Table S1. Genes with a recognizable association with macrocephaly, retrieved from OMIM and the scientific literature.

Gene	Gene/Locus name	Cytogenetic location (hg38)
ABCC9	ATP binding cassette subfamily C member 9	**12p12.1**
ACAN	Aggrecan	**15q26.1**
ACER3	Alkaline ceramidase 3	**11q13.5**
ADK	Adenosine kinase	**10q22.2**
ADNP	Activity dependent neuroprotector homeobox	**20q13.13**
AKT1	AKT serine/threonine kinase 1	**14q32.33**
AKT3	AKT serine/threonine kinase 3	**1q43-q44**
ALKBH8	AlkB homolog 8, tRNA methyltransferase	**11q22.3**
AMER1	APC membrane recruitment protein 1	**Xq11.2**
AMPD1	Adenosine monophosphate deaminase 1	**1p13.2**
ANKH	ANKH inorganic pyrophosphate transport regulator	**5p15.2**
ANKRD17	Ankyrin repeat domain 17	**4q13.3**
ANTXR1	Anthrax toxin receptor 1	**2p13.3**
APC2	APC regulator of WNT signaling pathway 2	**19p13.3**
APOC2	Apolipoprotein C-II	**19q13.32**
ARSB	Arylsulfatase B	**5q14.1**
ARSK	Arylsulfatase family member K	**5q15**
ASH1L	ASH1 like histone lysine methyltransferase	**1q22**
ASPA	aspartoacylase	**17p13.2**
ASXL2	ASXL transcriptional regulator 2	**2p23.3**
AUTS2	Activator of transcription and developmental regulator AUTS2	**7q11.22**
B3GLCT	Beta 3-glucosyltransferase	**13q12.3**
B4GALT1	Beta-1,4-galactosyltransferase 1	**9p21.1**
B4GALT7	Beta-1,4-galactosyltransferase 7	**5q35.3**
BAP1	BRCA1 associated protein 1	**3p21.1**
BGN	Biglycan	**Xq28**
BICD2	BICD cargo adaptor 2	**9q22.31**
BICRA	BRD4 interacting chromatin remodeling complex associated protein	**19q13.33**
BLTP1	Bridge-like lipid transfer protein family member 1	**4q27**
BRAF	B-Raf proto-oncogene, serine/threonine kinase	**7q34**
BRWD3	Bromodomain and WD repeat domain containing 3	**Xq21.1**
C12orf57	Chromosome 12 open reading frame 57	**12p13.31**
CACNA1E	Calcium voltage-gated channel subunit alpha1 E	**1q25.3**
CAMK2G	Calcium/calmodulin dependent protein kinase II gamma	**10q22.2**
CANT1	Calcium activated nucleotidase 1	**17q25.3**
CASK	Calcium/calmodulin dependent serine protein kinase	**Xp11.4**
CBL	Cbl proto-oncogene	**11q23.3**
CCND2	Cyclin D2	**12p13.32**
CCNK	Cyclin K	**14q32.2**
CDC42BPB	CDC42 binding protein kinase beta	**14q32.32**
CDH2	Cadherin 2	**18q12.1**
CDKN1C	Cyclin-dependent kinase inhibitor 1C	**11p15.4**
CEP120	Centrosomal protein, 120kD	**5q23.2**
CHD1	Chromodomain helicase DNA binding protein-1	**5q15-q21.1**
CHD3	Chromodomain helicase DNA binding protein-3	**17p13.1**
CHD4	Chromodomain helicase DNA-binding protein-4	**12p13.31**
CHD8	Chromodomain helicase DNA-binding protein 8	**14q11.2**
COL2A1	Collagen II, alpha-1 polypeptide	**12q13.11**
COL3A1	Collagen III, alpha-1 polypeptide	**2q32.2**
CPE	Carboxypeptidase E	**4q32.3**
CRPPA	CDP-L-ribitol pyrophosphorylase A	**7p21.2**
CSF1R	Colony stimulating factor 1 receptor	**5q32**

GALNACT1	Chondroitin sulfate N-acetylgalactosaminyltransferase 1	**8p21.3**
CSNK2A1	Casein kinase 2 alpha 1	**20p13**
CUL4B	Cullin 4B	**Xq24**
