A NOVEL MUTATION IN THE PANCREATIC DUODENAL HOMEOBOX-1 (PDX-1) GENE IN A PALESTINIAN FAMILY RESULTING IN NEONATAL DIABETES

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Background: Pancreatic duodenal homeobox-1 (PDX-1) gene is a transcription factor that is expressed in beta and δ cells of the islets of Langerhans and in dispersed endocrine cells of the duodenum.

It is involved in regulating the expression of a number of key beta-cell genes as well as somatostatin.

PDX-1 is involved in the early development of the pancreas and plays a major role in glucose-dependent regulation of insulin gene expression. Homozygous disruption of the gene results in pancreatic agenesis which can lead to early-onset insulin-dependent diabetes mellitus (IDDM), while heterozygous mutations in the gene result in impaired glucose tolerance and symptoms of diabetes as seen in MODY4 and late-onset type II DM.

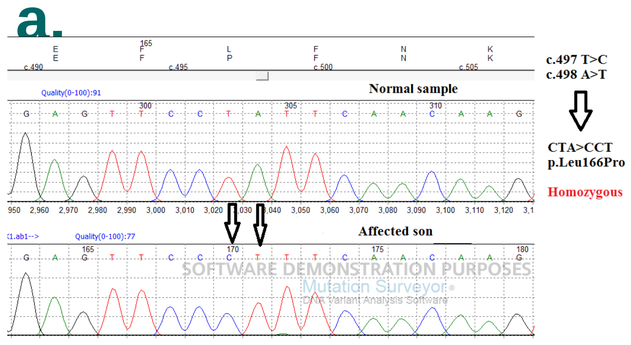
Here we describe a novel mutation in PDX-1 gene in a Palestinian family resulting in neonatal diabetes.

Clinical presentation and Methods: A 1-day-old male newborn, admitted to NICU due to antenatal diagnosis of duodenal atresia, polyhydramnios and IUGR. Following delivery initial abdomen x-ray showed classic double bubble sign, Laparotomy revealed duodenal web, resection was done with duodeno-duodenal anastomosis. He was noticed to have hyperglycemia since admission and clinical picture suggestive of neonatal diabetes, C-peptide: <0.02, Insulin level <0.5, normal thyroid function tests.

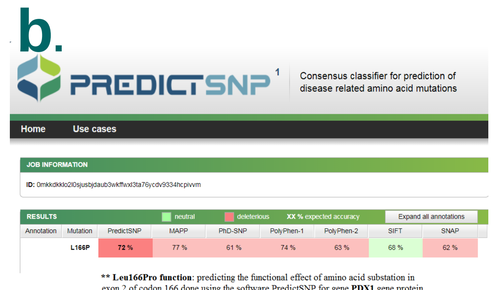
Abdomen CT was suggestive of dorsal pancreatic agenesis.

Results: DNA sequencing of the PDX-1gene for the patient revealed a novel homozygous mutation Leu166Pro in exon 2 of the PDX1 gene. Father & Mother were heterozygous for the same mutation.

a.



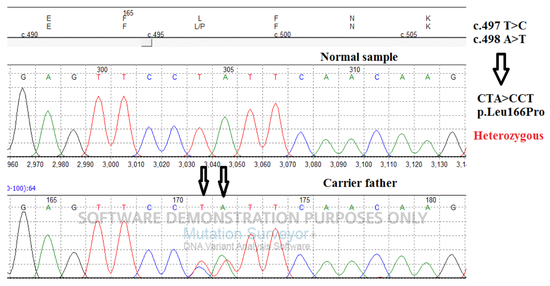
b.

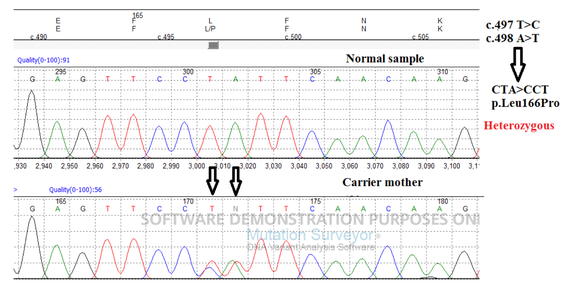


** **Leu166Pro function**: predicting the functional effect of amino acid substation in exon 2 of codon 166 done using the software PredictSNP for gene **PDX1** gene protein product, gave (72%) deleterious effect on the protein function of this gene.

a. The patient is *homozygous* for the mutation Leu166Pro in exon 2 of the PDX1 gene (Novel).

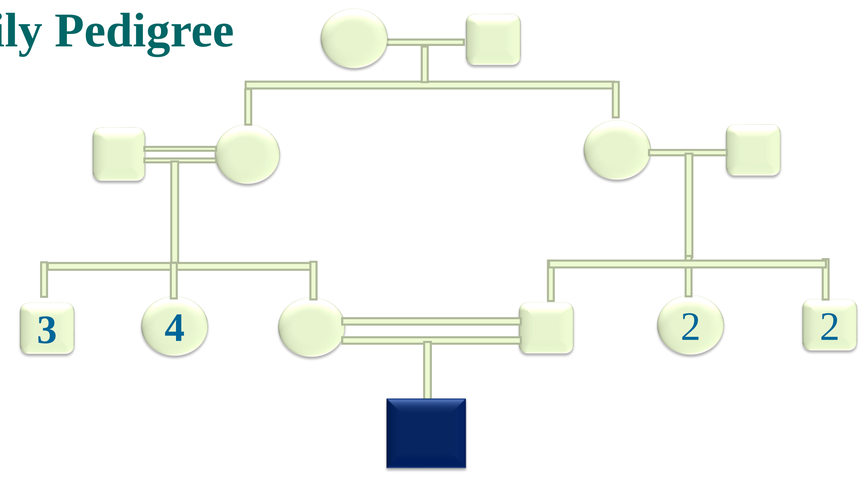
***b.* Leu166Pro function: predicting the functional effect of amino acid substation in exon 2 of codon 166 done using the software Predict SNP for gene PDX1 gene protein product, gave (72%) deleterious effect on the protein function of this gene.**





Segregation study showed that both parents were heterozygous for the mutation Leu166Pro in exon 2 of the PDX1 gene

Family Pedigree



Conclusions

- **Congenital absence of the pancreas is an extremely rare condition;**
- **To our knowledge, this is the first description of this disease in a Palestinian family with molecular confirmation, allowing accurate genetic counselling, early diagnosis of affected kindreds, early therapeutic interventions and avoiding complications.**

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Diabetes and insulin

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