SUPPLEMENTARY TABLE S2. PREDICTION OF FUNCTIONAL EFFECT OF THE VARIANTS BY *IN SILICO* ALGORITHMS AND ALLELE FREQUENCY

Gene	*Splicing variant*	*HSF*[a]
TPO	c.483-2A>G	–31.7% variation Alteration of the wild type acceptor site, most probably affecting splicing
TG	c.5042-2A>G	–30.62% variation Alteration of the wild type acceptor site, most probably affecting splicing

Gene	*Missense variants*		*RS number*	*SIFT*[b]	*PolyPhen2*[c]	*AAF*[d]
TPO	c.1535C>A	p.P512H	rs150489706	0.01, D	0.999, D	0.00001252
TPO	c.1759G>A	p.G587R	rs770562452	0.001, D	1.000, D	0.000
DUOX2	c.3329G>A	p.R1110Q	rs368488511	0.003, D	0.994, D	0.000
DUOX1	c.1525C>T	p.R509W	rs757808802	0.000, D	1.0, D	0.000

[a] The Human Splicing Finder. Possible predictions: site broken (variation score <–10%), new site (variation score >10%).

[b] The scores and predictions are separated by a comma. There are two possible predictions: D (damaging, score ≤0.05); T (tolerated, score >0.05).

[c] Polymorphism Phenotyping v2. The scores and predictions are separated by a comma. There are three possible predictions: D (probably damaging, score ≥0.909), P (possibly damaging, 0.447 ≤ score ≤0.909), B (benign, score ≤≤0.446).

[d] Alternative allele frequency in African population in The Genome Aggregation Database.

RS number, reference single nucleotide variants number.

SUPPLEMENTARY TABLE S3. SPLICING PREDICTION FOR THYROGLOBULIN ACCORDING TO THE FORMULA OF SHAPIRO AND SENAPATHY

Splicing
TG Intron between ex25 and ex26 c.5042-2A>G
5′ splice site—AAAAGG/gtaggttgg
3′ splice site—tgcctttccccc(a)g/GCCAAG
% Nucleotide at splice junction

Norm—5′

–3	A	28
–2	G	13
–1	G	81
+1	g	100
+2	t	100
+3	a	54
+4	g	11
+5	g	85
+6	t	45
T value		517

5′ T-min = 65
5′ T-max = 638
3′ T-min = 111
3′ T-max = 808

Norm—3′

–14	t	44
–13	g	14
–12	c	34
–11	c	34
–10	t	45
–9	t	44
–8	t	40
–7	c	41
–6	c	44
–5	c	40
–4	c	28
–3	c	79
–2	a	100
–1	g	100
+1	G	47
T value		734

Score normal = 5′ = 100(517 – 65)/(638 – 65) = 78.883
Score normal = 3′ = 100(734 – 111)/(808 – 111) = **89.383**

Mutated—3′

–14	t	44
–13	g	14
–12	c	34
–11	c	34
–10	t	45
–9	t	44
–8	t	40
–7	c	41
–6	c	44
–5	c	40
–4	c	28
–3	c	79
–2	g	0
–1	g	100
+1	G	47
T value		634

Score mutated = 5′ = 100(517 – 65)/(638 – 65) = 78.883
Score mutated = 3′ = 100(634 – 111)/(808 – 111) = **75.036**

Senapathy P, Shapiro MB, Harris NL 1990 Splice junctions, branch point sites, and exons: Sequence statistics, identification, and applications to genome project. Methods Enzymol **183:**252–278.

Supplementary Table S4. Splicing Prediction for Thyroperoxidase According to the Formula of Shapiro and Senapathy

Splicing
TPO ex6 c.483-2A>G
5′ splice site—AACAACAG/gtattgttt
3′ splice site—atttgtctccac(a)g/AGACCA
% Nucleotide at splice site junction

Norm—5′

–3	C	40
–2	A	59
–1	G	81
+1	g	100
+2	t	100
+3	a	54
+4	t	8
+5	t	4
+6	g	21
T value		467

5′ T-min = 65
5′ T-max = 638
3′ T-min = 111
3′ T-max = 808

Norm— 3′

–14	a	10
–13	t	43
–12	t	48
–11	t	52
–10	g	9
–9	t	44
–8	c	44
–7	t	41
–6	c	44
–5	c	40
–4	a	23
–3	c	79
–2	a	100
–1	g	100
+1	A	28
T value		705

Score normal = 5′ = 100(467 – 65)/(638 – 65) = 70.157
Score normal = 3′ = 100(705 – 111)/(808 – 111) = **85.222**

Mutated—3′

–14	a	10
–13	t	43
–12	t	48
–11	t	52
–10	g	9
–9	t	44
–8	c	44
–7	t	41
–6	c	44
–5	c	40
–4	a	23
–3	c	79
–2	g	0
–1	g	100
+1	A	28
T value		605

Score mutated = 5′ = 100(467 – 65)/(638 – 65) = 70.157
Score mutated = 3′ = 100(605 – 111)/(808 – 111) = **70.875**

Senapathy P, Shapiro MB, Harris N L 1990 Splice junctions, branch point sites, and exons: Sequence statistics, identification, and applications to genome project. Methods Enzymol **183:**252–278.