CUL7	Cullin 7	**6p21.1**
CWC27	CWC27 spliceosome associated cyclophilin	**5q12.3**
D2HGDH	D-2-hydroxyglutarate dehydrogenase	**2q37.3**
DAG1	Dystroglycan 1	**3p21.31**
DDX3X	DEAD-box helicase 3 X-linked	**Xp11.4**
DEAF1	DEAF1 transcription factor	**11p15.5**
DEPDC5	DEP domain containing 5	**22q12.2-q12.3**
DHCR24	24-dehydrocholesterol reductase	**1p32.3**
DICER1	Dicer 1, ribonuclease III	**14q32.13**
DIS3L2	DIS3 like 3'-5' exoribonuclease 2	**2q37.1**
DLX3	Distal-less homeobox 3	**17q21.33**
DMXL2	Dmx like 2	**15q21.2**
DNAJC21	DnaJ heat shock protein family (Hsp40) member C21	**5p13.2**
DNM1	Dynamin 1	**9q34.11**
DNMT3A	DNA methyltransferase 3 alpha	**2p23.3**
DOCK3	Dedicator of cytokinesis 3	**3p21.2**
DOCK6	Dedicator of cytokinesis 6	**19p13.2**
DPYSL5	Dihydropyrimidinase-like 5	**2p23.3**
DVL1	Dishevelled segment polarity protein 1	**1p36.33**
DVL3	Dishevelled segment polarity protein 3	**3q27.1**
DYNC2I1	Dynein 2 intermediate chain 1	**7q36.3**
DYNC2LI1	Dynein cytoplasmic 2 light intermediate chain 1	**2p21**
EBP	EBP cholestenol delta-isomerase	**Xp11.23**
EED	Embryonic ectoderm development	**11q14.2**
EHMT1	Euchromatic histone lysine methyltransferase 1	**9q34.3**
EIF2B1	Eukaryotic translation initiation factor 2B subunit alpha	**12q24.31**
EIF2B2	Eukaryotic translation initiation factor 2B subunit beta	**14q24.3**
EIF2B3	Eukaryotic translation initiation factor 2B subunit gamma	**1p34.1**
EIF2B4	Eukaryotic translation initiation factor 2B subunit delta	**2p23.3**
EIF2B5	Eukaryotic translation initiation factor 2B subunit epsilon	**3q27.1**
EML1	EMAP like 1	**14q32.2**
ERF	ETS2 repressor factor	**19q13.2**
ETFA	Electron transfer flavoprotein subunit alpha	**15q24.2-q24.3**
ETFB	Electron transfer flavoprotein subunit beta	**19q13.41**
ETFDH	Electron transfer flavoprotein dehydrogenase	**4q32.1**
EXT2	Exostosin glycosyltransferase 2	**11p11.2**
EZH2	Enhancer of zeste 2 polycomb repressive complex 2 subunit	**7q36.1**
FAM111A	FAM111 trypsin like peptidase A	**11q12.1**
FAM149B1	Family with sequence similarity 149 member B1	**10q22.2**
FAM20C	FAM20C golgi associated secretory pathway kinase	**7p22.3**
FAR1	Fatty acyl-CoA reductase 1	**11p15.3**
FBN1	Fibrillin 1	**15q21.1**
FBXW11	F-box and WD repeat domain containing 11	**5q35.1**
FGFR1	Fibroblast growth factor receptor 1	**8p11.23**
FGFR2	Fibroblast growth factor receptor 2	**10q26.13**
FGFR3	Fibroblast growth factor receptor 3	**4p16.3**
FH	Fumarate hydratase	**1q43**
FIBP	FGF1 intracellular binding protein	**11q13.1**
FKTN	Fukutin	**9q31.2**
FLNA	Filamin A	**Xq28**
FMR1	Fragile X messenger ribonucleoprotein 1	**Xq27.3**
FOXP1	Forkhead box P1	**3p13**
GABBR2	Gamma-aminobutyric acid type B receptor subunit 2	**9q22.33**
GATAD2B	GATA zinc finger domain containing 2B	**1q21.3**
GCDH	Glutaryl-coa dehydrogenase	**19p13.13**

GDF6	Growth differentiation factor 6	**8q22.1**
GFAP	Glial fibrillary acidic protein	**17q21.31**
