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Genetic Diversity of Interleukin Genes in Egyptian Goat Populations from Different Agro-Climatic Regions and Their Association with Disease Resistance

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Abstract

ENVIRONMENTAL stressor factors play an important role in shaping genetic diversity. The study aimed to assess the genetic diversity of IL genes and their association with disease resistance in six Egyptian goat populations. Blood samples were collected from six distinct goat populations to extract DNA. Data on of infectious diseases in animals were collected from owners. Polymerase chain reaction (PCR) amplification, sequencing, and bioinformatic analyses were conducted on four genes belonging to the IL family. The results revealed that the Interleukin 4 (IL4 exon3) gene was conserved among the Egyptian goat populations. While three haplotypes were observed for the Interleukin IL2 (exons 1 and 2) genes across the six breeds, 8 haplotypes were detected for IL2 (exon 3) and 4 haplotypes for Interleukin 13 (exon 4) genes. The phylogeny of Egyptian goat IL genes revealed more informative data for determining genetic distances between the populations. Based on the different genotypes of the studied IL genes and their association with the diseases in goats, the results suggested that the Hape_1 and Hap_3 of IL2 (exons 1 and 2) could be considered as candidate molecular markers for selecting goats with disease resistance in Aswani and Saedi and in Baladi, Barki, Sharkawi, and Zaribi, respectively. In conclusion, the results of the genetic analysis showed diversity of the IL genes among the Egyptian goat populations that may be associated with adaptation of each population to a specific environmental stress, including possible disease resistance.

Keywords: Interleukin genes, Goat breeds, genetic variation, agro-climates, innate immune.

Introduction

Diverse, locally adapted livestock breeds play an essential role in natural ecosystems. These breeds are impacted by random management practices as well as by the introduction of foreign breeds. Exotic breeds may have higher productivity; however, they may not be locally adapted to the environment [1]. In this context, the Food and Agriculture Organization of the United Nations (FAO) plays a major role in the genetic and phenotypic characterization of indigenous livestock breeds to ensure sustainable food production to promote healthy livelihoods and well-being for all [1].

One of the key objectives of livestock sustainable development is to minimize the depletion of animal genetic resources. One component is to compare the genetic variation within and between local breeds as well as to assess their adaptive traits in different climatic regions and diverse production systems. This type of data can provide new knowledge with regards to evolution, selection, and current and future conservation of animal genetic resources [2, 3]. Selection pressure on genes has been reported as an indicator of functional adaptation developed during the evolution of a breed to promote functional diversification [4]. The genes associated with the host's immune system are subjected to constant selective pressure from pathogens and environmental stress [5, 6].

The innate immune responses are the first line of defence against invading pathogens. Cytokines genes are responsible for communication with different

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immune cells during both acquired and innate immune responses. They are secreted by specific cells in the immune system [7]. It is known that cytokines genes regulate cell growth and proliferation of neuronal tissue and modify host responses to infection, inflammation, injury, and diseases of uncertain aetiology [8]. Interleukins (IL) are cytokine group that is expressed by white blood cells (leukocytes). IL can be divided into four major groups based on distinguishing structural features [9].

Goats are known to show a high degree of adaptation to extremely diverse environments, including poor-grazing grasslands and semi-harsh regions. The IL molecular evolution is an ideal model to provide evidence of significant positive selection in goats [9-11].

Previous studies reported that the positive selection of single-nucleotide polymorphism in IL32 and IL33 genes has an important role in disease control by enhancing the immune system in goat breeds [9, 12-14]. Bressani [15] reported IL2 (exons 1 and 2), IL2 (exon 3), and IL13 (exon 4) as candidate genes that could contribute to marker-assisted selection in animal breeding programs. McCormick and Heller [10] observed that the IL4 and IL13 genes have equal importance functions in the immune response to pathogenic infections.

In Egypt, goat has a high cultural and socio-economic significance in poor areas. The Egyptian environment has several geographic areas ranging from the Mediterranean climate in the north to tropical areas in the south. This contributes to differences in environmental stress and pathogen exposure of animals within and between the northern and southern regions. Three Egyptian goat populations are exposed to the agriculture Mediterranean climate (Baladi, Zaribi and Skarkawi), with the Barki exposed to the semi harsh Mediterranean climate, the Sadaei to the hot agro climate and the Aswani to the semi harsh hot climate [16].

In this study, we aimed to assess the genetic diversity of four IL genes in six goat populations from different climatic regions and their association with the data of disease resistance for sustainable goat management and genetics resources conservation.

Material and Methods

Sampling and genomic DNA extraction

Blood samples of six Egyptian goat populations aged from three months to four years (50 samples for each population) were collected in Ethylene diaminetetra acetic acid (EDTA) tubes from the different agro-climatic regions, the data related to history of infectious diseases in Egyptian goat populations were collected from owners (Table 1). DNA was extracted from whole blood as described by [11, 17,18].

