

CLINICAL MANIFESTATIONS & MOLECULAR ANALYSIS OF THIRTEEN PALESTINIAN FAMILIES WITH SANJAD-SAKATTI SYNDROME REVEALING A COMMON DELETION FOUNDER EFFECT AND ANOTHER TWO NOVEL MUTATIONS



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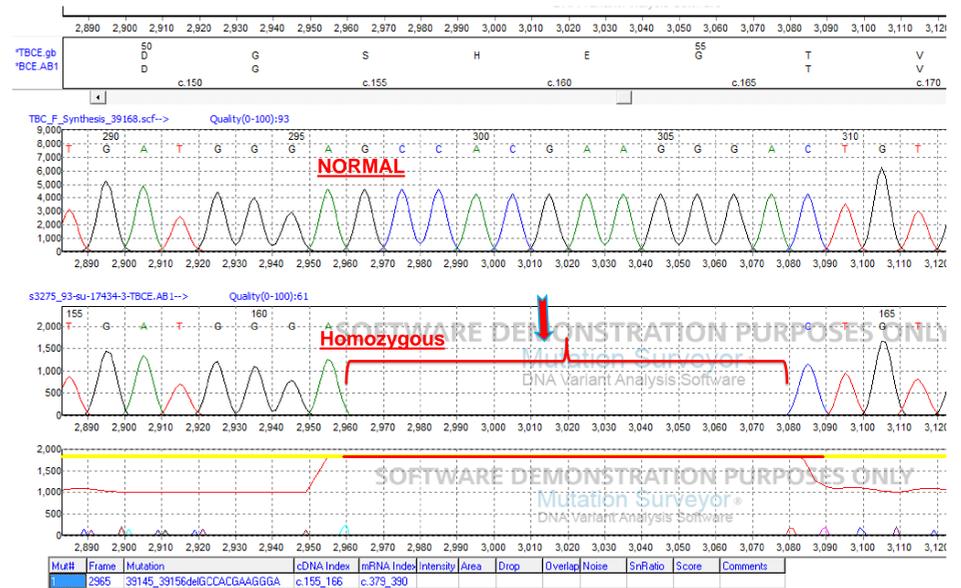
Objectives: Sanjad-Sakatti syndrome or hypoparathyroidism-retardation-dysmorphism syndrome (HDRs) is a rare autosomal recessive multisystemic disorder characterized by intrauterine and postnatal growth retardation, infantile-onset hypoparathyroidism that can result in severe hypocalcemic seizures, dysmorphic facial features, and developmental delay.

Clinical presentation and Methods: Thirteen unrelated Palestinian infants to a consanguineous Palestinian families presented in the first week of life with hypoparathyroidism, hypocalcemic seizures, dysmorphic features, growth retardation and developmental delay, assessed to have Sanjad-Sakatti syndrome and were managed accordingly. Clinical manifestations of all presenting patients and their molecular analysis has been checked to correlate clinical presentation with the specific genotype.

Results: Sequencing of the TBCE gene showed that eleven patients of our series of thirteen patients were homozygous for the mutation:

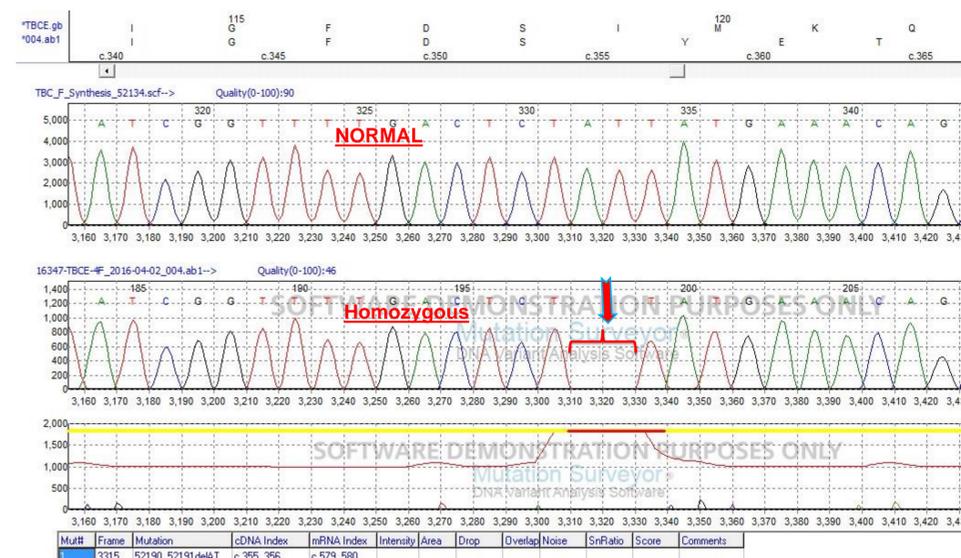
- ❖ (c.155-166del12;p.del52-55) in exon 3 of this gene, the common deletion founder effect of the TBCE gene in Arab patients, while the other two patients had novel mutations:
- ❖ c.355_356delAT in exon 4 of TBCE gene
- ❖ c.354-355del,p.S118fs of the TBCE gene (detected by whole exom sequencing).

