

Molecular Anthropology and Genetic Variation in Iran

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Abstract: Molecular anthropology is commonly defined, as the use of molecular genetics techniques in the analysis and interpretation of the patterns of genetic structure in various modern human populations; comparison of human and non-human primate genes and the retrieval of genetic information from fossil specimens to address questions that anthropologists are interested in concerning human evolution and diversity. By examining DNA sequences in different populations, molecular anthropologists can figure out how closely related those populations. Certain similarities in genetic makeup let to determine whether or not different groups of people belong to the same haplogroup and thus, if they share a common ancestor or are from the same geographical origin. This is significant because it allows anthropologists to trace back the patterns of migration and settlements which gives helpful insight, as to how contemporary populations have formed and progressed over time. Iranian and Caucasus gene pool have been at different times an important source of the Near Eastern and Eurasian Y chromosome variability, as well as a recipient of variation entered with different migratory events and the first region of the Asian continent occupied by modern humans. Consistency of genetic results with the archaeological findings or/and historical events could show a tangible and reasonable evidence to the anthropologist and may lead to the reconstruction of several stages in the history and prehistory. This essay by expression the principles of anthropology and some empirical research, examples of studding genetic structure of Iran tries to emphasize the collaboration of different fields of anthropology to detect the reasonable results and answers to questions about past and history of important regions, such as Iran.

Key words: Non-human, DNA, molecular, trace back, migration

INTRODUCTION

To understand the full sweep and complexity of cultures across the human history, it is necessary to draw and builds upon knowledge from the social and biological sciences, as well as the humanities and physical sciences, concerning the application of knowledge to the solution of human problems. Anthropology in the term of study humans past and present, provides this definition while due to fundamental questions about human origin and culture diversity in the world, also calls for clarification of what constitutes a culture of how an observer knows where his or her own culture ends and another begins and other crucial topics in writing history, anthropology has been central in the development of several new (late 20th century) interdisciplinary fields. However, it is possible to view all human cultures as part of one large, ever-changing global culture. These dynamic relationships, between what can be observed on the ground, as opposed to what can be observed by compiling many local observations remain fundamental in any kind of anthropology fields (Rosaldo, 1993; Inda and Rosaldo, 2007).

Focused in a positive light, anthropology as one of the few places where humanities, social and natural sciences are forced to confront one another is a global discipline that is traditionally divided into 4 sub-fields; cultural anthropology, archaeology, linguistic anthropology and biological anthropology.

According to history of anthropology, over the last several decades, sociocultural anthropology has been heavily influenced by structuralist and postmodern theories. In contrast, archaeology and biological anthropology remained largely positivist and there are several characteristics that tend to unite anthropological work. One of the central characteristics is that anthropology tends to provide a comparatively more holistic account of phenomena and tends to be highly empirical. The quest for holism leads most anthropologists to study a particular place, problem or phenomenon in detail, using a variety of methods, over a more extensive period than normal in many parts of academia (Eriksen, 2004).

Biological anthropology and physical anthropology are synonymous terms to describe anthropological research focused on the study of humans and non-human

primates in their biological, evolutionary and demographic dimensions. It examines the biological and social factors that have affected the evolution of humans and other primates and that generates, maintain or change contemporary genetic and physiological variation. The pattern of genetic variation in modern human populations depends on the demographic history (population migrations, bottlenecks and expansions) as well as gene specific factors such as mutation rates, recombination rates and selection pressure. By examining patterns of genetic polymorphisms researchers can infer how past demographic events and selection have shaped variation in the genome. Thus, molecular anthropology has important implications for evolutionary biology, disease analyses and forensics. In this study, first the anthropological and genomic basis for genetic variation is overviewed followed by some specific empirical research examples highlighting the usage of the molecular anthropological investigations. The focus here is on Iran and Caucasus studies but it cannot be exhaustive due to space considerations.