IL genes amplification and sequencing

Genetic diversity in the IL genes regions were analysed using sequences generated for IL2 (exons 1, 2, & 3), IL4 (exon 3) and IL13 (exon 4). The primers sequences according to Bressani [15] were used for PCR amplification. A PCR cocktail consisting of 2X power Taq PCR master mix (Bioteke Corporation, China), 1.0 µM of each primer and 100 ng of DNA. The reactions were run in a Coy Temp Cycler II (Bio Rad, USA). The cycling condition includes an initial denaturation step at 95 °C for 3 min followed by 35 cycles of 50 sec at 94°C, 50 sec at the annealing temperature (Table 2) and 1 min at 72°C. The final extension was 5 min at 72°C. 2% agarose gels (with 100-bp DNA ladder) were used to loaded the PCR products to ensure successful PCR reactions.

DNA sequencing

The samples were prepared for sequencing using the standard protocol for the BigDye Terminator v3.1 Cycle Sequencing Kit (Thermofisher Scientific, California, USA). The 3130 Genetic Analyzer (Thermofisher Scientific, California, USA) was used to visualize the sequences. Sequencing reactions were performed for both the forward and reverse directions.

Statistical analysis

GENEIOUS 6.0 software [19] was used for Sequences aligment, inspected and trimmed. Then exported in FASTA format. DnaSP ver6 [20] used to determine haplotype diversity (h) and to generate a haplotype file.

The ARLEQUIN software Version 3.5.2.2 [21] was used to calculate the nucleotide diversity (π) and to extract information on the genetic and demographic features of the samples. The hierarchical distribution of total genetic diversity was determined using an analysis of molecular variance (AMOVA), as implemented in ARLEQUIN.

Genetic diversity within populations was expressed as gene variation, which is equivalent to the expected heterozygosity for diploid data [22] Genetic differentiation between populations was calculated as FST (from ARLEQUIN) to determine the extent of population sub-structure due to drift or selection.

The Network software [23] was used to construct the phylogeny tree to identify the relationships between the populations sampled. The phylogenetic network using the Median Joining method was implemented in the program NETWORK. This model-free method uses a parsimony approach, based on pairwise differences, to connect each sequence to its closest neighbour, and allows the creation of

internal nodes, which could be interpreted as un-sampled or extinct ancestral genotypes to link the existing genotypes in the most parsimonious way.

The association of IL genes genotypes with the data of infectious diseases in Egyptian goat populations was calculated using mathematical formula: % change = (final value – initial value)/initial value x 100% [24].

Results

Genetic diversity of IL genes in Egyptian goat populations

Successful PCR amplification of IL genes revealed amplified fragments of 468 bp for IL2 (exons 1 and 2), 406 bp for IL2 (exon 3), 393 bp for IL4 (exon3) and 595 bp for the IL13 (exon 4) gene. A total of 15 unique haplotypes (Table 3) were identified for IL2 (exons 1 and 2), IL2 (exon 3), and IL13 (exon 4). The GenBank database for haplotypes are accession numbers MN427994–MN427996 for IL2 (exons 1 and 2), MN427997- MN428004 for IL2 (exon3), and MN428012-MN428015 for IL13 (exon 4). Analysis of the sequences revealed that the IL4 (exon 3) gene was conserved in all six Egyptian goat populations (accession numbers MN428006).

Table 3 illustrates that absence of genetic variation in the IL2 (exons 1 and 2) was observed in the Zaribi population, whereas the remaining populations displayed two to three haplotypes with variable frequencies.

The frequency of IL2 (exon3) alleles showed no genetic variation in Zaribi and Aswani goat populations while Barki goat population showed two haplotypes compared to three haplotypes for Baladi, Sharkawi and Saedi.

The IL13 exon 4 gene showed no genetic variation in Barki while three haplotypes were observed for Zaribi and two haplotypes with variant frequencies for Baladi, Sharkawi, Aswani and Saedi.

The inbreeding coefficient was 0.984, 0.995 and 0.976 for IL2 (exons 1 and 2), IL2 (exon 3), and IL13 (exon 4), respectively.

The gene variation and nucleotide diversity in Table 4 show that the Aswani, Saedi and Sharkawi populations recorded a high level of gene variation and nucleotide diversity in the IL2 (exons 1 and 2) compared to the other three populations. Barki population showed higher differences in gene variation (0.510) and nucleotide diversity (0.002) for IL2 (exon 3) while Baladi population showed a high level of gene variation (0.327) for IL13 (exon 4) compared to the other populations.

Pairwise differentiation (FST) for IL2 (exons 1 and 2) between different populations ranged from 0 to 0.737 (Table 5). The pairwise distance values between Zaribi and the other populations were comparatively high (average = 0.423), and with significance values that support the hypothesis of significant differentiation at $p<0.05$. The pairwise distance values between Barki and other populations varied from 0.116 to 0.737 (average = 0.248) and were significant at $p<0.05$. In addition, the Saedi goat population was significantly different at $p<0.05$.

