Supplementary Table S1. Clinical characteristics of children with HM

Sample number	Age [years]	Right eye				Left eye				Other eye disorders
		Spherical refractive error [D]	Cylindrical refractive error [D]	Ax [^{0}]	Spherical equivalent [D]	Spherical refractive error [D]	Cylindrical refractive error [D]	Ax [^{0}]	Spherical equivalent [D]	
UR-809	3	-11.50	1.50	132	-10.75	-13.0	+2.0	118	-12.00	strabismus
UR-810	10	-6.75	1.00	90	-6.25	-7.50	1.50	80	-6.75	
UR-813	10	-6.25	-	-	-6.25	-5.5	-	-	-5.50	
UR-814	10	-9.5	0.75	5	-9.25	-9.25	-	-	-9.25	
UR-816	10	-5.50	-	-	-5.50	-6.25	-	-	-6.25	
UR-817	11	-7.00	4.00	90	-5.00	-5.75	4.50	90	-3.50	retinal detachment
UR-818	12	-10.25	1.50	90	-9.50	-10.50	1.50	90	-9.75	
UR-819	12	-7.5	-	-	-7.50	-7	-	-	-7.00	
UR-821	4	-7.00	1.50	5	-6.25	-10.00	1.50	175	-9.25	
UR-822	11	-7.00	-	-	-7.00	-7	-	-	-7.00	
UR-823	12	-6.00	-	-	-6.00	-6.5	-	-	-6.50	
UR-824	12	-2.75	-	-	-2.75	-6.50	0.75	110	-6.25	
UR-825	8	-15.00	4.25	175	-13.00	-14.00	2.50	5	-12.75	
UR-826	11	-9.25	-	-	-9.25	-8.5	-	-	-8.50	
UR-827	8	-6.50	-	-	-6.50	-6.5	-	-	-6.50	
UR-829	8	-10.00	1.00	170	-9.50	-8.25	2.25	30	-7.25	retinopathy of prematurity
UR-831	9	-10.0	3.0	170	-8.50	-7.75	2.75	10	-6.50	
UR-832	12	-6.50	-	-	-6.50	-8.5	-	-	-8.50	

Supplementary Table S2. CG dinucleotides with at least 20% lower methylation level in HM cases when compared to controls, identified in gene sequence, including the promoter regions