DNA IS AN UNBROKEN LINK TO THE ANCESTORS, POPULATIONS AND RELATIVES

The inherited traits that shape human variation have been a major focus of anthropologists and biologists alike. Recently, molecular genetics tools have provided a massive array of possibilities to address anthropological questions in novel, powerful ways, leading to the formation of the young and exciting field of genetic anthropology. However, application of genetic knowledge to anthropology is still in its infancy and many methodological, theoretical, institutional and ethical issues remain to be addressed for a complete integration of genetics with anthropology. Still, over the past decades, several high-profile discoveries using genetic tools have changed the way anthropologists think about some of the fundamental questions related to human biological and cultural diversity.

Molecular anthropology, the study of human genetic polymorphisms is fast and ever-growing branch of anthropology that holds a great promise for both past and future. Some anthropologists believe that genetic/molecular anthropology is a science of future but it must be emphasized that it is a science of the past and present too. DNA as unbroken link to the ancestors, populations and relatives in molecular anthropology is useful to estimating the contribution of different gene pools to the make-up of present-day populations and test hypotheses about origin of linguistic and historical population movements. In addition, anthropology is playing a significant role in the understanding of

gene-environment interactions and contribution of populations to the detection of genes in common and complex diseases.

Anthropologists interested in reconstructing historical population movements and phylogenetic relationships initially used classical genetic data to achieve these aims. Classical genetic data uses proteins and blood groups and comprehensively provided the basis in the development of molecular anthropology. Hence, it have demonstrated by large-scale studies in human genome that the gene pool is not a simple sum of genes but is a dynamic system which is hierarchally organized and which maintains the memory of past events in the history of populations, the new field of molecular anthropology is utilizing DNA analysis for the reconstruction of human population structure, histories and evolution.

Biological and molecular anthropologists seek to understand how humans adapt to diverse environments, how biological and cultural processes work together to shape growth, development and behavior. In addition, they are interested in human biological origins, evolution and variation. They give primary attention to investigating questions having to do with evolutionary theory, the place in nature, adaptation and human biological variation. To understand these processes, biological anthropologists study other primates (primatology), the fossil record (paleoanthropology), prehistoric people (bioarchaeology) and the biology (e.g., health, cognition, hormones, growth and development) and genetics of living populations.

The human genome consists of 3 billion base pairs of nuclear DNA (nDNA) and around 16.6 Kb of extra-nuclear mitochondrial DNA (mtDNA). The completion of the human genome project and its descendant, the HapMap project has provided researchers with enormous opportunities and genetic markers for disease, population and evolutionary studies.

Evolution is regarded as a branching process, whereby populations are altered over time and may split into separate branches, hybridize together or terminate by extinction. This may be visualized in a phylogenetic tree, a hypothesis of the order in which evolutionary events are assumed to have occurred. Molecular phylogenetic is the analysis of hereditary molecular differences, mainly in DNA sequences, to gain information on an organism's evolutionary relationships. The result of a molecular phylogenetic analysis is expressed in a phylogenetic tree. Molecular phylogenetic is one aspect of molecular systematic, a broader term that also includes the use of molecular data in taxonomy and biogeography.

The mtDNA and Y chromosome analyses have proven to be the most useful for studying historical population movements because of their ease in analyses and non-recombining nature. In the absence of a recombination event both mitochondrial and Y chromosomes behave as single units and various markers stretched across are inherited as single blocks. A set of markers in these kind of DNA, generates haplotypes and the frequency of these haplotypes show great diversity in human populations.

Y chromosome DNA documents the paternal lineage and becoming a useful tool for tracing human evolution through male lineages. Using Y chromosome specific methods can improve the chances of detecting low levels of male DNA in a high background of female DNA. Since, the Y chromosome is passed down from father to son without any recombination can provide unique insights into the human past. Its long no recombining segment carries the most informative stable haplotypes in the genome whereas its permanent location in the male genome links these to male specific history. Consequently; it has been an attractive target for demographic inference. The Y chromosome consortium has established a system of defining Y-DNA haplogroups by letters A through to T with further subdivisions using numbers and lower case letters. Y chromosomal Adam is the name given by researchers to a theoretical male who is the most recent common patrilineal (male-lineage) ancestor of all living humans. Estimations of the date of this common ancestor have varied significantly in different studies (new binary polymorphisms reshape and increase resolution of the human Y chromosomal haplogroup tree). In contrast, for studying the female population history and determine matrilineal lineages, mitochondrial DNA is useful tool due to its maternally inheritance. mtDNA has been a crucial line of evidence in developing the current understanding of the genetic prehistory.

