

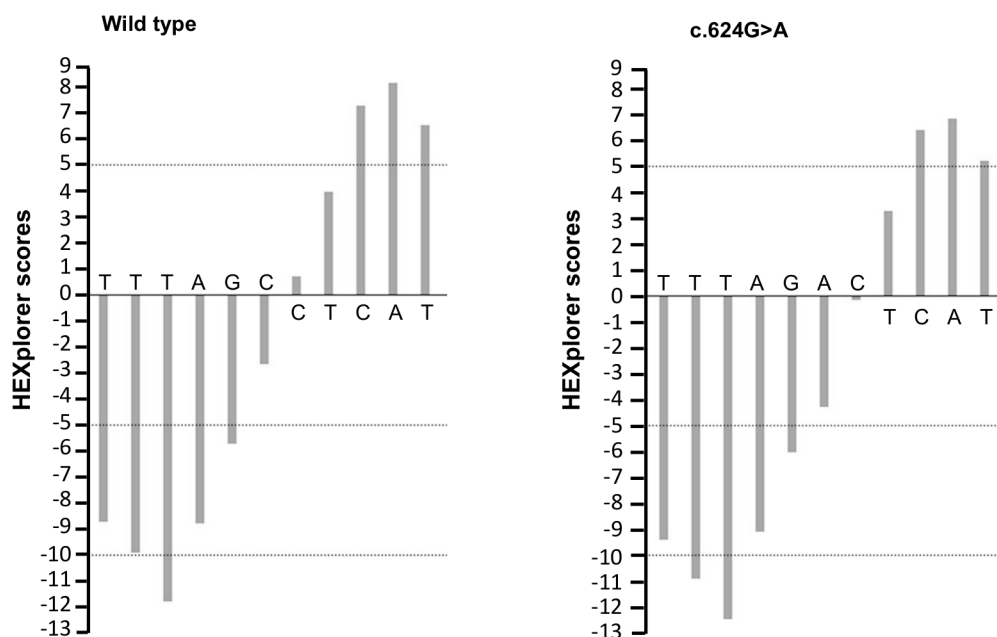
## SUPPLEMENTARY FIGURES

**Supplementary Figure 1: Predictions of exonic splicing regulator elements of the c.627C>T *TMCI* variant.**

**A**

Positions (wild type)	Hexamer seq wild type	ESRseq score wild type	Hexamer seq variant	ESRseq score variant	ESRseq score change (variant vs wild type)
c.619-624	TTTAG <u>C</u>	-0.5510	TTTAG <u>A</u>	-0.4845	+0.0665
c.620-625	TTAG <u>CC</u>	-0.5749	TTAG <u>AC</u>	-0.3924	+0.1825
c.621-626	TAG <u>CCT</u>	-0.2658	TAG <u>ACT</u>	0	+0.2658
c.622-627	AG <u>CCTC</u>	0	AG <u>ACTC</u>	0	0
c.623-628	GC <u>CTCA</u>	0	GA <u>CTCA</u>	0	0
c.624-629	<u>CCTCAT</u>	0	<u>ACTCAT</u>	0	0
Total		-1.3917		-0.8769	<b>+0.5148</b>

**B**



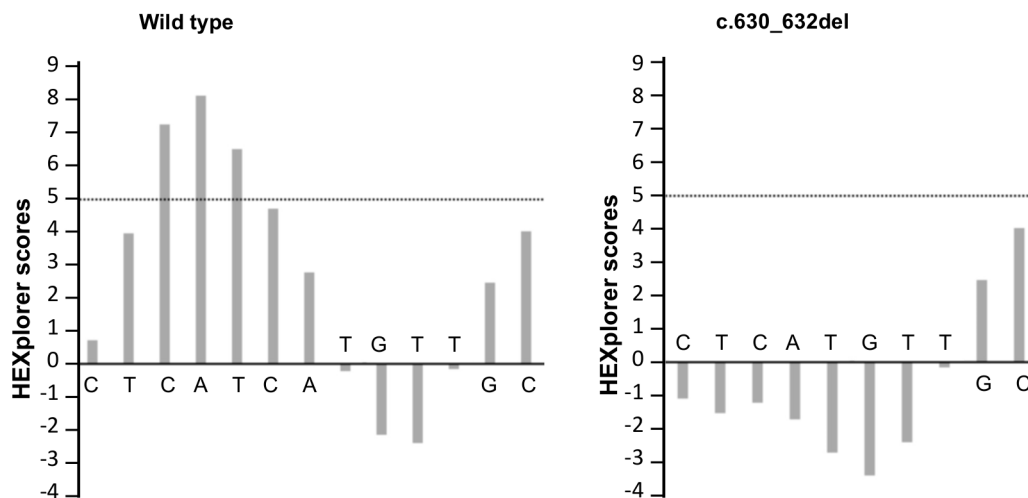
**A)** Data obtained from the HEXoSplice tool. The nucleotide change is indicated with underlined bold font;  $\Delta tESR_{seq}$  score: -1.31. **B)** Graphical presentation of data extracted from the HEXplorer algorithm for the wild type (c.622-632) and mutated sequences;  $\Delta HZ_{EI}$  value: -60.13.