Target ID	Chromosome	Gene	p-value	FDR p-value	Methylation level in HM cases [%]*	Methylation level in controls [%]*	Difference in methylation level	Localization in gene
cg02054572	4	*LINC01088*	2.21×10^{-27}	1.88×10^{-21}	52.63	81.71	**-29.08**	gene body
cg17651890	8	*RIMS2*	1.02×10^{-27}	8.66×10^{-22}	46.07	73.93	**-27.86**	gene body
cg15349655	5	*EPB41L4A*	9.95×10^{-28}	8.46×10^{-22}	59.43	86.62	**-27.20**	gene body
cg27494055	5	*PCDHA10*	5.26×10^{-28}	4.47×10^{-22}	29.63	56.70	**-27.07**	TSS1500
cg27494055	5	*PCDHA1;PCDHA2;PCDHA3; PCDHA4;PCDHA5;PCDHA6; PCDHA7;PCDHA8;PCDHA9*	5.26×10^{-28}	4.47×10^{-22}	29.63	56.70	**-27.07**	gene body
cg10162971	2	*GRHL1*	5.19×10^{-28}	4.41×10^{-22}	46.25	72.52	**-26.27**	gene body
cg09701422	14	*ADAM20*	7.47×10^{-28}	6.35×10^{-22}	63.66	89.87	**-26.21**	TSS1500
cg13953630	4	*OCIAD1*	4.47×10^{-28}	3.80×10^{-22}	53.11	78.94	**-25.84**	gene body
cg19976037	17	*CCDC57*	3.30×10^{-28}	2.81×10^{-22}	46.81	72.61	**-25.81**	gene body
cg18093771	10	*ADARB2*	4.82×10^{-28}	4.10×10^{-22}	58.25	84.01	**-25.76**	gene body
cg26069044	11	*NRGN*	3.97×10^{-28}	3.37×10^{-22}	50.88	76.55	**-25.67**	gene body
cg26700469	16	*WWOX*	4.21×10^{-28}	3.58×10^{-22}	56.32	81.91	**-25.59**	gene body
cg25543264	7	*COBL*	3.57×10^{-28}	3.03×10^{-22}	37.02	62.57	**-25.55**	gene body
cg18731202	2	*TGFA*	2.21×10^{-28}	1.88×10^{-22}	47.55	72.85	**-25.30**	gene body
cg06281409	5	*FBXO38*	4.58×10^{-28}	3.89×10^{-22}	63.52	88.79	**-25.27**	gene body
cg15049439	19	*INSR*	2.94×10^{-28}	2.50×10^{-22}	54.21	79.19	**-24.98**	gene body
cg02766704	7	*CTTNBP2*	2.57×10^{-28}	2.19×10^{-22}	49.73	74.50	**-24.77**	gene body
cg25010006	8	*PAG1*	2.42×10^{-28}	2.06×10^{-22}	62.06	86.48	**-24.43**	TSS1500
cg14197110	4	*CEP44*	1.94×10^{-28}	1.65×10^{-22}	62.53	86.39	**-23.87**	3'UTR
cg11603552	17	*APOH*	1.93×10^{-29}	1.64×10^{-23}	50.82	74.53	**-23.71**	gene body
cg24017056	15	*ZFAND6*	1.72×10^{-28}	1.46×10^{-22}	59.63	83.28	**-23.64**	5'UTR
cg23836814	11	*AGBL2*	1.33×10^{-28}	1.13×10^{-22}	44.55	68.16	**-23.61**	3'UTR
cg02137496	11	*DLG2*	1.30×10^{-28}	1.10×10^{-22}	61.18	84.41	**-23.23**	gene body
cg13432799	5	*SNX2*	1.69×10^{-28}	1.43×10^{-22}	66.44	89.65	**-23.21**	gene body
cg07736012	3	*MED12L*	1.27×10^{-28}	1.08×10^{-22}	68.25	91.16	**-22.91**	gene body
cg09925682	19	*NFIC*	3.07×10^{-29}	2.61×10^{-23}	56.15	79.06	**-22.91**	gene body
cg08913233	10	*VTI1A*	1.10×10^{-28}	9.32×10^{-23}	68.06	90.83	**-22.77**	gene body