ANTHROPOLOGICAL BASIS OF GENETIC VARIATION IN IRAN AND CAUCASUS

In Molecular anthropology projects Middle Eastern region and Caucasus is so important due to its central role in human evolution. It has been a passageway for Homo sapiens between Africa and the rest of Asia and in particular, the first region of the Asian continent occupied by modern humans (Lahr and Foley, 1998). This area was also one of the regions where agriculture began during the Neolithic period, in particular in the Fertile Crescent, from which it spread westwards and eastwards. Different pre-historic sites across the Iranian plateau point to the

existence of ancient cultures and urban settlements in the 6th millennium BP, perhaps even some centuries earlier than the earliest civilizations in nearby Mesopotamia (Ghirshman, 1961).

At present, the Iranian population is characterized by an extraordinary mix of different ethnic groups speaking a variety of Indo-Iranian, Semitic and Turkic languages. Despite these features, only few studies have investigated the multiethnic components of the Iranian gene pool. However, in order to shed some light on the genetic structure of the Iranian and Caucasus population, as well as on the expansion patterns and population movements which affected these regions, some scattered studies have been conducted.

The latest study on Iranian Y chromosome was done by Grugni *et al.* (2012) in the Università di Pavia, Italy. The results showed an autochthonous but non-homogeneous ancient background mainly composed by J2a sub-clades with different external contributions. The phylogeography of the main haplogroups allowed identifying post-glacial and neolithic expansions toward Western Eurasia but also recent movements towards the Iranian region from Western Eurasia (R1b-L23), Central Asia (Q-M25), Asia Minor (J2a-M92) and Southern Mesopotamia (J1-Page08). Results of this study were evidence the important role of the Iranian plateau as source and recipient of gene flow between culturally and genetically distinct populations.

In some other studies, frequency and variance distributions of the main haplogroups together with the network analyses and age estimates were suggestive of pre-agricultural expansions from the Iranian plateau toward Europe via Caucasus/Turkey (J2-M410*, J2-PAGE55*, J2- M530 and R1b-M269*), as well as more recent movements into the Iranian region from Asia Minor/Caucasus (J1-M267*, J2-M92), Central Asia (Q-M25), Southern Mesopotamia (J1-Page08) and from West Eurasia (R1b-L23 and probably part of R1a-M198*). As evidence, traces of recent gene flows from Arab countries and Anatolia are revealed. Afterwards that Iran was invaded by several populations, such as the Arabs, Mongols and Ottoman Turks, in the Iranian Y chromosome gene pool by the presence of the well resolved sub-haplogroups J1-Page08 and J2-M92, respectively. The Arab J1-Page 08, likely originated in the region at the border between South-Eastern Turkey and North Iraq, underwent an important Neolithic expansion in the southern countries of the Middle East and represents the most important haplogroup in the modern populations of the Arabian Peninsula and North Africa. This lineage is observed at an averaged frequency of 6% in Iran, reaching a value in the Khuzestan Arabs (31.6%)

which is comparable to that observed in the neighboring Iraqi population (Al-Zahery *et al.*, 2011; Chiaroni *et al.*, 2010). An origin of haplotype J2a-M92 (gene flows from Anatolia to Iran) is North-Western Turkey with a distribution restricted to Asia Minor, the Balkans and the North-Eastern Mediterranean coasts. Where the highest variance is registered and a subsequent migration to the Balkans and then to the Italian Peninsula. In Iran, it is sporadically observed with the only exception of Sistan Baluchestan where it reaches an incidence of 12.5%.