**Supplementary Figure 2: Predictions of exonic splicing regulator elements of the c.630\_632del *TMC1* alteration.**

**A**

Positions (wild type)	Hexamer seq wild type	ESRseq score wild type	Hexamer seq variant	ESRseq score variant	ESRseq score change (variant vs wild type)
c.625-630	CTC <u>ATC</u>	0	CTCATG	0	
c.626-631	TCAT <u>CA</u>	0	TCATGT	0	
c.627-632	CAT <u>CAT</u>	0	CATGTT	0	
c.628-633	AT <u>CATG</u>	0	ATGTTG	0	
c.629-634	TCAT <u>GT</u>	0	TGTTGC	0	
c.630-635	<u>CATGTT</u>	0			
c.631-636	<u>ATGTTG</u>	0			
c.632-637	<u>TGTTGC</u>	0			
Total		0		0	<b>0</b>

**B**



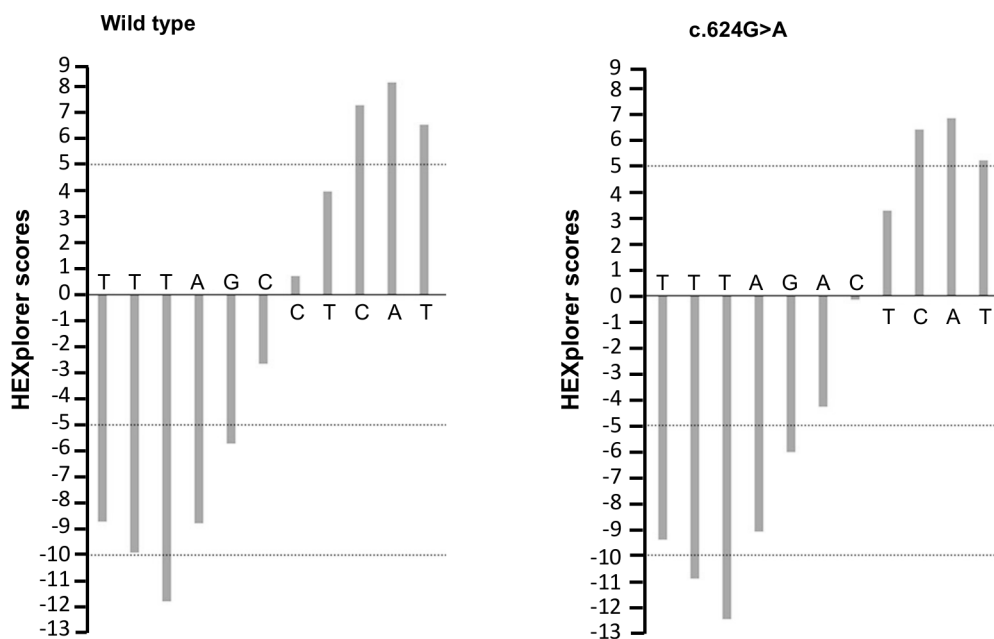
**A)** Data obtained from the HEXoSplice tool. The deletion is indicated with underlined bold font in the wild type sequence;  $\Delta$ tESR<sub>seq</sub> score: 0. **B)** Graphical presentation of data extracted from the HEXplorer algorithm for the wild type (c.625-637) and mutated sequences;  $\Delta$ HZ<sub>EI</sub> value: -43.76.

**Supplementary Figure 3: Predictions of exonic splicing regulator elements of the c.624C>A *TMC1* variant**

**A**

Positions (wild type)	Hexamer seq wild type	ESRseq score wild type	Hexamer seq variant	ESRseq score variant	ESRseq score change (variant vs wild type)
c.619-624	TTTAG <u>C</u>	-0.5510	TTTAG <u>A</u>	-0.4845	+0.0665
c.620-625	TTAG <u>CC</u>	-0.5749	TTAG <u>AC</u>	-0.3924	+0.1825
c.621-626	TAG <u>CTC</u>	-0.2658	TAG <u>ACT</u>	0	+0.2658
c.622-627	AG <u>CCTC</u>	0	AG <u>ACTC</u>	0	0
c.623-628	G <u>CCTCA</u>	0	G <u>ACTCA</u>	0	0
c.624-629	<u>CCTCAT</u>	0	<u>ACTCAT</u>	0	0
Total		-1.3917		-0.8769	<b>+0.5148</b>

**B**



**A)** Data obtained from the HExoSplice tool. The nucleotide change is indicated with underlined bold font;  $\Delta$ ESR<sub>seq</sub> score: +0.51. **B)** Graphical presentation of data extracted from the HExplorer algorithm for the wild type (c.619-629) and mutated sequences;  $\Delta$ HZ<sub>EI</sub> value: -9.82.