SUPPLEMENTARY INFORMATION

SUPPLEMENTARY TABLES

Supp. Table 1. Oligonucleotides for EMSA probe and competition experiments. Probes represented haplotypes containing *TMCO1* SNP variants at either rs4657473, rs116461237 or rs61058666.

EMSA Probes	Sequence		Description
Nppa	Forward 5′-TCTGCTCTTCTCACACCTTTGAAGTGGGGGCCTCTTG-3′		positive control (Postma et al 2008)
	Reverse 5′-CAAGAGGCCCCCACTTCAAAGGTGTGAGAAGAGCAGA-3′		
CGGA	Forward 5′-GCCCACCTCGGCCTCCCAAAGTTCTAGGATTACAGGTGTGAGCTACC-3′		Wildtype Alleles C,G,G
	Reverse 5′-GGTAGCTCACACCTGTAATCCTAGAACTTTGGGAGGCCGAGGTGGGC-3′		
TGGA	Forward 5′-GCCCACCTCAGCCTCCCAAAGTTCTAGGATTATAGGTGTGAGCTACC-3′		rs4657475 C>T
	Reverse 5′-GGTAGCTCACACCTATAATCCTAGAACTTTGGGAGGCTGAGGTGGGC -3′		
CAGA	Forward 5′-GCCCACCTCGGCCTCCCAAAGTTCTAGGATTACAGATGTGAGCTACC -3′		rs116461237 G>A
	Reverse 5′-GGTAGCTCACATCTGTAATCCTAGAACTTTGGGAGGCCGAGGTGGGC -3′		
CGCA	Forward 5′-GCCCACCTCGGCCTCCCAAAGTTCTAGGATTACAGGTGTCAGCTACC -3′		rs61058666 G>C
	Reverse 5′-GGTAGCTGACACCTGTAATCCTAGAACTTTGGGAGGCCGAGGTGGGC -3′		
Alu	Forward 5′-GCCCGCCTCGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACC-3′		Alu consensus
	Reverse 5′-GGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGC-3′		
ATTX	Forward 5′-GCCCACCTCGGCCTCCCAAAGTTCTAGGATTAAAGTTGTTAGCTACC -3′		3 SNP Mutations (A,T,T)
	Reverse 5′-GGTAGCTAACAACTTTAATCCTAGAACTTTGGGAGGCCGAGGTGGGC -3′		
CGTA	Forward 5′-GCCCACCTCGGCCTCCCAAAGTTCTAGGATTACAGGTGTTAGCTACC -3′		rs61058666 mutation G>T
	Reverse 5′-GGTAGCTAACACCTGTAATCCTAGAACTTTGGGAGGCCGAGGTGGGC-3′		
AGGA	Forward 5′-GCCCACCTCGGCCTCCCAAAGTTCTAGGATTAAAGGTGTGAGCTACC-3′		rs4657475 mutation C>A
	Reverse 5′-GGTAGCTCACACCTTTAATCCTAGAACTTTGGGAGGCCGAGGTGGGC-3′		

Supp. Table 2. Primers for Luciferase Assay PCR Constructs

PCR Construct (bp)	Primer Sequence	Chromosomal Position (GRCh38 assembly)
3337	5′ - AGTTTGGAACACTAAAGACCACTTT - 3′ (Acc65I)	1:1657,193,27 - 165,715,991
	5′ - CGAGACAGAGGTCCATCTCCA - 3′ (EcoRV)	
1274	5′ - CCTTAGTTCCTTTGGCTTGTTGG - 3′ (Acc65I)	1:165,718,361 - 165,717,088
	5′ - GACAAGAGAAGAGAAACAGCAGC - 3′ (EcoRV)	
703	5′ - TTTTCTGCAACTCAACTCACTGC - 3′ (Acc65I)	1:165,718,126 - 165,717,424
	5′ - TCTACCTGCTCTCTTTCTCTCCT - 3′ (EcoRV)	
703_Rev	5′ - TTTTCTGCAACTCAACTCACTGC - 3′ (EcoRV)	1:165,718,126 - 165,717,424
	5′ - TCTACCTGCTCTCTTTCTCTCCT - 3′ (Acc65I)	

Supplementary Table 3.