To consistent of historical events, age estimate of the microsatellite variation associated to J2a-M92 (gene flows from Anatolia to Iran) in different studies showed that this haplotypes emergence in Turkey is 15000 years ago (15 kya) (Cinnioglu *et al.*, 2004; Underhill *et al.*, 2010; Myres *et al.*, 2011) after that in Italy is 11.4 kya (Di Gaetano *et al.*, 2009) then in the Greece is 9.7 kya (King *et al.*, 2008; Underhill *et al.*, 2010) and in Iran is (1.3 kya (~1300 years ago) (totally reported in <1% in whole Iranian population and 3% in Iranian Azeries; Grugni *et al.*, 2012). Its presence in Iran is ascribable to recent gene flow and is completely accordance to history of entrance of Turkic invaders (Seljuk Empire (1037-1194 AD) to Iran.

To comprehensively evaluate diverse ethnicity in Iran by depicting a fine-grained picture of the Iranian mitochondrial landscape, some studies have conducted (Farjadian *et al.*, 2011; Metspalu *et al.*, 2004). According to their results, a discordant pattern of high ethno-linguistic and low mtDNA heterogeneity is observed in a large set of autochthonous groups from the Iranian plateau. Maternally transmitted genetic inheritance reflects the major role of the Iranian landmass, as a crossroad for human migrations since prehistoric times where the strong geographic and linguistic barriers were insufficient to generate a significant structure.

Also according to these projects, cultural, political and to a minor extent, geographical factors seem to have acted as an obstacle to maternal gene flow mostly in Balochis, Lurs from Yasouj, Qashqaees, Zoroastrians and Jews. In these few ethnic groups, deep rooting genealogies and endogamy might have preserved ancestral lineages that can be representative of Proto-Indo-Iranian or prehistoric mitochondrial profiles which survived more recent historical invasions of the Iranian territory. The majority of Iranian mtDNAs have reported belongs to Western Eurasian component represented by haplogroups N1, N2, X, R2'JT, U and R0. Other results of molecular dating of Iranian mtDNA lineages show that haplogroup N and its subgroups coalesce to the time of 45-60 kya, marking the first stages

of modern humans movement out of Africa. The ancient ancestry of Iranian gene pool is, also confirmed by revealing of the unique N23 lineage survived both in Persians and Qashqaies, albeit at low frequencies (Bahmanimehr *et al.*, 2012).

In the theory of ethnicity in anthropology, cultural pluralism has formulated and then recast boundaries to discuss the flow of culture and dynamic relationships between all human cultures by encompassing movements of people across the world. This aspect of mobility and boundaries are important because they make it possible to operationalize an epistemological shift toward social change, transition and transformation (Barth, 1969).

Human gene pool, also as a dynamic system in the history of populations, migration and colonization has restricted by some different boundaries for gene flows to different places. In addition to physical barriers like mountains and rivers, factors, such as linguistic, ethnic and religious restrictions should be considered as potential barriers to gene flows in analyzing genetic data and molecular anthropology studies.

The best examples of barriers to gene flow are observed in the contour plots of haplogroups J and I and of sub-haplogroups U2 and 7. Both haplogroups J and I are found in high frequencies in northern Iran and exhibit a dwindling cline toward the Levant/Anatolia region, Europe and Asia. A sharp decline is observed beyond the Dasht-e Kavir desert with some resurgence of haplogroup I in central Asia but no similar presence in southwest Asia, suggesting that this desert could have deterred migrants from traversing from one region to the other. On the other hand, haplogroups U2 and 7 exhibit the opposite demic pattern with high frequencies in Southwestern Asia and in the Indus Valley, experiencing a sharp decline/disappearance (it is especially notable for U7) upon arrival at the Zagros mountains/Dasht-e Kavir region. These mtDNA results are mirrored in the distribution of Y chromosomal haplogroup R which exhibits a dramatic drop in the Dasht-e Kavir zone.

The presence of haplogroups/sub-haplogroups J, I, U2 and 7 in the Arabian Peninsula again attests to the close genetic affiliation between Persia and Arabia and may suggest gene flow between the two regions. In connection with the putative migratory link between Persia and Arabia, it is noteworthy that high-frequency for haplogroups J and I, in the contour plots are observed in the Arabia Peninsula, again possible signals of gene flow between the two regions (Terreros *et al.*, 2011).