c.155-166del12 Mutation of TBCE gene



c.155-166del12 mutation was detected before in Sanjad Sakati Syndrome patients as a disease causing mutation.
(Reference: [Nat Genet.](#) 2002 Nov;32(3):448-52. Epub 2002 Oct 21)

c.355_356delAT Mutation of TBCE gene



c.355_356delAT mutation is a **novel mutation**, not documented before in Sanjad Sakati Syndrome patients.
c.355_356delAT mutation is a deletion mutation of AT at codon 119 that leads to frame shift and premature termination of protein translation after 26 codons (p.I119YfsX26).

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1  ATG AGT GAC ACT TTG ACA GCG GAT GTC ATT GGT CGA AGA GTT GAA 15
2  Met Ser Arg Thr Leu Thr Ala Arg Val Ile Gly Arg Arg Val Glu
3  16  GTT AAT GGA GAA CAT GCA ACA GTA CDT TTT GGT GGT GTT GTC CCT 30
4  Val Met Thr Gly Ala Ala Arg Thr Val Ala Thr Thr Thr Ala Thr Thr
5  31  CCC GCG GCA GCA CCC TGG TTA GGA GTA GAA TGG GAC AAT CCC GAG 45
6  Pro Val Ala Gly Pro Thr Ser Ser Gly Val Gly Thr Arg Asn Pro Gly
7  46  AGA GGA AAG CAT GAT GGG ACC CAC GAA GGG ATT GTG TAT TTT AAA 60
8  Arg Arg Thr Ala Arg Thr Thr
9  61  TGC AGG CAG CCG ACA GGA GCA TCC TTT ATT CCG CCG AAC AAG GTA 75
10 Cys Arg Ser Thr Thr
11 76  AAT TTT GGA ACA GAT TTT CTT ACT GCA ATT AAG AAC GCG TAT GTG 90
12 Asn Thr Gly Thr Asp Thr Ser Thr Thr Thr Thr Thr Thr Thr Thr Thr
13 91  TTA GAA GAT GCA CCA GCA GAA GAT AGA AAA GAG CAA ATT GTT ACA 105
14 Leu Thr Arg Thr Thr
15 106 ATT GGA AAT AAA CCT GTG GAG ACT ATC GGT TTT GAC TCT GAT AG 120
16 Ile Gly Asn Asp Ser Pro Val Gly Thr Thr Gly Thr Asp Ser Leu Met
17 121 AAA CAG CAG AAG CAG 135
18 Arg Ser Thr Thr
19 136 AAC TAT GCA GTA TAT TAT GAT GAT GAT GAT GAT GAT GAT GAT GAT 150
20 Asn Asp Thr Val Thr Thr
21 151 GCA TGT CCT AAT ATC AGA AAG GTA GAT TTT TCA AAA AAG CTT TGT 165
22 Ala Thr Thr Asp Thr Thr

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Conclusions

- ❖ To our knowledge, this is the first description of a series of eleven families of Palestinian origin of this disease with molecular confirmation, showing the common deletion founder effect, allowing accurate genetic counseling, early diagnosis of affected kindreds, early therapeutic interventions and avoiding complications.
- ❖ Checking novel mutations for this disease, allowing to check if clinical presentation does correlate well with the specific genotype, and paving the way to better understanding the molecular genotype vs clinical phenotype in Palestinian patients.