

The genetic determinants of cerebral palsy

**A thesis submitted for the degree of Doctor of
Philosophy (PhD) to the University of Adelaide**

By

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Statement of Declaration

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Gai Lisette McMichael

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Table of contents

Statement of declaration	i
Table of contents	ii
Acknowledgements	ix
Publications	xi
HUGO Gene Nomenclature gene symbol and gene name	xiii
Abbreviations	xvi
URLs	xix
Chapter 1 Introduction	1
1.1 Definition of cerebral palsy	2
1.2 Clinical classification of cerebral palsy	3
1.2.1 Gross motor function classification system	5
1.3 Neuroimaging	7
1.4 Incidence and economic cost of cerebral palsy	8
1.5 Known clinical risk factors for cerebral palsy	9
1.5.1 Preterm birth	9
1.5.2 Low birth weight	9
1.5.3 Multiple birth	10
1.5.4 Male gender	10
1.6 Other known clinical risk factors	11
1.6.1 Birth asphyxia	11
1.7 Other possible risk factors	12
1.8 Evidence for a genetic contribution to cerebral palsy causation	13
1.8.1 Sibling risks and twin studies	13
1.8.2 Effect of consanguinity	14
1.8.3 Associated congenital anomalies	15
1.8.4 Families providing evidence for Mendelian inheritance	16
1.9 Genetic disorders that can be mistaken for cerebral palsy	17
1.10 Approaches to identification of genes involved in cerebral palsy	19
1.10.1 Linkage analysis and homozygosity mapping	19
1.10.2 <i>GADI</i>	20
1.10.3 <i>KANK1</i>	20
1.10.4 Chromosome 9p12-q12	21
1.11 Candidate-gene association studies	22
1.12 Copy number variants	23
1.13 Massively parallel sequencing	28
1.14 Whole-exome sequencing	28

1.14.1	Whole-exome capture methods	29
1.15	Whole-exome sequencing identifying single gene mutations	32
1.16	Whole-exome sequencing identifying single gene mutations in cerebral palsy	33
1.16.1	AP-4 complex	33
1.16.2	<i>ADD3</i>	34
1.16.3	<i>KCNC3</i>	34
1.16.4	<i>ITPR1</i>	35
1.16.5	<i>SPTBN2</i>	36
1.17	Whole-exome sequencing vs whole genome sequencing	39
1.18	Summary	41
1.19	Hypotheses and aims	42
1.19.1	Hypotheses	42
1.19.2	Aims	42
1.20	References	43
Chapter 2 Clinical cohort		67
2.1	Sporadic cerebral palsy cases (n = 183)	68
2.2	Brain imaging details	69
2.3	Cerebral palsy cohort clinical characteristics	69
2.4	Cerebral palsy subtype	69
2.5	Gestational age	72
2.6	Birth weight distribution	74
2.7	Comorbidities distribution	76
2.8	Gender distribution	77
2.9	Familial cerebral palsy cases	78
2.10	References	80
Chapter 3 Materials and methods		82
3.1	Recruitment of cerebral palsy families	83
3.2	Blood collection	84
3.3	Lymphocyte cell line development	84
3.4	DNA extraction	85
3.5	Whole-exome sequencing	86
3.5.1	Illumina library construction	86
3.5.2	Illumina exome capture	87
3.5.3	Illumina sequencing	88
3.5.4	Read mapping and variant calling	89
3.5.5	Data interrogation and analysis	90
3.6	Validation of candidate variants for cerebral palsy	91
3.6.1	Human Genome Sequencing Centre, Baylor College of Medicine	91
3.6.2	The University of Adelaide	91
3.7	Polymerase Chain Reaction (PCR)	95