GJA1	Gap junction protein alpha 1	**6q22.31**
GLI2	GLI family zinc finger 2	**2q14.2**
GLI3	GLI family zinc finger 3	**7p14.1**
GNAI1	G protein subunit alpha i1	**7q21.11**
GNAI3	G protein subunit alpha i3	**1p13.3**
GNAQ	G protein subunit alpha q	**9q21.2**
GNE	Glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase	**9p13.3**
GPC3	Glypican 3	**Xq26.2**
GPC4	Glypican 4	**Xq26.2**
GPSM2	G protein signaling modulator 2	**1p13.3**
GRIA3	Glutamate ionotropic receptor AMPA type subunit 3	**Xq25**
GRIN2B	Glutamate ionotropic receptor NMDA type subunit 2B	**12p13.1**
GUSB	Glucuronidase beta	**7q11.21**
H1-4	H1.4 linker histone, cluster member	**6p22.2**
H3-3A	H3.3 histone A	**1q42.12**
H3-3B	H3.3 histone B	**17q25.1**
HADHA	oxyacyl-coa dehydrogenase trifunctional multienzyme complex subunit alpha	**2p23.3**
HDAC6	Histone deacetylase 6	**Xp11.23**
HECW2	HECT, C2 and WW domain containing E3 ubiquitin protein ligase 2	**2q32.3**
HEPACAM	Hepatic and glial cell adhesion molecule	**11q24.2**
HERC1	CT and RLD domain containing E3 ubiquitin protein ligase family member 1	**15q22.31**
HEXB	Hexosaminidase subunit beta	**5q13.3**
HMGA2	High mobility group AT-hook 2	**12q14.3**
HRAS	HRas proto-oncogene, GTPase	**11p15.5**
HSD17B4	Hydroxysteroid 17-beta dehydrogenase 4	**5q23.1**
HUWE1	HECT, UBA and WWE domain containing E3 ubiquitin protein ligase 1	**Xp11.22**
HYLS1	HYLS1 centriolar and ciliogenesis associated	**11q24.2**
IDS	Iduronate 2-sulfatase	**Xq28**
IDUA	Alpha-L-iduronidase	**4p16.3**
IFITM5	Interferon induced transmembrane protein 5	**11p15.5**
IFT43	Intraflagellar transport 43	**14q24.3**
IFT74	Intraflagellar transport 74	**9p21.2**
IFT81	Intraflagellar transport 81	**12q24.11**
IGBP1	Immunoglobulin binding protein 1	**Xq13.1**
IGF2	Insulin like growth factor 2	**11p15.5**
IL6ST	Interleukin 6 cytokine family signal transducer	**5q11.2**
INPP5E	Inositol polyphosphate-5-phosphatase E	**9q34.3**
INPPL1	Inositol polyphosphate phosphatase like 1	**11q13.4**
ITCH	Itchy E3 ubiquitin protein ligase	**20q11.22**
KCNH1	Potassium voltage-gated channel subfamily H member 1	**1q32.2**
KCNJ8	Potassium inwardly rectifying channel subfamily J member 8	**12p12.1**
KCTD13	Potassium channel tetramerization domain containing 13	**16p11.2**
KDM1A	Lysine demethylase 1A	**1p36.12**
KDM5B	Lysine demethylase 5B	**1q32.1**
KDM5C	Lysine demethylase 5C	**Xp11.22**
KIAA0753	KIAA0753	**17p13.1**
KIDINS220	Kinase D interacting substrate 220	**2p25.1**
KIF22	Kinesin family member 22	**16p11.2**
KIF7	Kinesin family member 7	**15q26.1**
KMT2E	Lysine methyltransferase 2E (inactive)	**7q22.3**
KMT5B	Lysine methyltransferase 5B	**11q13.2**
KPTN	Kaptin, actin binding protein	**19q13.32**
KRAS	KRAS proto-oncogene, GTPase	**12p12.1**
L1CAM	L1 cell adhesion molecule	**Xq28**
L2HGDH	L-2-hydroxyglutarate dehydrogenase	**14q21.3**
LAMB1	Laminin subunit beta 1	**7q31.1**

LBR	Lamin B receptor	**1q42.12**
LRP2	LDL receptor related protein 2	**2q31.1**