For IL2 (exon 3) pairwise differentiation (FST) between populations ranged from 0 to 0.276. The pairwise distances between Saedi and Aswani and the other goat populations were 0.012-0.035 and 0.0-0.035, respectively and with values that support significant differentiation ($p<0.05$) in and between each other. Also, the pairwise distances were significantly different between Baladi and Barki and Sharkawi and Zaribi. The Pairwise differentiation (FST) of the IL13 (exon 4) between populations ranged from 0.005 to 0.076. The differentiation of the IL13 (exon 4) between Egyptian goat populations at $p<0.05$ was not significant.

Genetic diversity of IL genes and their association with the infectious diseases in Egyptian goat populations.

Table 6 illustrates the association of IL genes diversity to the data of infectious diseases in animals (bacterial, viral and parasitic diseases). The IL2 (exons 1 and 2) gene variation showed that the Hap_1 recorded with high frequency for healthy goat in Aswani (40%) and Saedi (38%) populations while Hap_3 reported with high frequency for healthy goat in Baladi (56%), Barki (62%), Sharkawi (44%) and Zaribi (90%). Hap_2 showed with the infectious diseases in Baladi (42%) and Sharkawi (32%) goat.

The IL2 (exon 3) gene showed eight haplotypes, however, there was no association between the haplotypes and the data of infectious diseases whereas the frequency of Hap_1 was recorded in almost all goats. The same result was observed for IL13 (exon 4), the frequency for Hap_1 ranged from 46 to 76% compared to the other three haplotypes.

Phylogenetic analysis

The phylogram provided in Figure 1 shows the relationships between the Egyptian goat populations. The parsimony tree represents the preferred phylogenetic hypothesis of evolutionary changes among the Egyptian goat population from different agro-climatic regions depending on the sequences of the IL2 (exons 1 and 2), IL2 (exon 3) and IL13 (exon 4). The tree shows the Egyptian goat populations shared the ancestral character with variable relations and three unique sequence genotypes (Figure 1A) while Figure 1C shows four unique sequence genotypes.

Discussion

Many previous studies have shown the importance of characterizing the functional genes of local animals due to their adaptation to the surrounding environment and their resistance to diseases prevalent in the surrounding environment [1-6]. A recent study on the genotypes of sheep breeds using ovine 50K SNP chips to understand the genetic architecture and adaptability of native breeds revealed that a larger proportion of genetic variation was explained by developmental history and refined by geographical origin. The study emphasizes that local breeds' unique adaptability to specific climatic zones makes them valuable genetic resources for developing breeds capable of adapting to climate change [25].

The genetic diversity results of IL genes understudy revealed that the Aswani population was genetically conserved in the IL2 (exon 3) gene while the allele frequencies, and nucleotide diversities for the IL2 (exons 1 and 2) and IL13 (exon 4) were different compared to the other goat populations. The Baladi, Sharkawi and Saedi populations observed different allele frequencies and nucleotide diversities for IL2 (exons 1 and 2), IL2 (exon 3) and IL13 (exon 4) genes. The Zaribi population was genetically conserved in the IL2 (exons 1 and 2) and IL2 (exon 3) while the IL13 (exon 4) gene showed with three haplotypes compared to other goat populations. Barki population was genetically conserved in IL13 (exon 4) gene while the IL2 (exon 3) and IL2 (exons 1 and 2) genes represented three haplotypes and two haplotypes, respectively. The IL4 (exon 3) gene was genetically conserved in all six Egyptian goat populations. These results revealed that the IL genes have different genetic diversity between Egyptian goat breeds within the different agro-climatic regions, indicating the influence of environmental factors on genetic diversity and gene flow. The results pointed to importance of determining the genetic diversity of adaptive functional genes between different goat breeds to monitor management practices and ensure sustainable conservation of local genetic resources is critical.

The genetic diversity results showed polymorphic differences compared to Brazilian Saanen and Anglo-Nubian goats cross breeds [15] and Nigerian goats [26]. The differences could be related to the exposure of Egyptian goat breeds to different agroclimatic regions while the Brazilian and Nigerian goats are exposed to tropical weather. The Egyptian goat genotypes of the IL genes for each breed observed that the inbreeding coefficients and the pairwise differences (FST) among the six breeds confirmed the exposure of each breed to different environmental stresses and pathogens that caused gene variation. This is seen in the uniqueness of the Zaribi, Barki, Aswani, and Baladi, which showed significant pairwise divergence between populations.

In cattle, previous studies on the genetic diversity of IL genes reported no association was found between detected SNPs of IL12 and IL23 genes and resistance to mastitis based on the estimated breeding values for somatic cell score (SCS) [27], while the IL8 gene (SNP-180, G/A transition) tended to associate with SCS [28] and was suggested to be marker-assisted selection for mastitis resistance with IL6 and IL17A genes [29, 30]. In Nigerian cattle, SNPs in exon 1 of the IL10 gene was associated with trypanotolerance [31].

In goat, the IL2, IL4, IL13, and IFNG genes sequences were analyzed to identify SNPs that might be associated with resistance to gastrointestinal endoparasites in Saanen and Anglo-Nubian goats. They found that the SNPs in intron 1 of IL2, intron 3 of IL13 and exon 3 of IFNG were associated with gastrointestinal endoparasite resistance [32].