3.7.1	PCR product visualization	95
3.8	Sanger sequencing reaction and clean up	95
3.9	DNA variant and gene prioritization	97
3.10	References	98
Chapter 4	Whole exome sequencing points to considerable genetic heterogeneity of cerebral palsy	100
	Statement of authorship	101
4.1	Abstract	105
4.2	Introduction	106
4.3	Materials and methods	107
4.3.1	Study cohort	107
4.3.2	DNA extraction	107
4.3.3	Illumina library construction	108
4.3.4	Illumina exome capture	108
4.3.5	Illumina sequencing	109
4.3.6	Analysis	110
4.3.7	DNA variant and gene prioritization	111
4.4	Results	113
4.4.1	Case-parent trios (n=98)	113
4.4.1.1	<i>De novo</i> mutations	113
4.4.1.2	Inherited X-chromosome and recessive variants	114
4.4.2	Whole-exome sequencing	115
4.4.3	Pathway analysis	116
4.4.4	Clinical associations	116
4.5	Discussion	117
4.6	References	125
Chapter 5	A family diagnosed with cerebral palsy and intellectual disability with a X-linked mutation in ZC4H2	130
5.1	Introduction	131
5.2	Clinical reports	131
5.2.1	The family	131
5.2.2	The parents (I-1 and I-2)	132
5.2.3	The son with ‘cerebral palsy’ and intellectual disability (II-1)	132
5.2.4	The son with ‘cerebral palsy’ and intellectual disability (II-5)	135
5.2.5	The daughter with developmental delay (II-7)	136
5.2.6	Remaining siblings (II2, II3, II-4, II-6 and II-8)	136
5.3	Methods	138
5.3.1	DNA isolation	138
5.3.2	Whole-exome sequencing and analysis	138
5.3.3	Sanger sequencing	138

5.4	Results	140
5.5	Discussion	142
5.6	References	144
Chapter 6	NK2 homeobox 1 gene mutations in a family diagnosed with ataxic dyskinetic cerebral palsy	146
	Statement of authorship	147
6.1	Abstract	149
6.2	Introduction	150
6.3	Clinical report	151
	6.3.1 The family	151
	6.3.2 The affected father	151
	6.3.3 The affected son	152
	6.3.4 The affected daughter	152
	6.3.5 Other cases of dyskinetic or ataxic cerebral palsy	153
6.4	Methods	154
	6.4.1 DNA isolation	154
	6.4.2 Whole-exome sequencing and analysis	154
	6.4.3 Sanger sequencing	155
6.5	Results	156
6.6	Discussion	158
6.7	References	160
Chapter 7	A family with autism spectrum disorder and spasticity with novel compound heterozygous mutation in the sodium channel gene SCN2A	162
7.1	Abstract	163
7.2	Introduction	164
7.3	Clinical report	165
	7.3.1 The family	165
	7.3.2 The parents	165
	7.3.3 The 13-year-old son with ASD only	166
	7.3.4 The 9-year-old daughter with ASD and spasticity	166
	7.3.5 The 7-year-old son with ASD and spasticity	167
7.4	Methods	169
	7.4.1 Whole-exome sequencing and analysis	169
	7.4.2 Sanger sequencing	170
7.5	Results	171
7.6	Discussion	172
7.7	References	179
Chapter 8	Discussion and future directions	184
8.1	Discussion and future prospects	185
8.2	Sporadic cases	186

8.3	Familial cases	190
8.3.1	Family 1 with <i>ZC4H2</i> mutation	190
8.3.2	Family 2 with <i>NKX2-1</i> mutation	191
8.3.3	Family 3 with <i>SCN2A</i> mutation	192
8.4	Limitations of this study	194
8.5	Future prospects	195
8.5.1	Whole-exome and whole-genome sequencing	196
8.5.2	Custom gene-panels	197
8.5.3	Central data repository	198
8.5.4	Genome-wide expression profiling (RNA sequencing)	198
8.5.5	Epigenetics and cerebral palsy	200
8.6	Conclusion	204
8.7	References	207
Appendix	Supplementary data	217
9.1	References	260

List of Tables

Table 1.1	Summary of potentially pathogenic CNVs encompassing genes previously associated with cerebral palsy	27
Table 1.2	Summary of the different solution-based commercial exome capture kits	31
Table 1.3	Summary of novel single gene mutations, in known (OMIM) genes, in cerebral palsy cases	38
Table 2.1	Type of cerebral palsy in 183 sporadic cases	70
Table 2.2	Gestational age distribution of 183 sporadic cases with cerebral palsy compared with South Australian (SA) pregnancy outcome data	73
Table 2.3	Birth weight distribution in 183 sporadic cases with cerebral palsy compared with South Australian (SA) pregnancy outcome data	75
Table 2.4	Distribution of co-morbidities in 183 sporadic cases with cerebral palsy	76
Table 2.5	Gender distributions in 183 sporadic cases with cerebral palsy	77
Table 2.6	Summary of the clinical characteristics for three families With more than one individual with a diagnosis of cerebral Palsy	79
Table 3.1	Primer sequences for validating candidate variants from whole blood (The University of Adelaide)	92
Table 4.1	Clinical characteristics of 183 individuals with cerebral palsy	122
Table 4.2	Novel variants in known (OMIM) genes in CP cases identified in 98 trios: CADD score > 10 and RVIS % < 50	123