cg27078890	11	*ETS1*	1.06×10^{-28}	9.04×10^{-23}	65.25	88.02	**-22.76**	TSS200
cg10025778	7	*CCDC146*	9.61×10^{-29}	8.16×10^{-23}	63.16	85.79	**-22.63**	gene body
cg15039162	13	*ABHD13*	9.49×10^{-29}	8.07×10^{-23}	62.27	84.72	**-22.46**	5'UTR
cg15039162	13	*LIG4*	9.49×10^{-29}	8.07×10^{-23}	62.27	84.72	**-22.46**	TSS1500
cg21610839	3	*UBE2E1*	6.90×10^{-29}	5.87×10^{-23}	42.87	65.24	**-22.37**	gene body
cg19518093	8	*SBSPON*	8.99×10^{-29}	7.64×10^{-23}	67.98	90.18	**-22.20**	TSS1500
cg21494160	18	*PTPRM*	7.78×10^{-29}	6.61×10^{-23}	66.49	88.70	**-22.20**	gene body
cg27374674	17	*GAS7*	6.84×10^{-29}	5.82×10^{-23}	56.08	78.23	**-22.16**	gene body
cg27262015	4	*SORBS2*	6.53×10^{-29}	5.55×10^{-23}	64.35	86.16	**-21.82**	TSS200
cg25885356	21	*RUNX1*	4.47×10^{-29}	3.80×10^{-23}	51.60	73.15	**-21.55**	gene body
cg00571519	7	*SRPK2*	3.65×10^{-29}	3.11×10^{-23}	63.58	85.11	**-21.52**	gene body
cg21047322	6	*AKAP12*	3.86×10^{-29}	3.28×10^{-23}	48.67	70.16	**-21.49**	gene body
cg24562221	1	*CACYBP*	4.78×10^{-29}	4.06×10^{-23}	59.35	80.79	**-21.44**	gene body
cg11683966	1	*SLC25A3P1*	4.41×10^{-29}	3.75×10^{-23}	49.46	70.84	**-21.38**	TSS200
cg18556587	2	*TANC1*	4.05×10^{-29}	3.44×10^{-23}	53.42	74.74	**-21.32**	5'UTR
cg12836825	3	*LMOD3*	4.92×10^{-29}	4.18×10^{-23}	66.22	87.39	**-21.16**	TSS1500
cg26393261	6	*ATXN1*	3.82×10^{-29}	3.24×10^{-23}	43.33	64.38	**-21.05**	5'UTR
cg15144397	3	*SPATA16*	3.76×10^{-29}	3.20×10^{-23}	59.88	80.86	**-20.98**	gene body
cg15357273	3	*CCDC50*	4.73×10^{-29}	4.02×10^{-23}	63.24	84.19	**-20.95**	gene body
cg14540736	18	*ZNF516*	2.71×10^{-29}	2.31×10^{-23}	50.55	71.30	**-20.75**	gene body
cg19032370	1	*EVI5*	3.05×10^{-29}	2.59×10^{-23}	64.94	85.40	**-20.47**	gene body
cg11755269	21	*CRYZL1*	3.74×10^{-29}	3.18×10^{-23}	65.43	85.88	**-20.46**	gene body
cg24684709	2	*FARP2*	7.03×10^{-25}	5.97×10^{-19}	45.02	65.44	**-20.42**	5'UTR
cg07418777	10	*CCDC3*	2.61×10^{-29}	2.22×10^{-23}	54.30	74.70	**-20.40**	gene body
cg21537492	8	*SNTB1*	3.00×10^{-29}	2.55×10^{-23}	70.86	91.17	**-20.31**	gene body
cg21685655	7	*PON2*	3.14×10^{-29}	2.67×10^{-23}	69.00	89.30	**-20.29**	3'UTR
cg05939089	14	*ARMH4*	2.32×10^{-29}	1.98×10^{-23}	55.25	75.45	**-20.20**	gene body
cg05740739	2	*OR6B3*	2.25×10^{-29}	1.92×10^{-23}	55.98	76.12	**-20.14**	TSS1500
cg17721001	8	*UBR5*	2.14×10^{-29}	1.82×10^{-23}	54.75	74.78	**-20.03**	gene body

FDR - false discovery rate, HM - high myopia, TSS200 - 0-200 bases upstream of the transcriptional start site, TSS1500 - 200-1500 bases upstream of the transcriptional start site

* Methylation levels in children are presented as mean values

Supplementary Table S3. Additional information about genes overlapping the highest-ranked differentially methylated CG dinucleotides located in promoter regions with at least 20% decrease in the methylation level when compare HM cases to controls

Gene	OMIM accession number	Coding protein	*Locus*	Nearby myopia *locus*	Gene function (GeneCards[*], NCBI Gene database[†])	Eye related phenotypes/myopia risk factors (GWAS Catalog[‡])	Mouse ocular phenotype (Mouse Genome Informatics[§])
Genes related to myopia, eye structure or function							
PCDHA10	606316	protocadherin alpha 10	5q31.3	MYP25: 5q31	Encoded neural cadherin-like cell adhesion protein is most likely involved in the establishment and maintenance of specific neuronal connections in the brain.	Refractive error (Europeans, GCST010002)	nd
ADAM20	603712	ADAM metallopeptidase domain 20	14q24.2	MYP18: 14q22.1-q24.2	Encode membrane-anchored protein structurally related to snake venom disintegrins, and have been implicated in a variety of biological processes involving cell-cell and cell-matrix interactions, including fertilization, muscle development, and neurogenesis. May be involved in sperm maturation and/or fertilization.	nd	nd
ZFAND6	610183	zinc finger AN1-type containing 6	15q25.1		Involved in regulation of TNF-alpha induced NF-kappa-B activation and apoptosis. Required for PTS1 target sequence-dependent protein import into peroxisomes and PEX5 stability; may cooperate with PEX6. In vitro involved in PEX5 export from the cytosol to peroxisomes	nd	expressed in mouse whole eye, retina and neural retina (MGI:1929510)
ETS1	164720	ETS proto-oncogene 1, transcription factor	11q24.3		The protein is a transcription factor that directly controls the expression of cytokine and chemokine genes in a wide variety of different cellular contexts. May control the differentiation, survival and proliferation of lymphoid cells. May also regulate angiogenesis through regulation of expression of genes controlling endothelial cell migration and invasion.	Intraocular pressure (Europeans, GCST006394, GCST009725, GCST006412, GCST005580, GCST010376), glaucoma (Europeans, GCST006395, GCST009726, GCST009722, GCST90011770, GCST011439, GCST011438)	low expression in mouse whole eye, retina and neural retina (MGI:95455)
ABHD13	-	abhydrolase domain containing 13	13q33.3		nd	nd	expressed in mouse whole eye, retina and neural retina, mutation in this gene cause abnormal eye morphology (MGI:1916154)