		TMCO1 rs11430311				Age and Sex Adjusted Differences vs insT/insT		
		insT/insT	insT/WT	WT/WT	p-val	insT/WT	WT/WT	p-val
CCT (mean)	mean (stddev)	531.5 (37.9)	529.3 (40.2)	535.7 (41.4)	0.33	-2.2 (-6.4, 2.0)	4.3 (-5.0, 13.6)	0.32
	n	887	508	71				
CDR (mean)	mean (stddev)	0.71 (0.16)	0.72 (0.16)	0.72 (0.16)	0.92	0.00 (-0.02, 0.02)	0.01 (-0.03, 0.04)	0.95
	n	901	517	72				
Max IOP (mean)	mean (stddev)	25.7 (7.9)	26.1 (8.1)	25.9 (8.4)	0.63	0.4 (-0.5, 1.2)	0.2 (-1.7, 2.1)	0.68
	n	925	531	75				
RNFL (mean)	mean (stddev)	73.1 (13.5)	72.5 (12.9)	73.7 (14.1)	0.67	-0.4 (-2.1, 1.2)	0.6 (-2.9, 4.2)	0.80
	n	668	369	56				

		TMCO1 rs4657473				Age and Sex Adjusted Differences vs C		
		C	Y	T	p-val	Y	T	p-val
CCT (mean)	mean (stddev)	530.9 (39.2)	532.2 (37.8)	506.7 (19.5)	0.12	1.3 (-3.9, 6.4)	-21.2 (-45.3, 2.9)	0.19
	n	1196	263	10				
CDR (mean)	mean (stddev)	0.72 (0.15)	0.71 (0.18)	0.75 (0.15)	0.66	-0.01 (-0.03, 0.01)	0.02 (-0.08, 0.12)	0.70
	n	1217	266	10				
Max IOP (mean)	mean (stddev)	25.8 (7.9)	26.2 (8.0)	29.6 (11.0)	0.24	0.4 (-0.6, 1.5)	3.8 (-1.2, 8.7)	0.24
	n	1250	274	10				
RNFL (mean)	mean (stddev)	72.8 (13.4)	73.4 (12.9)	82.8 (11.8)	0.21	0.7 (-1.3, 2.7)	11.4 (0.0, 22.8)	0.12
	n	889	201	5				

		TMCO1 rs4657474				Age and Sex Adjusted Differences vs G		
		G	R	A	p-val	R	A	p-val
CCT (mean)	mean (stddev)	531.5 (37.9)	529.4 (40.1)	535.6 (41.7)	0.38	-2.0 (-6.2, 2.2)	4.1 (-5.3, 13.5)	0.38
	n	888	511	70				
CDR (mean)	mean (stddev)	0.71 (0.16)	0.72 (0.16)	0.72 (0.16)	0.92	0.00 (-0.02, 0.02)	0.01 (-0.03, 0.04)	0.95
	n	902	520	71				
Max IOP (mean)	mean (stddev)	25.7 (7.9)	26.1 (8.1)	25.9 (8.5)	0.65	0.4 (-0.5, 1.2)	0.1 (-1.8, 2.0)	0.70
	n	926	535	73				
RNFL (mean)	mean (stddev)	73.1 (13.5)	72.4 (12.9)	73.9 (14.2)	0.62	-0.4 (-2.1, 1.2)	0.8 (-2.8, 4.4)	0.76
	n	668	372	55				

		TMCO1 rs4657475			Age and Sex Adjusted Differences vs C		
		C	Y	T	p-val	Y	T	p-val
CCT (mean)	mean (stddev)	531.5 (37.9)	529.4 (40.1)	536.0 (41.9)	0.34	-2.1 (-6.3, 2.1)	4.3 (-5.1, 13.8)	0.35
	n	888	512	69				
CDR (mean)	mean (stddev)	0.71 (0.16)	0.72 (0.16)	0.72 (0.16)	0.91	0.00 (-0.02, 0.02)	0.01 (-0.03, 0.04)	0.94
	n	902	521	70				
Max IOP (mean)	mean (stddev)	25.7 (7.9)	26.1 (8.1)	25.8 (8.5)	0.67	0.3 (-0.5, 1.2)	0.1 (-1.8, 2.0)	0.72
	n	926	536	72				
RNFL (mean)	mean (stddev)	73.1 (13.5)	72.5 (12.9)	73.8 (14.3)	0.67	-0.4 (-2.0, 1.2)	0.7 (-2.9, 4.3)	0.80
	n	668	373	54				