MAB21L2	mab-21 like 2	**4q31.3**
MADD	MAP kinase activating death domain	**11p11.2**
MAN1B1	Mannosidase alpha class 1B member 1	**9q34.3**
MAN2B1	Mannosidase alpha class 2B member 1	**19p13.13**
MAN2C1	Mannosidase alpha class 2C member 1	**15q24.2**
MAP2K1	Mitogen-activated protein kinase kinase 1	**15q22.31**
MAP2K2	Mitogen-activated protein kinase kinase 2	**19p13.3**
MCCC2	Methylcrotonyl-coa carboxylase subunit 2	**5q13.2**
MCEE	Methylmalonyl-coa epimerase	**2p13.3**
MECP2	Methyl-cpg binding protein 2	**Xq28**
MED12	Mediator complex subunit 12	**Xq13.1**
MESD	Mesoderm development LRP chaperone	**15q25.1**
MGAT2	alpha-1,6-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase	**14q21.3**
MITF	Melanocyte inducing transcription factor	**3p13**
MLC1	Modulator of VRAC current 1	**22q13.33**
MOCS1	Molybdenum cofactor synthesis 1	**6p21.2**
MOCS2	Molybdenum cofactor synthesis 2	**5q11.2**
MPDZ	Multiple PDZ domain crumbs cell polarity complex component	**9p23**
MRAS	Muscle RAS oncogene homolog	**3q22.3**
MSL3	MSL complex subunit 3	**Xp22.2**
MTOR	Mechanistic target of rapamycin kinase	**1p36.22**
MTM1	Myotubularin 1	**Xq28**
MUSK	Muscle associated receptor tyrosine kinase	**9q31.3**
MYCN	MYCN proto-oncogene, bHLH transcription factor	**2p24.3**
MYH8	Myosin heavy chain 8	**17p13.1**
MYMK	Myomaker, myoblast fusion factor	**9q34.2**
NBPF1	NBPF member 1	**1p36.13**
NDN	Necdin, MAGE family member	**15q11.2**
NDUFAF3	NADH:ubiquinone oxidoreductase complex assembly factor 3	**3p21.31**
NDUFAF5	NADH:ubiquinone oxidoreductase complex assembly factor 5	**20p12.1**
NDUFS4	NADH:ubiquinone oxidoreductase subunit S4	**5q11.2**
NDUFV1	NADH:ubiquinone oxidoreductase core subunit V1	**11q13.2**
NEK1	NIMA related kinase 1	**4q33**
NF1	Neurofibromin 1	**17q11.2**
NFIA	Nuclear factor I A	**1p31.3**
NFIB	Nuclear factor I B	**9p23-p22.3**
NFIX	Nuclear factor I X	**19p13.13**
NKX3-2	NK3 homeobox 2	**4p15.33**
NONO	Non-POU domain containing octamer binding	**Xq13.1**
NR2F1	Nuclear receptor subfamily 2 group F member 1	**5q15**
NRAS	NRAS proto-oncogene, GTPase	**1p13.2**
NSD1	Nuclear receptor binding SET domain protein 1	**5q35.3**
NXN	Nucleoredoxin	**17p13.3**
OBSL1	Obscurin like cytoskeletal adaptor 1	**2q35**
ODC1	Ornithine decarboxylase 1	**2p25.1**
OFD1	OFD1 centriole and centriolar satellite protein	**Xp22.2**
OPHN1	Oligophrenin 1	**Xq12**
OTUD5	OTU deubiquitinase 5	**Xp11.23**
P4HB	Prolyl 4-hydroxylase subunit beta	**17q25.3**
PAK1	P21 (RAC1) activated kinase 1	**11q13.5-q14.1**
PAK3	P21 (RAC1) activated kinase 3	**Xq23**
PAM16	Presequence translocase associated motor 16	**16p13.3**
PC	Pyruvate carboxylase	**11q13.2**
PCGF2	Polycomb group ring finger 2	**17q12**
PDSS1	Decaprenyl diphosphate synthase subunit 1	**10p12.1**
PEX1	Peroxisomal biogenesis factor 1	**7q21.2**

PHF21A	PHD finger protein 21A	**11p11.2**
PHF6	PHD finger protein 6	**Xq26.2**
PIGA	Phosphatidylinositol glycan anchor biosynthesis class A	**Xp22.2**