The obtained results of genetic diversity and their association with the data of infectious diseases reported that genetic diversity of IL2 (exons 1 and 2) gene Hape_1 in Aswani and Saedi and Hap_3 in Baladi, Barki, Sharkawi, and Zaribi were with high frequencies in in health goat compared to other genotypes. The IL2 (exon 3) and IL13 (exon 4) genes showed with no association between the haplotypes and the data of infectious diseases. The results suggested that the two haplotypes could be considered as candidate molecular markers for selecting the goat with a high immune response to pathogenic infections. The diversity in populations is related to the adaptation of each population to specific environmental stress including exposure to pathogens [25].

The goat IL genes phylogeny is poorly described in scientific reports compared to the studies reported in other mammalian species [9]. A previous genetic study on the mtDNA D-loop of the same goat populations reported that most of the Egyptian goats representing different agro-climatic regions have a shared maternal origin [16]. However, the results obtained in this study showed that while the majority of the Egyptian goat populations have the same maternal origin (Haplogroup A), variable relations and three unique populations were observed. The results revealed that additional genetic analysis of the adaptive functional genes such as the immune genes is more informative for determining genetic distances between the populations.

Conclusion

This study demonstrated that analysis of adaptive functional genes reveals genetic diversity in the Interleukin genes among the six Egyptian goat

populations. These populations have a long history of selection, both natural and artificial with each population of goat adapting to environmental stress including exposure to pathogens. The importance of determining the genetic diversity of adaptive functional genes between different goat populations to monitor management practices and ensure sustainable conservation of local genetic resources is critical. The results suggested that the Hape_1 of IL2 (exons 1 and 2) in Aswani and Saedi and Hap_3 of IL2 (exons 1 and 2) in Baladi, Barki, Sharkawi, and Zaribi could be considered as candidate molecular markers for selecting goats with disease resistance.

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Declaration of Conflict of Interest

The authors declare that they have no competing financial interests.

Ethical of approval

This study was approved by Ethics Committee of National Research Centre, Egypt (reference 14512012023).

TABLE 1. The agro- climatic regions of the Egyptian goat populations and the data of infectious diseases

Goat population	Healthy	Infectious diseases			Agro-climatic region description
		Bacterial (corynebacterium, brucellosis, mycoplasmosis)	Viral (pox, PPR)	Parasitic (coccidiosis, Faciolaiasis, mange)	
Aswani	35 (70%)	5 (10%)	--------	10 (20%)	Very hot climate, dry weather and semi-arid conditions
Baladi	33 (66%)	5 (10%)	4 (8%)	8 (16%)	Moderate climate and intensive agriculture
Barki	37 (74%)	4 (8%)	--------	9 (18%)	North coast climate
Saedi	30 (60%)	7 (14%)	--------	13 (26%)	Hot climate with high humidity and intensive agriculture
Sharkawi	34 (68%)	6 (12%)	5 (10%)	5 (10%)	Intensive agriculture and reclaimed land
Zaribi	45 (90%)	5 (10%)	----------	----------	Moderate climate with reference to cross b breed between Nubian and Jamnapari goat (Mason, 1984)

TABLE 2. Primers used to amplify the IL genes in six populations of Egyptian goats

Primers	Sequences 5'–3'	Location	Annealing temperature (°C)
IL2F1	GAA CTT CCT ATC TGC TTC TCT AA	Exons 1 & 2	55
IL2R1	TGA AGT TAC TAT TTC TTC TCC TC		
IL2F2	CGG GCA GCT AAA CTC TAA TTT TT	Exon 3	55
IL2R2	CAA TGT TAA AAT GCC CTT CCA T		
IL4F	CCC CCT GGA AAG AAG AAA TC	Exon 3	56
IL4R	TCC CCA GTG CCT AGA ACA GT		
IL13F2	TGC ACT CTG TCC TCA CAA GC	Exon 4	53
IL13R2	CCC TCC CTA ACC CTC CTT TA		

TABLE 3. The presence and frequency of alleles and the Single Nucleotide Polymorphism (SNP) substitution for IL2 (exons 1 and 2), IL2 (exon 3) and IL13 (exon 4) in Egyptian goat populations

Haplotype	SNPs	Aswani	Balade	Barki	Saedi	Sharkawi	Zaribi
IL2 (exons 1 and 2)							
Hap_1	A/T	0.2	0	0	0.1	0	0
Hap_2	T/G	0.46	0.34	0.76	0.46	0.44	0
Hap_3	G/T	0.34	0.66	0.24	0.44	0.56	1
IL2 (exon 3)							
Hap_1	T/T	1	0.9	0.66	0.9	0.9	1
Hap_2	A/T	0	0.1	0	0	0	0
Hap_3	T/G	0	0	0	0.05	0	0
Hap_4	A/T	0	0	0	0.05	0	0
Hap_5	T/G	0	0	0	0	0.05	0
Hap_6	A/T	0	0	0	0	0.05	0
Hap_7	A/C	0	0	0.3	0	0	0
Hap_8	A/T	0	0	0.04	0	0	0
IL13 (exon 4)							
Hap_1	T/T	0.9	0.8	1	0.9	0.9	0.8
Hap_2	C/T	0.1	0.2	0	0	0.1	0.12
Hap_3	T/G	0	0	0	0.1	0	0
Hap_4	A/G	0	0	0	0	0	0.08

