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.

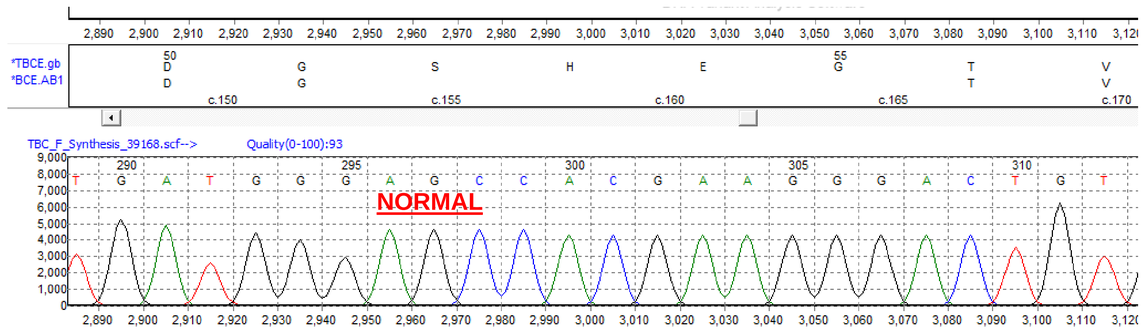
Clinical presentation and Methods: Thirteen unrelated Palestinian infants to a consanguineous Palestinian families presented in the first week of life with hypoparathyroidism, hypocalcemic seizures, dysmorphic features, growth retardation and developmental delay, assessed to have Sanjad-Sakatti syndrome 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.

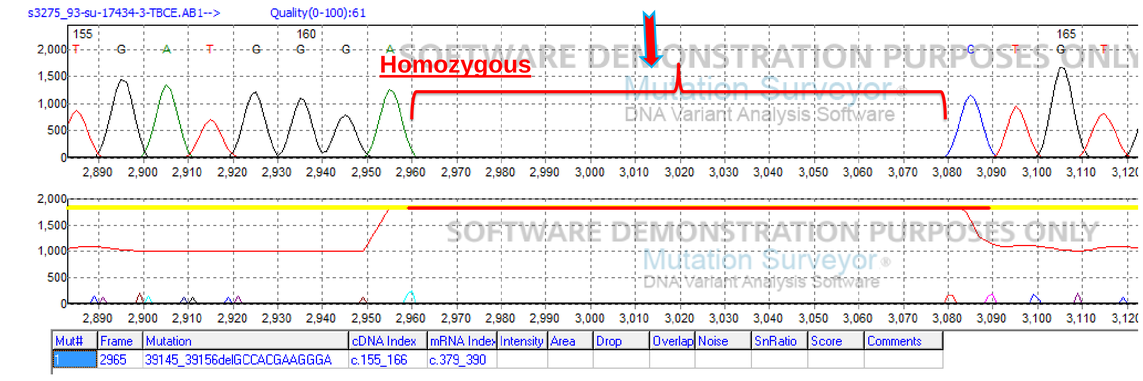
Results: Sequencing of the TBCE gene showed that eleven patients of our series of thirteen patients were homozygous for the mutation:

- (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).

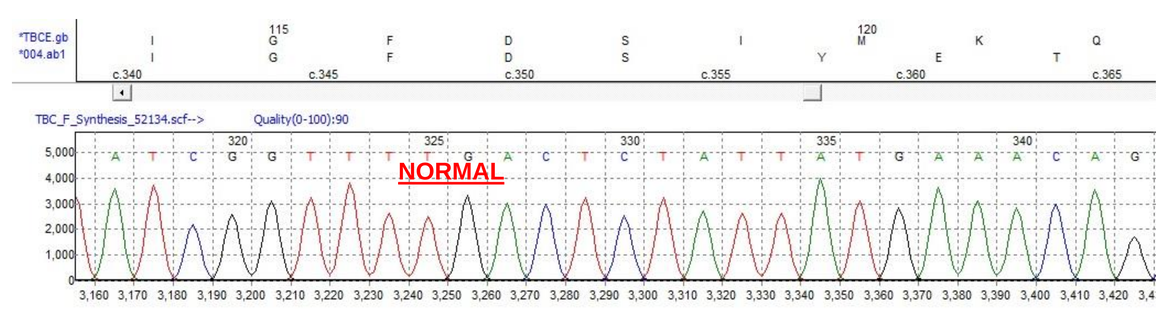
c.155-166del12 Mutation of TBCE gene

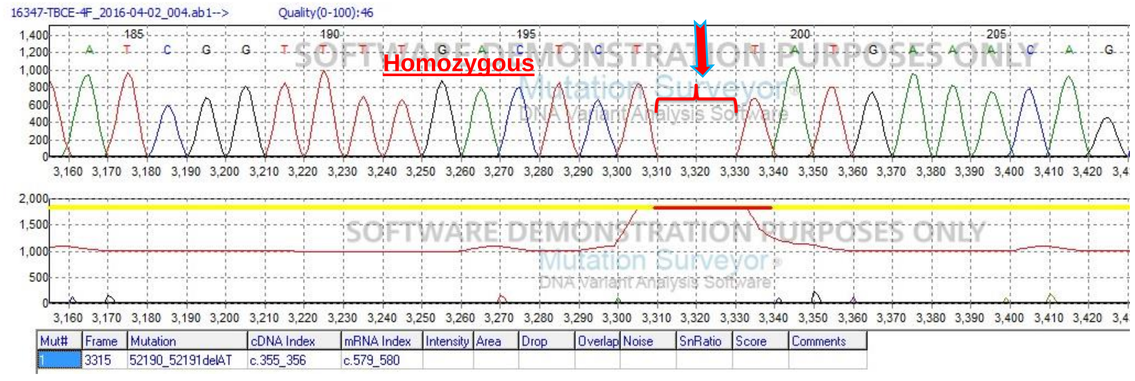




c.155-166del12 mutation was detected before in Sanjad Sakati Syndrome patients as a disease causing mutation.
(Reference: Nat Genet. 2002 Nov;32(3):448-52. Epub 2002 Oct 21)

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).

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.**