the Indo-European language family. The population historically occupies the area stretching from the Eastern Caucasus to Anatolia and from the Black Sea to Mesopotamia, an important region in the context of the theories of ancient human migration and language dispersal. Previous genetic studies of the Armenians confirm a significant geographic stratification of the population and identify

their mainly unadmixed pattern at least over the past 4 kya [1, 2, 3]. However, the question of the origin of Armenians still remains a subject of hot debates among scholars of various disciplines.

The impressive advances of molecular genetic technique in recent years have enabled an increasing number of applications in reconstructing of genetic history of human populations [4, 5]. Though maternally inherited mitochondrial DNA (mtDNA) and paternally transmitted non-recombining Y chromosome (NRY) variation have provided a valuable insight into human origins and migration events, however uniparental markers are limited by the content of genome information [6]. In this context, the fast-growing whole genome sequencing has become a powerful tool in population genetics.

Currently, few genome-wide association studies of Armenian population have been performed. It was shown that general Armenian population follows clustering patterns similar to the Caucasus and the Levantine ones, and did not exhibit explicit genetic affinity to other Indo-European-speaking populations [7, 8]. However, the growing number of genome-wide data from several neighboring populations requires new genetic comparisons with these datasets.

In the present study, we aim to analyze genetic relationships between the populations of South-West Asia and, in particular, to reveal the location of Armenians on the genetic landscape of the region. Based on genome-wide autosomal DNA typing data we examine genetic variation of the considered populations and compare the results obtained with those based on uniparental genetic system.

Materials and methods. The genome-wide SNP data of a total of 331 samples from 18 populations were assembled from previously published studies. The Armenian samples (n=16) [8] were compared with those of other ethnic groups – Lebanese (n=8) [9], Palestinians (n=51) [10], Jordanians (n=20) [9], Syrians (n=16) [9], Turks (n=19) [9], Kurds (n=6) [8], Iranians (n=20) [9], Azeris (n=16) [11], Georgians (n=20) [9], Abkhazians (n=20) [8], Balkars (n=19) [8], Adygeis (n=17) [10], Northern Ossetians (n=15) [8], Chechens (n=20) [8], Lezgins (n=18) [9], Kumiks (n=14) [8], Nogais (n=16) [8].

For data management and quality control we used PLINK software [12]. SNPs genotyping success rate was set to > 97% and minor allele frequency >1%. Individuals with genotyping success rate less than 97% were excluded from the analysis. After LD pruning and filtering out sex-linked and mitochondrial SNPs, the data contained 208,459 autosomal SNPs.

To study the genetic relationships of Armenians to neighboring populations, we applied Principal Component Analysis (PCA) using the *smartpca* program (EIGENSOFT package) [13].

Results and Discussion. The principal components (PCs) of autosomal variation in the considered populations are shown on the PCA plot (fig. 1). We detected a distinct cluster of Armenians, a pattern that is consistent with the previous studies reporting Armenians as a genetic isolate of the region since the end of the Bronze Age [2, 14]. The reason of the lack of significant mixture signals with surrounding populations may be explained by cultural, linguistic, and religious peculiarities of Armenians [14]. However, genetic admixtures with several Eurasian populations were detected in the Armenian gene pool between ca. 4,000 – ca. 1,000 BC [14]. This time span almost comprises the temporal extent of Bronze Age, a period characterized by mass population movements after the invention of wheel, chariots, domestication of horse, and the appearance of powerful states in the West Asia [15, 16]. These events explain the reason of considerable genetic sharing of the modern Armenian population with ancient European agriculturalists, thus pointing to the possible routes of Neolithic farmers from the Near East via the Armenian Highland to Europe and the North Caucasus [3, 17].

On the whole, the PCA analysis places the studied populations along the South-North geographic axis. Notable that Armenians are located between the populations of the Near East and the Caucasus that coincides with the published results based on Y-chromosomal markers [3]. We observe that the populations of the North Caucasus appear relatively far from other populations and form a tight cluster, reflecting an isolation role of the geographic barrier: the Greater Caucasus mountain range. Moreover, the populations of Kurds, Turks, Azeris, and Iranians are located in close proximity to each other, flanked by Armenians.

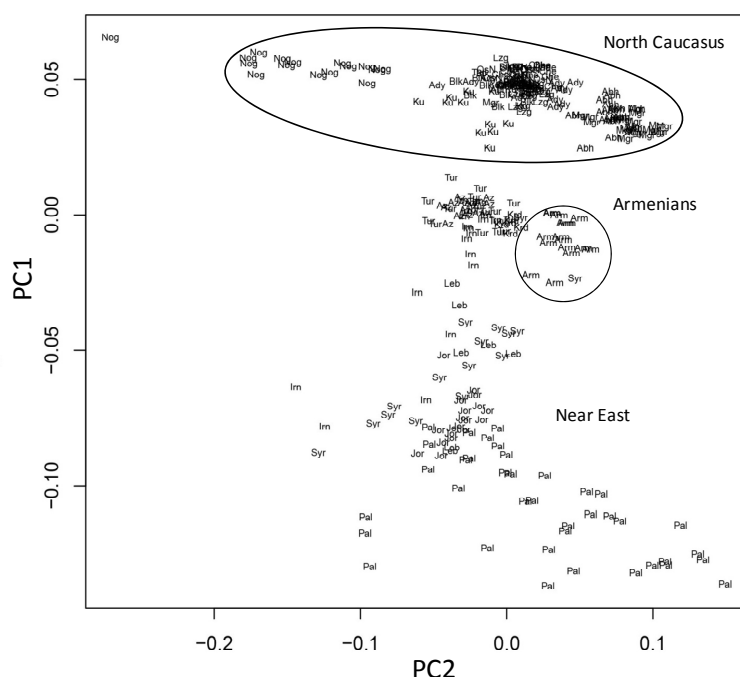


Figure 1. PCA plot based on autosomal SNPs frequencies in the populations studied.

In conclusion, the results of our study have shown that Armenians are genetically isolated in the South-West Asian region. Moreover, we found an agreement between the results based on biparentally and paternally inherited systems. In particular, the comparison reveals an intermediate position of Armenians between the populations of the Near East and the South Caucasus. Further studies with sufficiently larger samples from different regions within the Armenian Highland will provide deeper insights to the genetic peculiarities of the population.

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