PIGM	Phosphatidylinositol glycan anchor biosynthesis class M	**1q23.2**
PIGN	Phosphatidylinositol glycan anchor biosynthesis class N	**18q21.33**
PIGT	Phosphatidylinositol glycan anchor biosynthesis class T	**20q13.12**
PIGV	Phosphatidylinositol glycan anchor biosynthesis class V	**1p36.11**
PIK3CA	Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha	**3q26.32**
PIK3R1	Phosphoinositide-3-kinase regulatory subunit 1	**5q13.1**
PIK3R2	Phosphoinositide-3-kinase regulatory subunit 2	**19p13.11**
PKDCC	Protein kinase domain containing, cytoplasmic	**2p21**
PLAG1	PLAG1 zinc finger	**8q12.1**
PLCB4	Phospholipase C beta 4	**20p12.3-p12.2**
PLCH1	Phospholipase C eta 1	**3q25.31**
PLG	Plasminogen	**6q26**
POC1A	POC1 centriolar protein A	**3p21.2**
POLE	DNA polymerase epsilon, catalytic subunit	**12q24.33**
POLR3A	RNA polymerase III subunit A	**10q22.3**
POMK	Protein O-mannose kinase	**8p11.21**
POMT1	Protein O-mannosyltransferase 1	**9q34.13**
POP1	POP1 homolog, ribonuclease P/MRP subunit	**8q22.2**
PPP1CB	Protein phosphatase 1 catalytic subunit beta	**2p23.2**
PPP1R12A	Protein phosphatase 1 regulatory subunit 12A	**12q21.2-q21.31**
PPP2CA	Protein phosphatase 2 catalytic subunit alpha	**5q31.1**
PPP2R5D	Protein phosphatase 2 regulatory subunit b'delta	**6p21.1**
PTCH1	Patched 1	**9q22.32**
PTCH2	Patched 2	**1p34.1**
PTEN	Phosphatase and tensin homolog	**10q23.31**
PTPN11	Protein tyrosine phosphatase non-receptor type 11	**12q24.13**
PUF60	Poly(U) binding splicing factor 60	**8q24.3**
RAB39A	RAB39A, member RAS oncogene family	**11q22.3**
RAB39B	RAB39B, member RAS oncogene family	**Xq28**
RAC1	Rac family small GTPase 1	**7p22.1**
RAF1	Raf-1 proto-oncogene, serine/threonine kinase	**3p25.2**
RALA	RAS like proto-oncogene A	**7p14.1**
RHEB	Ras homolog, mTORC1 binding	**7q36.1**
RIN2	Ras and Rab interactor 2	**20p11.23**
RIT1	Ras like without CAAX 1	**1q22**
RNF125	Ring finger protein 125	**18q12.1**
RNF135	Ring finger protein 135	**17q11.2**
ROR2	Receptor tyrosine kinase like orphan receptor 2	**9q22.31**
RPS6KA3	Ribosomal protein S6 kinase A3	**Xp22.12**
RRAS2	RAS related 2	**11p15.2**
RXYLT1	Ribitol xylosyltransferase 1	**12q14.2**
SATB2	SATB homeobox 2	**2q33.1**
SEC23A	SEC23 homolog A, COPII coat complex component	**14q21.1**
SEC23B	SEC23 homolog B, COPII coat complex component	**20p11.23**
SEC24D	SEC24 homolog D, COPII coat complex component	**4q26**
SERPINH1	serpin family H member 1	**11q13.5**
SETD2	SET domain containing 2, histone lysine methyltransferase	**3p21.31**
SGSH	N-sulfoglucosamine sulfohydrolase	**17q25.3**
SHANK3	SH3 and multiple ankyrin repeat domains 3	**22q13.33**
SHOC2	SHOC2 leucine rich repeat scaffold protein	**10q25.2**
SIX3	SIX homeobox 3	**2p21**
SLC25A1	Solute carrier family 25 member 1	**22q11.21**
SLC2A1	Solute carrier family 2 member 1	**1p34.2**
SLC2A10	Solute carrier family 2 member 10	**20q13.12**
SLC44A1	Solute carrier family 44 member 1	**9q31.1-q31.2**