TABLE 4. Genetic diversity at IL2 (exons 1 and 2), IL2 (exon 3) and IL13 (exon 4) in six Egyptian goat populations, expressed as gene and nucleotide diversity

Goat population	IL2 (exons 1 and 2)		IL2 (exon 3)		IL13 (exon 4)	
	Gene variation	Nucleotide diversity	Gene variation	Nucleotide diversity	Gene variation	Nucleotide diversity
Aswani	0.668± 0.053	0.002±0.002	0.000 ± 0.000	0.000 ± 0.000	0.248 ± 0.130	0.001 ± 0.001
Baladi	0.442± 0.087	0.001± 0.001	0.189± 0.108	0.001± 0.001	0.327± 0.153	0.001± 0.001
Barki	0.394± 0.100	0.001± 0.001	0.510± 0.090	0.002± 0.002	0.000 ± 0.000	0.000± 0.000
Saedi	0.616± 0.058	0.002± 0.002	0.195± 0.114	0.001± 0.001	0.143± 0.119	0.001± 0.001
Sharkawi	0.521± 0.042	0.001± 0.001	0.195± 0.114	0.001± 0.001	0.154± 0.126	0.001± 0.001
Zaribi	0.000 ± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.353± 0.123	0.0015±0.002

TABLE 5. Pairwise difference (FST) between the six Egyptian goat populations for IL genes expressed as the average number of pairwise differences between populations (below the diagonal), with significance values (above the diagonal)

IL2 (exons 1 and 2)						
	Aswani	**Baladi**	**Barki**	**Saedi**	**Sharkawi**	**Zaribi**
Aswani	--	0.216	0.018*	0.864	0.387	0.000*
Baladi	0.044	--	0.009*	0.324	0.432	0.009*
Barki	0.136*	0.303*	--	0.063	0.144	0.000*
Saedi	0.037	0.006	0.116*	--	0.864	0.000*
Sharkawi	0.008	0.421*	0.128*	0.035*	--	0.000*
Zaribi	0.340*	0.263*	0.737*	0.354*	0.003	--
IL2 (exon 3)						
	Aswani	**Baladi**	**Barki**	**Saedi**	**Sharkawi**	**Zaribi**
Aswani	--	0.396	0.276	0.035*	0.000*	0.000*
Baladi	0.052	--	0.009*	0.216	0.549	0.468
Barki	0.276	0.232*	--	0.210	0.170	0.276
Saedi	0.035*	0.042	0.211	--	0.012*	0.035*

Sharkawi	0.000*	0.015	0.170	0.012*	--	0.000*
Zaribi	0.000*	0.053	0.276	0.035*	0.000*	--
IL13 (exon 4)						
	Aswani	**Baladi**	**Barki**	**Saedi**	**Sharkawi**	**Zaribi**
Aswani	--	0.990	0.450	0.504	0.990	0.990
Baladi	0.076	--	0.504	0.144	0.504	0.990
Barki	0.012	0.059	--	0.990	0.990	0.504
Saedi	0.035	0.058	0.045	--	0.711	0.144
Sharkawi	0.059	0.038	0.042	0.002	--	0.756
Zaribi	0.052	0.064	0.005	0.043	0.037	--

TABLE 6. Genetic diversity of IL genes and their association with the data of infectious diseases

Haplotype %		**Aswani**	**Baladi**	**Barki**	**Saedi**	**Sharkawi**	**Zaribi**
IL2 (exons 1 and 2)							
Hap_1	Healthy	18	-------	-------	3	--------	--------
	Infectious diseases	2	-------	-------	2	--------	--------
Hap_2	Healthy	40	10	14	38	12	--------
	Infectious diseases	6	24	10	8	32	--------
Hap_3	Healthy	20	56	62	16	44	90
	Infectious diseases	14	10	14	28	12	10
IL2 (exon 3)							
Hap_1	Healthy	70	60	46	54	60	90
	Infectious diseases	30	30	20	36	30	10
Hap_2	Healthy	--------	6	--------	--------	--------	--------
	Infectious diseases	--------	4	--------	--------		
Hap_3	Healthy	--------	--------	--------	2	--------	--------
	Infectious diseases	--------	--------	--------	2		
Hap_4	Healthy	--------	--------	--------	2	--------	--------
	Infectious diseases	--------	--------	--------	4	--------	--------
Hap_5	Healthy	--------	--------	--------	--------	6	--------
	Infectious diseases					2	--------
Hap_6	Healthy	--------	--------	--------	--------	2	--------
	Infectious diseases	--------	--------	--------	--------	--------	--------
Hap_7	Healthy	--------	--------	30	--------	--------	--------
	Infectious diseases	--------	--------	--------	--------	--------	--------
Hap_8	Healthy	--------	--------	--------	--------	--------	--------
	Infectious diseases	--------	--------	4	--------	--------	--------
IL13 (exon 4)							
Hap_1	Healthy	60	46	76	58	60	74
	Infectious diseases	30	34	24	32	30	6
Hap_2	Healthy	10	20	--------	--------	6	10
	Infectious diseases	--------	--------	--------	--------	4	2
Hap_3	Healthy	--------	--------	--------	2	--------	--------
	Infectious diseases	--------	--------	--------	8	--------	--------
Hap_4	Healthy	--------	--------	--------	--------	--------	6
	Infectious diseases	--------	--------	--------	--------	--------	2