		TMCO1 rs116461237			Age and Sex Adjusted Differences vs G	
		G	R	p-val	R	p-val
CCT (mean)	mean (stddev)	530.8 (38.9)	538.9 (37.4)	0.20	7.6 (-4.7, 19.8)	0.23
	n	1429	39			
CDR (mean)	mean (stddev)	0.71 (0.16)	0.72 (0.15)	0.67	0.01 (-0.04, 0.06)	0.75
	n	1449	43			
Max IOP (mean)	mean (stddev)	25.9 (8.0)	23.9 (7.5)	0.11	-2.1 (-4.5, 0.3)	0.09
	n	1490	43			
RNFL (mean)	mean (stddev)	72.9 (13.3)	72.3 (13.5)	0.80	-0.6 (-5.2, 4.1)	0.81
	n	1063	31			

		TMCO1 rs61058666			Age and Sex Adjusted Differences vs G		
		G	S	C	p-val	S	C	p-val
CCT (mean)	mean (stddev)	530.8 (38.8)	531.6 (38.1)	543.7 (69.4)	0.66	0.8 (-5.2, 6.7)	11.9 (-16.8, 40.6)	0.70
	n	1276	185	7				
CDR (mean)	mean (stddev)	0.71 (0.16)	0.72 (0.16)	0.71 (0.10)	0.71	0.01 (-0.01, 0.04)	-0.01 (-0.13, 0.10)	0.64
	n	1298	187	7				
Max IOP (mean)	mean (stddev)	25.8 (8.0)	26.7 (8.0)	23.2 (4.1)	0.20	1.0 (-0.2, 2.2)	-3.0 (-8.9, 2.9)	0.17
	n	1334	192	7				
RNFL (mean)	mean (stddev)	73.1 (13.4)	71.9 (13.1)	66.3 (7.7)	0.28	-1.2 (-3.6, 1.1)	-5.7 (-16.1, 4.7)	0.34
	n	951	137	6				

|		TMCO1 rs4656461			Age and Sex Adjusted*Differences vs A		
		A	R	G	p-val	R	G	p-val
CCT (mean)	mean (stddev)	531.5 (37.9)	529.5 (40.1)	536.0 (41.9)	0.36	-2.0 (-6.2, 2.2)	4.4 (-5.1, 13.8)	0.36
	n	887	512	69				
CDR (mean)	mean (stddev)	0.71 (0.16)	0.72 (0.16)	0.72 (0.16)	0.92	0.00 (-0.02, 0.02)	0.01 (-0.03, 0.04)	0.94
	n	901	521	70				
Max IOP (mean)	mean (stddev)	25.7 (7.9)	26.2 (8.2)	25.8 (8.5)	0.59	0.4 (-0.4, 1.3)	0.1 (-1.8, 2.0)	0.64
	n	925	536	72				
RNFL (mean)	mean (stddev)	73.1 (13.5)	72.5 (12.9)	73.8 (14.3)	0.71	-0.4 (-2.0, 1.3)	0.7 (-2.9, 4.3)	0.82
	n	667	373	54				

