Ribosomal protein S19 - 631 insertion is an African-originated mutation

Afrika kökenli toplumlarda ribozomal protein S19- 631 insersiyonu

Özge Cumaoğulları[1], Ayşenur Öztürk[1], Nejat Akar[1], Solaf Elsayed[2], Ezzat Elsobky[2], Bakhouche Houcher[3]

[1]*Pediatric Molecular Genetic Department, Ankara University, Ankara, Turkey*

[2]*Pediatric Hospital, Ain Shams University, Cairo, Egypt*

[3]*Department of Biology, University of Sétif, Faculty of Sciences, Sétif, Algeria*

To the Editor,

Ribosomes, the organelles that catalyze protein synthesis, consist of a small 40S subunit and a large 60S subunit. *RPS19* gene encodes a ribosomal protein (RP) that is a component of the 40S subunit. The protein belongs to the S19E family of RPs. It is located in the cytoplasm. Mutations in this gene cause Diamond-Blackfan anemia (DBA), a constitutional erythroblastopenia characterized by absent or decreased erythroid precursors in 25% of the patients. This suggests a possible extra-ribosomal function for this gene in erythropoietic differentiation and proliferation, in addition to its ribosomal function [1,2].

The *RPS19* gene is located on chromosome 19q13.2 and has six exons and spans 11 kb. The first exon is untranslated, and the start codon (AUG) is located at the beginning of exon 2 [1]. *RPS19* has three annotated pseudogenes. The *RPS19* gene has 196 sequence variants, of which 65 had no known pathogenicity. Recent studies have provided evidence for an association between common polymorphic markers in the *RPS19* exon 1 gene -631 locus insertion (ins) GCCA, AGCC and African origin [3]. At the same location, there are two common polymorphisms, -631 ins GCCA, AGCC refsnp:34020014 [4]. As previously reported, these polymorphisms do not have any effect on phenotype. The common polymorphism -631 ins GCCA was found in African-Americans with an allele frequency of 0.09 [3].

We aimed to study the frequency of this polymorphism in North African countries and also in Turkish Cypriots.

In this study, 280 Egyptians, 105 Algerians, 92 Turkish Cypriots and 6 Hemoglobin (Hb) O_{Arab} cases were included. *RPS19* gene exon 1 was amplified with "F5'TTA CTA CTC CCA CTT CCG GCC AGG GAA CAG 3', R5'TCA GGC ACG CGC GCT CTG AGG CTT CGG CGT C3' " primers followed by digestion with the restriction enzymes HpyF10VI (MwoI, Fermentas, USA). HpyF10VI recognizes 5'-G C N N N N N^N N G C-3'. 3% agarose gel electrophoresis was used to show the fragments, which are 295bp, 158bp and 73bp for normal sample and 173bp, 158bp, 126bp, and 73bp for homozygous sample.

In this study, we aimed to analyze the -631 ins GCCA mutation in three different Mediterranean populations, of which two were North African countries. Table 1 shows the genotype distribution in the three countries.

Previously, the RPS19 gene -631 ins was reported as an African marker in African-Americans in the United States population [3]. In order to test this hypothesis, we analyzed individuals from two different North African countries. Although rare, we found this polymorphism in Algerians and Egyptians. Our finding supported the hypothesis.

Address for Correspondence: Özge Cumaoğulları, MD, Ankara Üniversitesi Tıp Fakültesi, Pediatrik Moleküler Genetik Bilim Dalı Dikimevi 06100 Ankara, Turkey
Phone: +90 312 595 63 48 E-mail: ozge_cuma@yahoo.com

doi:10.5152/tjh.2010.12

Table 1. RPS gene -631 GCCA insertion genotype and allele frequency in Egyptians, Algerians and Turkish Cypriots

		Genotype Frequency		Allele Frequency
Country of origin	n	N/N (%)	4bpINS (%)	INS
Egypt	280	98.21 (275)	1.78 (5)	0.8
Algeria	105	96.2 (101)	3.8 (4)	1.9
North Cyprus	92	100 (92)	-	-

RPS gene -631 GCCA insertion genotype and allele frequency in Egyptians, Algerians and Turkish Cypriots

Further, we previously noted the Hb O_{Arab} mutation in the Turkish Cypriot population, hypothesizing that there could be an admixture of African descent [5]. We thus included samples from North Cyprus; however, we were unable to find this polymorphism in Turkish Cypriots.

Hb O_{Arab} was first detected in an Arab living in Israel, then in Egypt, Aden (Yemen), Bulgaria, Romania, Hungary, among American-Africans, and in Turkey. It is believed to have originated in the Sudan and to have spread from there to west Africa and to many countries once occupied by or in close contact with the Ottoman Empire [6,7]. For this reason, we screened six Hb O_{Arab} samples but none had this polymorphism. This may be due to the few samples analyzed.

In conclusion, we can say that this polymorphism is an indicator of African origin. However, it may also have spread to other Mediterranean countries, which will be the subject of another research.

Conflict of interest

No author of this paper has a conflict of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included in this manuscript.

References

1. Draptchinskaia N, Gustavsson P, Andersson B, Pettersson M, Willig T-N, Dianzani I, Ball S, Tchernia G, Klar J, Matsson H, Tentler D, Mohandas N, Carlsson B, Dahl N. The gene encoding ribosomal protein S19 is mutated in Diamond-Blackfan anaemia. Nature Genet 1999;21:169-75.
2. Cmejla R, Blafkova J, Stopka T, Zavadil J, Pospisilova D, Mihal V, Petrtylova K, Jelinek J. Ribosomal protein S19 gene mutations in patients with Diamond-Blackfan anemia and identification of ribosomal protein S19 pseudogenes. Blood Cells Mol Dis 2000;26:124-32.
3. Huang Q, Robledo S, Wilson DB, Bessler M, Mason PJ. A four base pair insertion in exon 1 of the RPS19 gene is a common polymorphism in African-Americans. Br J Haematol. 2006;135:745-6.
4. Ramenghi U, Campagnoli MF, Garelli E, Carando A, Brusco A, Bagnara GP, Strippoli P, Izzi GC, Brandalise S, Riccardi R, Dianzani I. Diamond-Blackfan anemia: report of seven further mutations in the RPS19 gene and evidence of mutation heterogeneity in the Italian population. Blood Cells Mol Dis 2000;26:417-22.
5. Cin S, Akar N, Arcasoy A, Çavdar A, Dedeoğlu S. Haemoglobin O Arab (B121 Glu-Lys) in Turkish Cypriot population. J Med Genet 1984;21:158.
6. Prozorova-Zamani V, Özsoylu Ş, Aksoy M, Headlee MG, Lam H, Wilson JB, Altay C, Huisman TH. Hb E and Hb E like in individuals from Turkey. Hemoglobin 1981;5:743-8.
7. Vella F, Beale D, Lehmann H. Hemoglobin O Arab in Sudanese. Nature 1966;209:308.