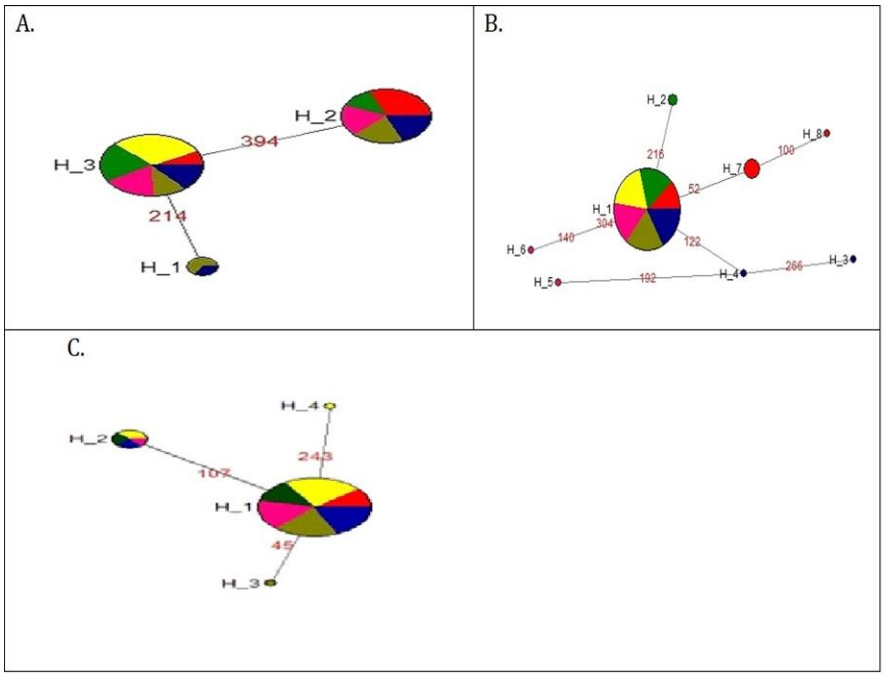

Fig. 1. Median-joining phylogenetic network of the Egyptian goat populations. This network includes all the most parsimonious trees linking the sequences of the (A) IL2 (exons 1 and 2), (B) IL2 (exon 3) and (C) IL13 (exon 4). Each unique sequence genotype is represented by a coloured circle sized relative to its frequency in the dataset. Genotypes are coloured according to the goat population from different locations. Each branch contains the specific substitution SNPs. Nodes are coloured according the different goat population from different agro-climatic regions. Yellow (Zaribi), Blue (Saedi), red (Barki), pink (Sharkawi), green (Baladi) and yellowish green (Aswani). H= haplotype.