SBSPON	-	somatomedin B and thrombospondin type 1 domain containing	8q21.11		nd	Corneal curvature/corneal topography (Australians, GCST001680)	low expression in mouse whole eye, retina and neural retina (MGI:2684952)
SORBS2	616349	sorbin and SH3 domain containing 2	4q35.1	MYP22: 4q35	Adapter protein that plays a role in the assembling of signaling complexes, being a link between ABL kinases and actin cytoskeleton. Can form complex with ABL1 and CBL, thus promoting ubiquitination and degradation of ABL1. May play a role in the regulation of pancreatic cell adhesion, possibly by acting on WASF1 phosphorylation, enhancing phosphorylation by ABL1, as well as dephosphorylation by PTPN12.	Iris color/eye color measurement (South Asians, GCST007740), Educational attainment (years of education) (Europeans, GCST006442, GCST006571)	expressed in mouse whole eye, retina and neural retina, mutation in this gene cause abnormal retina morphology (MGI:1924574)
LMOD3	616112	leiomodin 3	3p14.1		Essential for the organization of sarcomeric actin thin filaments in skeletal muscle. Increases the rate of actin polymerization.	nd	expressed in eye skeletal muscle and retina in mouse embryo, low expression in eye of adult mouse (not detected in retina), mutation in this gene cause abnormal eye morphology (MGI:2444169)
ATXN1	601556	ataxin 1	6p22.3		Chromatin-binding factor that repress Notch signaling in the absence of Notch intracellular domain by acting as a CBF1 corepressor. Binds to the HEY promoter and might assist, along with NCOR2, RBPJ-mediated repression. Binds RNA in vitro. May be involved in RNA metabolism. In concert with CIC and ATXN1L, involved in brain development.	Central corneal thickness (multiethnic cohort, GCST90000654), educational attainment (years of education) (Europeans, GCST003676, GCST006442, GCST006571)	expressed in mouse whole eye, retina and neural retina (MGI:104783)
FARP2	617586	FERM, ARH/RhoGEF and pleckstrin domain protein 2	2q37.3	MYP12: 2q37.1	Functions as guanine nucleotide exchange factor that activates RAC1. Plays a role in the response to class 3 semaphorins and remodeling of the actin cytoskeleton. Plays a role in TNFSF11-mediated osteoclast differentiation, especially in podosome rearrangement and reorganization of the actin cytoskeleton. Regulates the activation of ITGB3, integrin signaling and cell adhesion.	Educational attainment (years of education) (Europeans, GCST006442, GCST006571)	expressed in mouse whole eye, retina and neural retina (MGI:2385126)
Genes expressed in the eye but with unknown association with myopia/eye							
PAG1	605767	phosphoprotein membrane anchor with	8q21.13		Negatively regulates T-cell antigen receptor-mediated signaling in T-cells and FCER1-mediated signaling in mast cells. Inhibits immunological synapse formation by preventing	nd	expressed in mouse whole eye, retina and neural retina

