Location	Care	Amino acids		Mutation	REVEL	MCAD	MaxEntSca		NetGene
Location	Gene	change	PolyPhen-2	Taster	(>0.5)	M-CAP	n	BDGP	2
chr14:8155	TOUD	C17(D	PROBABLY	Disease	0.710	Possibly			
8933	TSHR	p.C176R	DAMAGING	causing	0.718	Pathogenic			
chr14:8160	TCUD	D 45011	PROBABLY	Disease	0.042	Possibly			
9751	TSHR	p.R450H	DAMAGING	causing	0.943	Pathogenic			
chr14:8160	TCUD	- D5290		Disease	0.202	Possibly			
9984	TSHR	p.R528S	BENIGN	causing	0.303	Pathogenic			
chr14:8161	TCUD			Disease					
0254	TSHR	p.K618*		causing					
chr15:4540	DUOX	p.D137E	PROBABLY	Disease	0.53	Possibly			
4068	2	p.D15/E	DAMAGING	causing	0.55	Pathogenic			
chr15:4540	DUOX	• D276W	p.R376W PROBABLY Disease Possibly 0.421						
2093	2	p.R376W	DAMAGING	causing	0.421	Pathogenic			
chr15:4540	DUOX	F2001/		Polymorphi	0.111	1 111 .			
1791	2	p.E389K	BENIGN	sm	0.111	Likely Benign			
chr15:4540	DUOX	• V407E	PROBABLY	Disease	0.27	Possibly			
1737	2	p.V407F	DAMAGING	causing	0.37	Pathogenic			
chr15:4538	DUOX	p.G1521*		Disease					

Table SVI. In silico analysis of variants detected in the present study.

6434	2			causing		
chr15:4540	DUOX	- D 42211	PROBABLY	Disease	0.296	Possibly
1090	2	p.R432H	DAMAGING	causing	0.296	Pathogenic
chr15:4540	DUOX	D 42 4¥		Disease		
1085	2	p.R434*		causing		
chr15:4540	DUOX	p.R434_S440de		Disease		
1064	2	1		causing		
chr15:4539	DUOX	- V520*		Disease		
9648	2	p.K530*		causing		
chr15:4539	DUOX	56016	PROBABLY	Disease	0. (01	Possibly
9089	2	p.F591S	DAMAGING	causing	0.691	Pathogenic
chr15:4539	DUOX			Disease		
8800	2	p.G624fs		causing		
chr15:4539	DUOX			Disease		
8798	2	p.R625*		causing		
chr15:4539	DUOX			Disease	0.070	
6563	2	p.V779M	BENIGN	causing	0.079	
chr15:4539	DUOX	T 0026		Disease		
6491	2	p.T803fs		causing		
chr15:4539	DUOX	50704	PROBABLY	Disease	0.702	Possibly
6177	2	р.Е879К	DAMAGING	causing	0.793	Pathogenic
chr15:4539	DUOX	p.R885L	PROBABLY	Disease	0.22	Possibly

6158	2		DAMAGING	causing		Pathogenic			
chr15:4539	DUOX	a D11100	PROBABLY	Disease	0.91	Possibly			
1946	2	p.R1110Q	DAMAGING	causing	0.91	Pathogenic			
chr15:4538	DUOX	A 120/T	PROBABLY	Disease	0.201	Possibly			
9889	2	p.A1206T	DAMAGING	causing	0.381	Pathogenic			
chr15:4538	DUOX								
9811	2	IVS28+1G>T					8.72/0.22	0.91/-	0.82/-
chr15:4538	DUOX	V1 41 CO	PROBABLY	Disease	0.012	Possibly			
7285	2	p.Y1415C	DAMAGING	causing	0.913	Pathogenic			
chr15:4540	DUOX	DAAG	PROBABLY	Polymorphi	0.000	Possibly			
8396	A2	p.R94C	DAMAGING	sm	0.222	Pathogenic			
chr15:4540	DUOX	XO 4 C ¥		Disease					
9472	A2	p.Y246*		causing					
chr19:1800	SLC5A	0(20*		Polymorphi					
4669	5	p.Q639*		sm					
chr2:14809				Polymorphi		Possibly			
63	TPO	p.S309P	BENIGN	sm	0.351	Pathogenic			
chr2:14811			PROBABLY	Disease					
20	TPO	p.R361L	DAMAGING	causing	0.311				
chr2:14917		0.571 D		Polymorphi	0.146	Possibly			
08	TPO	p.S571R	BENIGN	sm	0.146	Pathogenic			
chr2:15004	TPO	p.E757fs		Disease					

18				causing
chr2:15206	TPO	p.R846W	PROBABLY	Polymorphi
72	IFO	p.K840W	DAMAGING	sm
chr2:15443	TPO	p.P883S		Polymorphi
94	IFO	p.r 8855	BENIGN	sm
chr5:17742	PROP1	p.G51V		Polymorphi
1297	TROTT	p.031 v	BENIGN	sm
chr7:10730	SLC26	p.Y78H	PROBABLY	Disease
3808	A4	p. 1 / 811	DAMAGING	causing
chr7:10733	SLC26	p.A434T		Disease
4884	A4	p.A4341	BENIGN	causing
chr7:10734	SLC26	p.Y578H	PROBABLY	Disease
1570	A4	p. 1 <i>5</i> / 811	DAMAGING	causing
chr8:11010	TRHR	p.I168M		Polymorphi
0245	IMIK	p.1106W	BENIGN	sm
chr8:13388	TG	p.N212S		Polymorphi
5463	10	p.112125	BENIGN	sm
chr8:13390	TG	p.R896Q	PROBABLY	Disease
0739	10	p.1090Q	DAMAGING	causing
chr8:13390	TG	p.E955fs		Disease
6036	10	p.199918		causing
chr8:13395	TG	p.V1738I	BENIGN	Polymorphi

Possibly Pathogenic Likely Benign Possibly Pathogenic Possibly Pathogenic Possibly Pathogenic Possibly Pathogenic Likely Benign Possibly Pathogenic Possibly

Pathogenic

Likely Benign

0.215

0.317

0.166

0.96

0.602

0.507

0.068

0.065

0.325

0.078

3766				sm		
chr8:13398	ТC	n \$1012N		Polymorphi		Likaly Danian
0087	TG	p.S1912N	BENIGN	sm	0.071	Likely Benign
chr8:13398	ТC	n 11021V		Polymorphi	0.361	Likely Benign
0143	TG	p.I1931V	BENIGN	sm	0.301	LIKELY Delligh
chr8:13403	TG	p.L2282fs		Disease		
1903	10	p.L226218		causing		
chr8:13404	TG	p.I2394M	PROBABLY	Disease	0.397	Possibly
2211	10	p.12394WI	DAMAGING	causing	0.397	Pathogenic
chr8:13412	TG	p.R2585W	PROBABLY	Disease	0.117	Possibly
5846	10	p.r.2383 w	DAMAGING	causing	0.117	Pathogenic

PolyPhen-2, MutationTaster, REVEL and M-CAP were used to predict the effects of missense and indel mutations; MaxEntScan, BDGP, and NetGene-2 were used to predict the damaging effects of splicing mutations with a wild-type/mutant score; – means depletion of the 5' splice site. PolyPhen-2, Polymorphism Phenotyping v2; REVEL, Rare Exome Variant Ensemble Learner; M-CAP, Mendelian Clinically Applicable Pathogenicity; BDGP, Berkeley Drosophila Genome Project; NA: not available.