SMAD4	SMAD family member 4	**18q21.2**
SMO	Smoothened, frizzled class receptor	**7q32.1**
SNRPN	Small nuclear ribonucleoprotein polypeptide N	**15q11.2**
SNX10	Sorting nexin 10	**7p15.2**
SNX14	Sorting nexin 14	**6q14.3**
SON	SON DNA and RNA binding protein	**21q22.11**
SOS1	SOS Ras/Rac guanine nucleotide exchange factor 1	**2p22.1**
SOST	Sclerostin	**17q21.31**
SOX9	SRY-box transcription factor 9	**17q24.3**
SPINT2	Serine peptidase inhibitor, Kunitz type 2	**19q13.2**
SPOP	Speckle type BTB/POZ protein	**17q21.33**
SPRED1	Sprouty related EVH1 domain containing 1	**15q14**
SPRED2	Sprouty related EVH1 domain containing 2	**2p14**
STRADA	STE20 related adaptor alpha	**17q23.3**
STT3A	STT3 oligosaccharyltransferase complex catalytic subunit A	**11q24.2**
SUFU	SUFU negative regulator of hedgehog signaling	**10q24.32**
SUZ12	SUZ12 polycomb repressive complex 2 subunit	**17q11.2**
SYN1	Synapsin I	**Xp11.3-p11.23**
SZT2	SZT2 subunit of KICSTOR complex	**1p34.2**
TAOK1	TAO kinase 1	**17q11.2**
TBC1D2B	TBC1 domain family member 2B	**15q24.3-q25.1**
TBC1D7	TBC1 domain family member 7	**6p24.1**
TBCK	TBC1 domain containing kinase	**4q24**
TBL1X	Transducin beta like 1 X-linked	**Xp22.31-p22.2**
TCF20	Transcription factor 20	**22q13.2**
TCIRG1	T cell immune regulator 1, ATPase H+ transporting V0 subunit a3	**11q13.2**
TET3	Tet methylcytosine dioxygenase 3	**2p13.1**
THRA	Thyroid hormone receptor alpha	**17q21.1**
TMCO1	Transmembrane and coiled-coil domains 1	**1q24.1**
TMEM53	Transmembrane protein 53	**1p34.1**
TMEM165	Transmembrane protein 165	**4q12**
TMEM216	Transmembrane protein 216	**11q12.2**
TNFRSF11B	TNF receptor superfamily member 11b	**8q24.12**
TONSL	Tonsoku like, DNA repair protein	**8q24.3**
TPI1	Triosephosphate isomerase 1	**12p13.31**
TRIM37	Tripartite motif containing 37	**17q22**
TRIO	Trio Rho guanine nucleotide exchange factor	**5p15.2**
TRIP11	Thyroid hormone receptor interactor 11	**14q32.12**
TRIP12	Thyroid hormone receptor interactor 12	**2q36.3**
TSC1	TSC complex subunit 1	**9q34.13**
TSC2	TSC complex subunit 2	**16p13.3**
UPF3B	UPF3B regulator of nonsense mediated mRNA decay	**Xq24**
USP9X	ubiquitin specific peptidase 9 X-linked	**Xp11.4**
VPS35L	VPS35 endosomal protein sorting factor like	**16p12.3**
VPS4A	Vacuolar protein sorting 4 homolog A	**16q22.1**
WASHC5	WASH complex subunit 5	**8q24.13**
WDR81	WD repeat domain 81	**17p13.3**
WNT5A	Wnt family member 5A	**3p14.3**
XYLT1	Xylosyltransferase 1	**16p12.3**
YME1L1	YME1 like 1 ATPase	**10p12.1**
ZBTB20	Zinc finger and BTB domain containing 20	**3q13.31**
ZBTB42	Zinc finger and BTB domain containing 42	**14q32.33**
ZBTB7A	Zinc finger and BTB domain containing 7A	**19p13.3**
ZDHHC9	Zinc finger DHHC-type palmitoyltransferase 9	**Xq26.1**
ZIC2	Zic family member 2	**13q32.3**
ZNF469	Zinc finger protein 469	**16q24.2**
ZSWIM6	Zinc finger SWIM-type containing 6	**5q12.1**

Figure S1. Enriched biological processes of the gene set related to macrocephaly