Geneticists and anthropologists often expect that human language groups and gene pools will share a common structure. It is noted that both language and genes are passed from parents to children, mating tends

to be endogamous with respect to linguistic groups and splits in linguistic communities usually occur with splits in breeding populations. Cavalli-Sforza (2007) have reported that genetic trees of major geographic populations correlate well with language families. They argue that a process consisting of population fissions, expansion into new territories and isolation between ancestral and descendant groups will produced a tree-like structure common to both genes and languages.

Linguists agree that population fissions and range expansions play an important role in the generation of linguistic diversity. One informative approach toward disentangling the relative impact of geography and linguistic relationships is to analyze the genetic relationships of groups whose geographic neighbors are not their linguistic neighbors (Stoneking, 2000). In some experiments such examples of neighboring groups who speak different languages have analyzed (Nasidze *et al.*, 2001, 2004, 2006) in some cases have found geographical proximity of linguistically-different groups best explains their genetic relationships, e.g., Turkic-speaking Azerbaijanians in the Caucasus or Turkic-speaking Gagauz in Moldavia (Nasidze *et al.*, 2008) while in other cases, the linguistic similarity of geographically-distant groups best explains the genetic relationships, e.g., Mongolian-speaking Kalmyks who are surrounded by Slavic-speaking groups (Nasidze *et al.*, 2004).

In addition, in order to investigate the genetic relationships of two neighboring groups in South West Iran (Khuzestan Province) who speak languages belonging to different linguistic families; Semitic-speaking Iranian Arabs and Indo-European-speaking Bakhtiari with their geographic and linguistic neighbors, mtDNA and Non-Recombining Y chromosome (NRY) variation of the population have analyzed. The genetic results are in good agreement with the below historical information. The Iranian Arab group shows close affinities with the Bakhtiari and other Iranian Indo-European-speaking groups for both mtDNA and the Y chromosome. In fact, for both mtDNA and the Y chromosome, all of the Indo-Europeanspeaking and Semitic-speaking groups from West Asia exhibit generally low levels of differentiation.

History has left considerable records that indicate intensive contacts between Arabs and different groups in Iran. Much of the current region known as Iran was conquered by Arab armies of the early Islamic state in the 7th-8th centuries AD (Morony, 2005). However, there may also have been contact with Arabic groups before these conquests. Since the time of the conquests, there have been numerous migrations of Arab settlers to Iran, resulting eventually in the spread of Islam and in Arabic

becoming the language of religion and literature in Iran. Therefore, the Arabic presence, beginning at least 1400 years ago is clearly a major turning point in the history of Iran.

The correlation between patterns of linguistic and genetic variation has been studied by many researchers in different world regions with mixed positive and negative findings. Regional differences in population history are likely to explain some of the discrepant results. However, it is difficult to draw firm conclusions because these studies are heterogeneous with respect to the genetic and population sampling units, definition of linguistic variables and analytical methods. Researchers on this topic have identified the need for a method to directly compare language trees with population genetic trees.

CONCLUSION

A generation or so ago, anthropology still concentrated almost exclusively on detailed studies of local life in traditional societies and ethnographic fieldwork was its main in some cases its sole method. The situation is more complex now because anthropologists now study all kinds of societies and also because the methodological repertoire has become more varied and modern techniques in molecular genetics, anthropology as global discipline become a places where humanities, social and natural sciences are forced to confront one another and seems that history or human anthropology is rewriting in modern methods.

For reconstructing the history and studding rise and fall of great civilizations and geographical migration and cultural movements in important and civilization prone regions, such as Iran and Caucasus, need to define the larger and complex projects in these area. Previous Scattered and non-consistent studies on the genetic structure, phylogenetic and phylogeographic of Iran and Caucasus have certain problems and restrictions, such as small target population in most projects, superficial and mix sampling from society and ethnic groups, also a low and limit knowledge and information of genetics researchers in anthropology cultural feature, ethnicity of these regions that have led to unavailable tangible and comprehensive results for molecular anthropology studies of Iran and Caucasus.

In opinion of researchers, by considering these points and making inter disciplinary collaboration in different field of anthropology could observe the evolution in studding anthropology of this region and illuminate the historical events and human migration through this great gate way of Asia and Europe.

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