		glycosphingolipid microdomains 1			dynamic arrangement of lipid raft proteins. May be involved in cell adhesion signaling.		(MGI:2443160)
LIG4	601837	DNA ligase 4	13q33.3				expressed in mouse whole eye, retina and neural retina (MGI:1929510)
TANC1	611397	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 1	2q24.2		May be a scaffold component in the postsynaptic density.	nd	expressed in mouse whole eye, retina and neural retina (MGI:1914110)
Genes not expressed in the eye or not associated with myopia/eye							
SLC25A3P1	-	solute carrier family 25 member 3 pseudogene 1	1p32.3		nd	nd	nd
OR6B3	-	olfactory receptor family 6 subfamily B member 3	2q37.3	MYP12: 2q37.1	Olfactory receptor interact with odorant molecules in the nose, to initiate a neuronal response that triggers the perception of a smell. Olfactory receptors share a 7-transmembrane domain structure with many neurotransmitter and hormone receptors and are responsible for the recognition and G protein-mediated transduction of odorant signals.	DNA methylation variation (age effect) (Europeans, GCST006660)	nd

nd – no data

[*]GeneCards (https://www.genecards.org/)

[†]National Center for Biotechnology Information (NCBI), Gene database (https://www.ncbi.nlm.nih.gov/)

[‡]GWAS Catalog (https://www.ebi.ac.uk/gwas/)

[§]Mouse Genome Informatics (MGI, http://www.informatics.jax.org/)

Supplementary Table S4. Expression of genes overlapping the highest-ranked CG dinucleotides with at least 20% decreased methylation level in promoter region, based on data of the ARPE-19 cell line [35]

Expression in the cell line is presented as transcripts per million reads (TPM) after four days and after four months of culture

Gene	4 days culture [TPM]				4 months culture [TPM]			
	1 rep	**2 rep**	**3 rep**	**Mean**	**1 rep**	**2 rep**	**3 rep**	**Mean**
ZFAND6	93.09	102.79	98.71	98.20	82.47	92.81	94.45	89.91
ETS1	37.18	42.46	41.09	40.24	16.63	15.09	17.61	16.44
TANC1	20.59	22.35	23.37	22.10	42.46	39.44	45.35	42.42
ABHD13	14.41	16.37	15.32	15.37	23.2	22.33	24.16	23.23
LIG4	9.62	11.57	10.7	10.63	9.92	10.26	10.54	10.24
FARP2	5.96	6.97	7.49	6.81	7.18	6.39	7.13	6.90
PAG1	5.55	6.75	6.43	6.24	13.76	15.62	15.77	15.05
SBSPON	5.36	5.95	5.85	5.72	6.11	7.06	6.65	6.61
ATXN1	4.76	5.81	4.78	5.12	10.76	9.62	10.46	10.28
SORBS2	0.63	0.48	0.76	0.62	9.16	9	9.76	9.31
LMOD3	0.2	0.33	0.21	0.25	0.31	0.26	0.35	0.31
PCDHA10	0.17	0.17	0.31	0.22	0.13	0.24	0.20	0.19
ADAM20	0.25	0.14	0.16	0.18	0.35	0.3	0.32	0.32
SLC25A3P1	0	0	0	0	0	0	0	0
OR6B3	0	0	0	0	0	0	0	0

nd - no data

Supplementary Table S5. Results of Sanger sequencing of SNVs rs1581364290, rs200661444 and rs246073 located in *PCDHA10*, including its promoter region, in children with HM and children without HM

Children with HM				Children without HM			
Sample number	**rs1581364290 C>T**	**rs200661444 C>T**	**rs246073 T>C**	**Sample number**	**rs1581364290 C>T**	**rs200661444 C>T**	**rs246073 T>C**
UR-809	CC	CC	TC	**UR-837**	CC	CC	TC
UR-810	CC	CC	TT	**UR-838**	CC	CC	TC
UR-813	CC	CC	TC	**UR-839**	CC	CC	TC
UR-814	CC	CC	TC	**UR-840**	CC	CC	TC
UR-816	CC	CC	TT	**UR-842**	CC	CC	TC
UR-817	CC	CC	TC	**UR-843**	CC	CC	TC
UR-818	CC	CC	TC	**UR-844**	CC	CC	CC
UR-819	CC	CC	TT	**UR-845**	CC	CC	CC
UR-821	CC	CC	TT	**UR-846**	CC	CC	TC
UR-822	CC	CC	TT	**UR-847**	CC	CC	TC
UR-823	CC	CC	TT	**UR-848**	CC	CC	TT
UR-824	CC	CC	CC	**UR-849**	CC	CC	TC
UR-825	CC	CC	TT	**UR-850**	CC	CC	CC
UR-826	CC	CC	TT	**UR-851**	CC	CC	TT
UR-827	CC	CC	TC	**UR-852**	CC	CC	TC
UR-829	CC	CC	TT	**UR-853**	CC	CC	CC
UR-831	CC	CC	TC	**UR-854**	CC	CC	TC
UR-832	CC	CC	TC	**UR-855**	CC	CC	TT