Table 4.3	Novel candidate genes in CP cases identified in 98 trios; CADD score > 20 and RVIS % < 50	124
Table 5.1	Multispecies alignment around p.Arg213 of <i>ZC4H2</i>	141
Table 7.1	Clinical characteristics, <i>SCN2A</i> variants and segregation pattern and pathogenicity predictions and scores	178
Table 7.2	Fragments of sequence chromatograms from 5'-3'	178
Table 9.1	Supplementary Table A	224
Table 9.2	Supplementary Table B	242
Table 9.3	Supplementary Table C	243
Table 9.4	Supplementary Table D	247
Table 9.5	Supplementary Table E	248
Table 9.6	Supplementary Table F	249
Table 9.7	Supplementary Table G	250
Table 9.8	Supplementary Table H	253
Table 9.9	Supplementary Table I	254
Table 9.10	Supplementary Table J	255
Table 9.11	Supplementary Table K	258
Table 9.12	Supplementary Table L	259

List of Figures

Figure 1.1	Different types of cerebral palsy and the regions of the body affected	5
Figure 1.2	Prevalence of cerebral palsy rates per 1000 live births compared with caesarean rates over the past 50 years	12
Figure 1.3	The prevalence and type of co-morbidities seen in individuals diagnosed with cerebral palsy	16
Figure 1.4	Allele frequency correlated with effect size	23
Figure 2.1	Type of cerebral palsy in 183 sporadic cases	71
Figure 2.2	Gestational age distribution of 183 sporadic cases with cerebral palsy compared with South Australian (SA) pregnancy outcome data	73
Figure 2.3	Birth weight distribution in 183 sporadic cases with cerebral palsy compared with South Australian (SA) pregnancy outcome data	75
Figure 2.4	Distribution of co-morbidities in 183 sporadic cases with cerebral palsy	76
Figure 2.5	Gender distributions in 183 sporadic cases with cerebral palsy	77
Figure 2.6-2.8	Overview of the pedigree details for three families with a diagnosis of cerebral palsy	78
Figure 5.1	Two generation pedigree with two brothers (II-1 and II-5) diagnosed with 'cerebral palsy' and intellectual disability and a sister (II-7) significantly behind in language, cognitive and personal/social skills	132

Figure 5.2	Representative sequence chromatograms of <i>ZC4H2</i> wildtype, mutations and heterozygous variants identified in nine out of the ten family members	141
Figure 6.1	Three generation pedigree with de novo mutation in II-1 and subsequent autosomal dominant transmission in III-2 and III-3	153
Figure 6.2(A)	Fragments of sequence chromatograms from an affected individual (heterozygous mutation) and an unaffected individual (normal homozygous) from 5'–3' and corresponding amino acid sequences	157
Figure 6.2(B)	Comparison of amino acid sequences of wildtype and mutant NKX2-1 proteins	157
Figure 7.1	Two-generation pedigree	177
Figure 7.2	Fragments of sequence chromatograms from 5'–3'	177
Figure 9.1	Supplementary Figure A	218
Figure 9.2	Supplementary Figure B	219
Figure 9.3	Supplementary Figure C	219
Figure 9.4	Supplementary Figure D	220
Figure 9.5	Supplementary Figure E	220
Figure 9.6	Supplementary Figure F	221
Figure 9.7	Supplementary Figure G	221
Figure 9.8	Supplementary Figure H	222
Figure 9.9	Supplementary Figure I	222
Figure 9.10	Supplementary Figure J	223