SUPPLEMENTARY FIGURES:
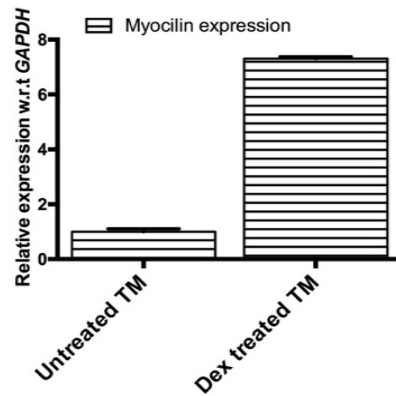
Supp. Fig. S1. Realtime PCR profiles showing the induction of Myocilin in TM cultures (P2 to P4 cultures) with 100mM Dexamethasome treatment for 3 days. The relative expression profiles of *Myocylin* transcript are presented with respect to GAPDH transcript.
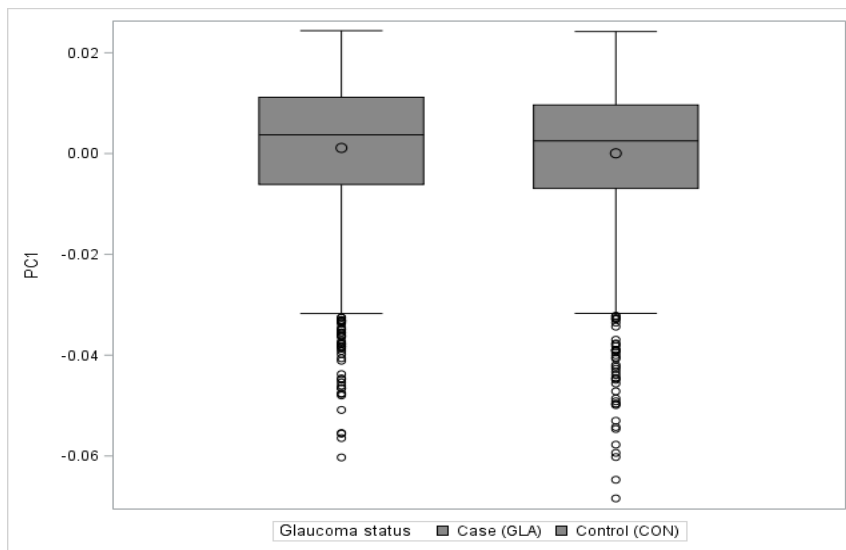