Supplementary Table S6. Significantly overrepresented biological processes (q-value<0.01) predicted by GO and GOrilla enrichment analyses of genes with CG dinucleotides with at least 20% methylation difference

Biological process	p-value	q-value	Genes
Homophilic cell adhesion via plasma membrane adhesion molecules	4.01×10^{-12}	6.22×10^{-8}	*PCDHA10*, *PCDHA9*, *PCDHA8*, *PCDHA7*, *PCDHA6*, *PCDHA5*, *PCDHA4*, *PCDHA3*, *PCDHA2*, *PCDHA1*, *PTPRM*
Cell-cell adhesion via plasma-membrane adhesion molecules	4.1×10^{-10}	3.18×10^{-6}	*PCDHA10*, *PCDHA9*, *PCDHA8*, *PCDHA7*, *PCDHA6*, *PCDHA5*, *PCDHA4*, *PCDHA3*, *PCDHA2*, *PCDHA1*, *PTPRM*
Nervous system development	4.91×10^{-9}	2.54×10^{-5}	*PCDHA10*, *PCDHA8*, *PCDHA7*, *PCDHA6*, *PCDHA5*, *PCDHA4*, *PCDHA3*, *PCDHA2*, *PCDHA1*, *ATXN1*, *NRGN*
Cell-cell adhesion	5.23×10^{-8}	2.03×10^{-4}	*PCDHA10*, *PCDHA9*, *PCDHA8*, *PCDHA7*, *PCDHA6*, *PCDHA5*, *PCDHA4*, *PCDHA3*, *PCDHA2*, *PCDHA1*, *DLG2*, *PTPRM*
Developmental process	1.39×10^{-6}	4.3×10^{-3}	*PCDHA10*, *PCDHA8*, *PCDHA7*, *PCDHA6*, *PCDHA5*, *PCDHA4*, *PCDHA3*, *PCDHA2*, *PCDHA1*, *ZNF516*, *CACYBP*, *SPATA16*, *DLG2*, *LIG4*, *ATXN1*, *PTPRM*, *RIMS2*, *FARP2*, *ETS1*, *LMOD3*, *ADAM20*, *COBL*, *CTTNBP2*, *SORBS2*, *SRPK2*, *INSR*, *GRHL1*, *TANC1*, *RUNX1*, *NRGN*, *SNX2*, *WWOX*, *GAS7*
System development	1.87×10^{-6}	4.83×10^{-3}	*PCDHA10*, *PCDHA8*, *PCDHA7*, *PCDHA6*, *PCDHA5*, *PCDHA4*, *PCDHA3*, *PCDHA2*, *PCDHA1*, *LIG4*, *ATXN1*, *NRGN*
Cell adhesion	4.58×10^{-6}	1.01×10^{-2}	*PCDHA10*, *PCDHA9*, *PCDHA8*, *PCDHA7*, *PCDHA6*, *PCDHA5*, *PCDHA4*, *PCDHA3*, *PCDHA2*, *PCDHA1*, *DLG2*, *PTPRM*, *FARP2*
Biological adhesion	4.91×10^{-6}	9.53×10^{-3}	*PCDHA10*, *PCDHA9*, *PCDHA8*, *PCDHA7*, *PCDHA6*, *PCDHA5*, *PCDHA4*, *PCDHA3*, *PCDHA2*, *PCDHA1*, *DLG2*, *PTPRM*, *FARP2*