References

1. Bélanger, J. and Pilling, D. The state of the world's biodiversity for food and agriculture. FAO, (2019).
2. Barendse, W., Harrison, B.E., Bunch, R.J., Thomas, M.B. and Turner, L.B. Genome wide signatures of positive selection: the comparison of independent samples and the identification of regions associated to traits. *BMC Genomics*, 10, 178 (2009).
3. Zhao, W., Zhong, T., Wang, L.J., Li, L. and Zhang, H.P. Extensive female-mediated gene flow and low phylogeography among seventeen goat breeds in southwest China. *Biochemical Genetics*, **52**, 355-364 (2014).
4. Ijaz, N., Liu, G., Jiang, X., Tesema, B., Wang, D., Xu, F., Zhao, Q. and Huang, H. Genetic signature of strong recent positive selection at fshβ gene in goats. *Pakistan Journal of Agricultural Sciences*, **52** (4),1109-1114 (2015).
5. Graham, A.L., Cattadori, I.M., Lloyd-Smith, J.O., Ferrari, M.J. and Bjornstad, O.N. Transmission consequences of coinfection: cytokines writ large? *Trends in Parasitology*, **23** (6), 284-291 (2007).
6. Neves, F., Abrantes, J., Steinke, J.W. and Esteves, P.J. Maximum-likelihood approaches reveal signatures of positive selection in IL genes in mammals. *Innate Immunity*, **20** (2), 184-191 (2014).
7. Turner, A.K., Begon, M., Jackson, J.A., Bradley, J.E. and Paterson, S. Genetic diversity in cytokines associated with immune variation and resistance to multiple pathogens in a natural rodent population. PLoS Genetics, 7 (10), e1002343 (2011).
8. Xu, N., Li, X. and Zhong, Y. Inflammatory cytokines: potential biomarkers of immunologic dysfunction in autism spectrum disorders. *Mediators of inflammation*, **2015** (1), 531518 (2015).
9. Asif, A.R., Qadri, S., Ijaz, N., Javed, R., Ansari, A.R., Awais, M., Younus, M., Riaz, H. and Du, X. Genetic signature of strong recent positive selection at interleukin-32 gene in goat. *Asian-Australasian Journal of Animal Sciences*, **30** (7), 912 (2016).
10. McCormick, S.M. and Heller, N.M. Commentary: IL-4 and IL-13 receptors and signaling. *Cytokine*, **75** (1), 38-50 (2015).
11. Ahmed, S.S., Abdel-Rahman, S.M., Grobler, P.J. and Kotzé, A. Allelic diversity of DQA2 exon 2 gene in Egyptian goat populations. *Indian Journal of Animal Research*, **52** (8), 1101-1106 (2018).
12. Ilie, D.E., Kusza, S., Sauer, M. and Gavojdian, D. Genetic characterization of indigenous goat breeds in Romania and Hungary with a special focus on genetic resistance to mastitis and gastrointestinal parasitism based on 40 SNPs. *PLoS One*, **13** (5), e0197051 (2018).
13. Luigi-Sierra, M.G., Fernandez, A., Martinez, A., Guan, D., Delgado, J.V., Alvarez, J.F., Landi, V., Such, F.X., Jordana, J., Saura, M. and Amills, M. Genomic patterns of homozygosity and inbreeding

depression in Murciano-Granadina goats. *Journal of Animal Science and Biotechnology*, **13** (1), 35 (2022).

14. Amiri Ghanatsaman, Z., Ayatolahi Mehrgardi, A., Asadollahpour Nanaei, H. and Esmailizadeh, A. Comparative genomic analysis uncovers candidate genes related with milk production and adaptive traits in goat breeds. *Scientific Reports*, **13** (1), 8722 (2023).
15. Bressani, F.A., Tizioto, P.C., Giglioti, R., Meirelles, S.L., Coutinho, R., Benvenuti, C.L., Malago, W., Jr., Mudadu, M.A., Vieira, L.S., Zaros, L.G., Carrilho, E. and Regitano, L.C. Single nucleotide polymorphisms in candidate genes associated with gastrointestinal nematode infection in goats. *Genetics and Molecular Research*, **13** (4), 8530-8536 (2014).
16. Ahmed, S., Grobler, P., Madisha, T. and Kotze, A. Mitochondrial D-loop sequences reveal a mixture of endemism and immigration in Egyptian goat populations. *Mitochondrial DNA A DNA Mapp Seq Anal*., **28** (5), 711-716 (2017).
17. John, S.W., Weitzner, G., Rozen, R. and Scriver, C.R. A rapid procedure for extracting genomic DNA from leukocytes. *Nucleic Acids Research*, **19** (2), 408 (1991).
18. Ahmed, S., Ali, N.I., Darwish, H.R., Salem, L.M., Elsayad, R.I. and El-Keredy, A. Genetic Characterization of Myf5 and POU1F1 Genes in Different Egyptian Local Rabbit Breeds and Their Association with Growth Traits. *Biochemical Genetics*, **62** (5), 3540-3556 (2024).
19. Kearse, M., Moir, R., Wilson, A., Stones-Havas, S., Cheung, M., Sturrock, S., Buxton, S., Cooper, A., Markowitz, S., Duran, C., Thierer, T., Ashton, B., Meintjes, P. and Drummond, A. Geneious Basic: an integrated and extendable desktop software platform for the organization and analysis of sequence data. *Bioinformatics*, **28** (12), 1647-1649 (2012).
20. Rozas, J., Ferrer-Mata, A., Sanchez-DelBarrio, J.C., Guirao-Rico, S., Librado, P., Ramos-Onsins, S.E. and Sanchez-Gracia, A. DnaSP 6: DNA Sequence Polymorphism Analysis of Large Data Sets. *Molecular Biology and Evolution*, **34** (12), 3299-3302 (2017).
21. ExcoYer, L., Laval, G. and Schneider, S. Arlequin ver 3.01. An integrated software package for population genetics data analysis. Bern, Switzerland: Computational Molecular Population Genetics Lab, Institute of Zoology, University of Bern, (2006).
22. Nei, M. Molecular evolutionary genetics. Columbia university press, (1987).
23. . Meißner, T., Mark, A., Williams, C., Berdel, W.E., Wiebe, S., Kerkhoff, A., Wardelmann, E., Gaiser, T., Müller-Tidow, C. and Rosenstiel, P. Metastatic triple-negative breast cancer patient with TP53 tumor mutation experienced 11 months progression-free survival on bortezomib events after ending standard treatments with grade 3 adverse events. *Molecular Case Studies*, **3** (4), a001677 (2017).
24. Bennett, J. and Briggs, W. Using & understanding mathematics: a quantitative reasoning approach. Pearson, eTextbook.(2019).
25. Wanjala, G., Bagi, Z., Gavojdian, D., Badaoui, B., Astuti, P.K., Mizeranschi, A., Ilisiu, E., Ohran, H., Juhas, E.P. and Loukovitis, D. Genetic diversity and adaptability of native sheep breeds from different climatic zones. *Scientific Reports*, **15** (1), 14143 (2025).
26. Yakubu, A., Salako, A., Donato, M., Takeet, M., Peters, S., Wheto, M., Okpeku, M. and Imumorin, I. Interleukin-2 ((IL-2) gene polymorphism and association with heat tolerance in Nigerian goats. *Small Ruminant Research*, **141**, 127-134 (2016).
27. Skelding, A., Schenkel, F., Sharma, B., Verschoor, C., Pant, S., Biggar, G., Boermans, H. and Karrow, N. Identification of single nucleotide polymorphisms in the bovine interleukin-12 and interleukin-23 receptor genes and their associations with health and production traits in Holstein cows. *Journal of Dairy Science*, **93** (10), 4860-4871 (2010).
28. Muhaghegh, D.M. Single nucleotide polymorphism in the promoter region of bovine Interleukin 8 gene and its association with milk production traits and somatic cell score of Holstein cattle in Iran. *Iran. J. Biotech.*, **12**(3),e1016 (2014).
29. Khan, M.Z., Wang, J., Ma, Y., Chen, T., Ma, M., Ullah, Q., Khan, I.M., Khan, A., Cao, Z. and Liu, S. Genetic polymorphisms in immune-and inflammation-associated genes and their association with bovine mastitis resistance/susceptibility. *Frontiers in Immunology*, **14**, 1082144 (2023).
30. Dusza, M., Pokorska, J. and Makulska, J. Identification of polymorphism in the bovine interleukin-17A gene and its association with mastitis in Polish Holstein? Friesian cattle. *Turkish Journal of Veterinary Animal Sciences*, **42** (4), 346-352 (2018).
31. Okweluma, N., Onagbesanb, O.M., Akinkuotuc, O.A., Bemjib, M.N., Daramolab, J.O. and Osinowoa, O.A. Variations in Interleukin-10 Gene Underlying monotherapy without adverse Trypanotolerance in Nigerian Indigenous Cattle. *Alexandria Journal of Veterinary Sciences*, **64** (2), 9-9 (2020).
32. Mandal, M., Mishra, C., Dash, S.K., Priyadarshini, P., Sabat, S.S., Swain, L. and Sahoo, M. Genomic insight to the disease resistance in goat. *The Pharma Innovation*, **7**, 98-103 (2018).