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2. **McMichael, G.L.**, Hirata, H., Nanda, I., van Riesen, A. *et al.* ZC4H2 mutations are associated with arthrogyriposis multiplex congenita and intellectual disability through impairment of central and peripheral synaptic plasticity. *Am J Hum Genet* **92**, 681-95 (2013).
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HUGO Gene Nomenclature gene symbol and gene name

ADD3 – Adducin 3 (Gamma)

AGAP1 – ArfGAP with GTPase Domain, Ankyrin Repeat and PH Domain 1

AHII – Abelson Helper Integration Site 1

ANKRD15 – KN Motif And Ankyrin Repeat Domains 1 (KANK1)

AP-4 – AP-4 Complex

AP4B1 – Adaptor-related Protein Complex 4, β 1 subunit

AP4E1 – Adaptor-related Protein Complex 4, ϵ 1 subunit

AP4M1 – Adaptor-related Protein Complex 4, μ 1 subunit

AP4S1 – Adaptor-related Protein Complex 4, σ 1 subunit

CDK17 – Cyclin-Dependent Kinase 17

CD99L2 – CD99 Molecule-Like 2

CEP290 – Centrosomal Protein 290KDa

COPS3 – COP9 Signalosome Subunit 3

CTNND2 – Catenin (Cadherin-Associated Protein), Delta 2

CUL4B – Cullin 4B

ENPP4 – Ectonucleotide Pyrophosphatase/Phosphodiesterase 4 (Putative)

FLNB – Filamin B (Beta)

GAD1 – Glutamate Decarboxylase 1

GCH1 – GTP Cyclohydrolase 1

HSPA4 – Heat Shock 70kDa Protein 4

HSPG2 – Heparan Sulfate Proteoglycan 2

ITPR1 – Inositol 1,4,5-Trisphosphate Receptor, Type 1

JHDM1D – Lysine (K)-Specific Demethylase 7A

KANK1 – KN Motif And Ankyrin Repeat Domains 1 (ANKRD15)

HUGO Gene Nomenclature gene symbol and gene name (continued)

KDM5C – Lysine (K)-Specific Demethylase 5C

KCNC3 – Voltage-Gated Potassium Channel Subunit Kv3.3

LICAM – L1 Cell Adhesion Molecule

LTN1 – Listerin E3 Ubiquitin Protein Ligase 1

MAOA – Monoamine Oxidase A

MAOB – Monoamine Oxidase B

MAST1 – Microtubule Associated Serine/Threonine Kinase 1

MCPH1 – Microcephalin 1

MED17 – Mediator Complex Subunit 17

MEF2C – Myocyte Enhancer Factor 2C

MIIP – Migration and Invasion Inhibitory Protein

MUM1L1 – Melanoma Associated Antigen (Mutated) 1-Like 1

MYH14 – Myosin, Heavy Chain 14, Non-Muscle

NAA35 – N(Alpha)-Acetyltransferase 35, NatC Auxiliary Subunit

NEMF – Nuclear Export Mediator Factor

NPHP1 – Nephronophthisis 1 (Juvenile)

NKX2-1 – NK2 Homeobox 1

PAK3 – P21 Protein (Cdc42/Rac)-Activated Kinase 3

PACRG – PARK2 Co-Regulated

PARK2 – Parkin RBR E3 Ubiquitin Protein Ligase

PAX5 – Paired Box 5

PLAC4 – Placenta-Specific 4

PLP1 – Proteolipid Protein 1

PCDH11X – Protocadherin 11 X-Linked

HUGO Gene Nomenclature gene symbol and gene name (continued)

RFX2 – Factor X, 2 (Influences HLA Class II Expression)

SCN2A – Sodium Channel, Voltage Gated, Type II Alpha Subunit

SCN8A – Sodium Channel, Voltage Gated, Type VIII Alpha Subunit

SLC11A2 – Solute Carrier Family 11 (Proton-Coupled Divalent Metal Ion
Transporter), Member 2

SPAST – Spastin

SPR – Sepiapterin Reductase (7,8-Dihydrobiopterin:NADP+ Oxidoreductase)