Supp. Fig. S2. Boxplots showing the comparison of the PC1 score between the cases and controls. No statistically significant difference was found between cases and controls (p=0.06).
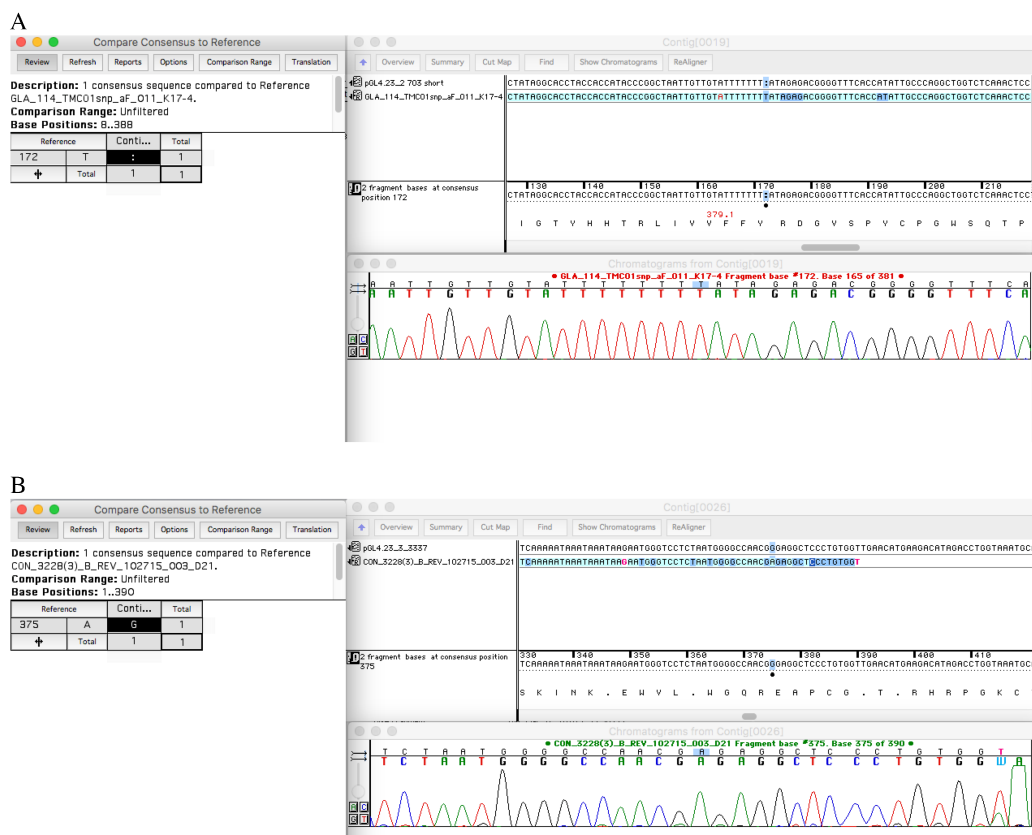
Supp. Fig. 3. Sequencing traces showing (a) Insert 2_703 has variant rs11430311 (WT/WT) which is not expected from the haplotype associated with SNP rs 4657473. This variant is not seen in the other Insert 2 sequences as expected. (b) All Insert 3 sequences have a discrepancy in sequencing between previous genotyping and sequenced insert 201bp upstream of SNP rs11430311 (A>G). This may represent an introduced mutation at this location.
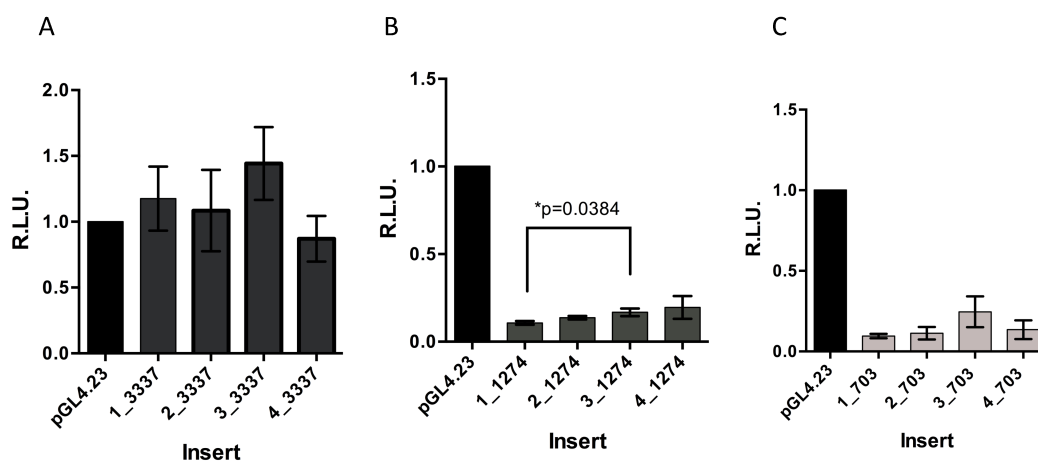
Supp. Fig. 4. Luciferase assays on TM cells showing, (A) 3337bp inserts does not have an effect on luciferase expression and (B) 1274bp and (C) 703bp inserts show repression of luciferase expression.
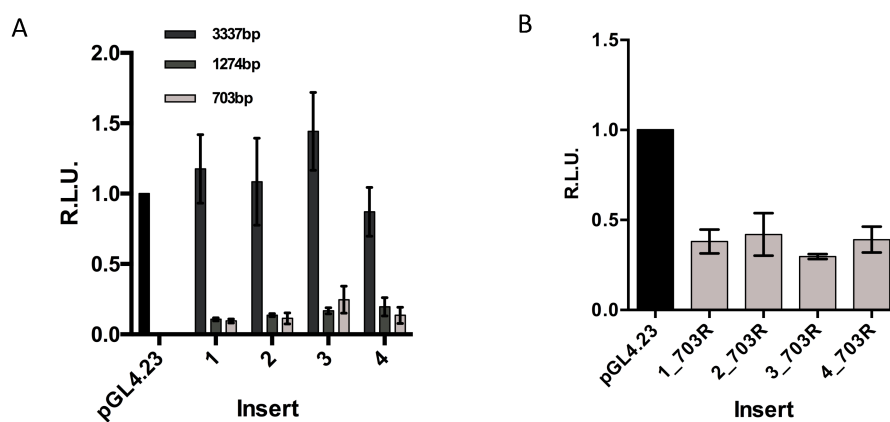
Supp. Fig. 5. Luciferase assays on TM cells showing, (A) a pattern of core repression with serial deletion of 3337bp insert is not evident and (B) 703bp insert does not demonstrate enhancer activity in the reverse orientation.

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