التنوع الوراثي لجينات الإنترلوكين في مجموعات الماعز المصرية من مناطق مناخية مختلفة وعلاقته بمقاومة الأمراض

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الملخص

تلعب عوامل الإجهاد البيئي دورًا مهمًا في تشكيل التنوع الوراثي. هدفت الدراسة إلى تقييم التنوع الوراثي لجينات الإنترلوكين وعلاقته بمقاومة الأمراض في ست مجموعات من الماعز المصري من مناطق مناخية مختلفة. تم جمع عينات الدم للماعز لاستخلاص الحمض النووي لاجراء تحليل البلمرة المتسلسل (PCR)، وتحليل المعلوماتية الحيوية و كذلك تحليل شجرة التطور الوراثية لاربعة جينات تنتمي إلى عائلة الإنترلوكين. كما تم جمع بيانات حول الأمراض المعدية في الحيوانات لكل بيئة.

كشفت النتائج أن جين الإنترلوكين ٤ (exon3) ذا نمط وراثي واحد فى سلالات الماعز المصرية المختلفة. في حين لوحظ وجود ثلاثة أنماط وراثية لجين IL2 (exons 1 and 2)، وثمانية انماط وراثية لجين IL2 (exon 3) ، و اربعة انماط وراثية لجين الإنترلوكين ١٣(exon 4).

بناءً على الأنماط الجينية في السلالات المختلفة كشف تحليل شجرة التطور الوراثية لجينات الإنترلوكين في الماعز المصري عن بيانات أكثر لتحديد المسافات الوراثية بين المجموعات. ، و اظهرت النتائج أن النمطين الوراثيين ١ و ٣ لجين IL2 (exons 1 and 2) يمكن اعتبارهما كعلامات وراثية جزيئية مرشحة لاختيار الماعز المقاومة للأمراض في سلالات الأسواني والصعيدي، بالإضافة إلى البلدى، البرقى، الشرقاوي، والزرايبى. كما اوضحت النتائج أن التنوع في جينات الإنترلوكين لسلالات الماعز المصرى مرتبطٌ بتكيف كل سلالة مع الظروف البيئية المحيطة، بما في ذلك مقاومة الأمراض المحتملة.

الكلمات الدالة: جينات الإنترلوكين، سلالات الماعز، التباين الوراثي، المناخات الزراعية، المناعة الفطرية.