SPTBN2 – Spectrin, beta, non-erythrocytic 2

SSPO – SCO-Spondin

SYNGAP1 – Synaptic Ras GTPase Activating Protein 1

TBC1D24 – TBC1 Domain Family, Member 24

TENM1 – Teneurin Transmembrane Protein 1

TGM6 – Transglutaminase 6

TUBA1A – Tubulin, Alpha 1a

UBE3A – Ubiquitin Protein Ligase E3A

UBQLN3 – Ubiquilin 3

WDR45 – WD Repeat Domain 45

WIP1 – WD Repeat Domain, Phosphoinositide Interacting 2

ZC4H2 – Zinc Finger, C4H2 Domain Containing

ZNF674 – Zinc Finger Protein 674

Abbreviations

ACD – Acid citrate dextrose

AMC – Arthrogryposis multiplex congenita

ASD – Autism spectrum disorder

ATLAS – SNP

BCM – Baylor College of Medicine

BHC – Benign Hereditary Chorea

BWA – Burrows-Wheeler Aligner

CADD – Combined Annotation-Dependent Depletion

CGH – Comparative Genomic Hybridisation

ChIP – Chromatin immunoprecipitation

CNVs – Copy Number Variants

CNS – Central nervous system

CP – Cerebral palsy

DNA – Deoxyribonucleic acid

EDTA – Ethylenediaminetetraacetic acid

EVS – Exome Variant Server

ExAC – Exome Aggregation Consortium

GA – General anaesthetic

GABA – Gamma-aminobutyric acid

GATK – Genome Analysis Toolkit

GERP – Genomic Evolutionary Rate Profiling

GMFCS – Gross Motor Function Classification System

GRA – Genetic Repositories Australia

HGMD – Human Genome Mutation Database

Abbreviations (continued)

HGSC – Human Genome Sequencing Center

HSP – Hereditary Spastic Paraplegia

ID – Intellectual disability

IQ – Intelligence quotient

IUGR – Intrauterine growth restriction

IVF – *In vitro* fertilization

IVH – Intraventricular haemorrhage

LCLs – Lymphoblastoid cell lines

LM-PCR – Ligation mediated-polymerase chain reaction

LOF – Loss of function

MAF – Minor allele frequency

MIM – Mendelian Inheritance in Man

MPS – Massively parallel sequencing

mRNA – Messenger ribonucleic acid

miRNA – Micro ribonucleic acid

MRI – Magnetic resonance imaging

ncRNA – Non-coding ribonucleic acid

NGS – Next generation sequencing

NHLBI – National Heart, Lung, and Blood Institute

OMIM – Online Mendelian Inheritance in Man

OR – Odds ratio

PCR – Polymerase chain reaction

PE – Paired-end

PMD – Pelizaeus-Merzbacher disease

Abbreviations (continued)

POSU – Pregnancy Outcome in South Australia

PVL – Periventricular leukomalacia

RNA – Ribonucleic acid

rRNA – Ribosomal ribonucleic acid

tRNA – Transfer ribonucleic acid

RVIS – Residual Variation Intolerance Score

SHRs – Standardized hospitalisation ratios

SIFT – Scale-invariant feature transform

SNPs – Single nucleotide polymorphisms

SPG4 – Spastic paraplegia 4

UCSC – University of California, Santa Cruz Genome Browser

UTRs – Untranslated regions

WES – Whole-exome sequencing

WGS – Whole-genome sequencing

XLID – X-linked intellectual disability

URLs

Allen Human Brain Atlas – www.brainspan.org/

Australian Bureau of Statistics – www.abs.gov.au

BCM-HGSC protocol – https://hgsc.bcm.edu/sites/default/files/documents/Illumina_Barcoded_PairedEnd_Capture_Library_Preparation.pdf Barcoded Paired-End Capture Library Preparation.pdf

Cerebral Palsy Research Report – www.cerebralpalsy.org.au/wp-content/uploads/2013/04/ACPR/

dbSNP – <http://www.ncbi.nlm.nih.gov/projects/SNP/>

Ensembl – www.ensembl.org/

EVS – <http://evs.gs.washington.edu/EVS/>

ExAC database – exac.broadinstitute.org/

OMIM – www.omim.org/

Partek – <http://www.partek.com/>

RefSeq – www.ncbi.nlm.nih.gov/refseq/

1000 Genomes – <http://browser.1000genomes.org/index.html>

UCSC – <https://genome.ucsc.edu/>