

# **Sox3 dosage regulation is important for roof plate specification during central nervous system development**

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Philosophy

By

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# **Errata**

**The following corrections have been made in the final version of the thesis: --**

## **Table of Contents**

“5.4.1 Bmp and Wnt RP expression was diminished transgenic embryos” to “5.4.2 Bmp and Wnt RP expression was diminished in transgenic embryos”

“5.4.2” to “5.4.3”

“5.4.3” to “5.4.4”

“5.4.4” to “5.4.5”

“5.4.5” to “5.4.6”

“APPENDIX IV: AN OUTLINE OF THE MICROARRAY EXPERIEMNT” to

“APPENDIX IV: AN OUTLINE OF THE MICROARRAY EXPERIMENT”

## **Summary**

Third paragraph, line 8: “have similar role” to “have a similar role”

## **Abbreviations**

Title: “Abbreviations Abbreviations” to “Abbreviations

Anatomical terms: “MZ mantel zone” to “MZ mantle zone”

## **Chapter 1: Introduction**

Page 3, line 6: “subfamily” to “subfamilies”

Page 4, line 14: “to minor groove of DNA helix” to “to the minor groove of the DNA helix”

Page 5, line 6: “activate” to “activates”

Page 5, line 11: “These indicate” to “These data indicate”

Page 5, line 29: “target genes” to “target gene”

Page 6, line 1: “target genes” to “target gene”

Page 6, line 1-2: “function specialisation” to “the functional specialisation”

Page 7, line 7: “study on the abnormal development” to “study the abnormal development”

Page 7, line 8: “the discussion” to “the following discussion”

Page 7, line 25: “the formation of DV is” to “the formation of DV axis is”

Page 8, line 16: “with respects to” to “with respect to”

Page 8, line 21: :”(blastocoels)” to “(blastocoel)”

Page 8, line 24: “process which some epithelial cells” to “process by which some epithelial cells”

Page 10, line 13: “mesenchyme” to “mesoderm”

Page 10, line 26: “a node explants from a late-streak embryo has” to “node explants from late-streak embryos have”

Page 10, line 27: “the expression of neural marker” to “the expression of the neural marker”

Page 11, line 14: “The following few section” to “The following section”

Page 13, line 10: “binds to Ephrin” to “binds to Eph”

Page 14, line 3: “NC cells migration” to “NC cell migration”

Page 15, line 21: “as well as constitutive” to “as well as constitutively active”

Page 15, line 25: “dysplasic” to “dysplastic”

Page 16, line 4: “part of” to “part of the”

Page 16, line 7: “with onset of” to “with the onset of”

Page 16, line 18: “domain of dorsal” to “domain of the dorsal”

Page 17, line 2: “may involve in” to “may be involved in”

Page 18, line 1: “CNS needs to be” to “the CNS needs to be”

Page 18, line 5: “referred as” to “referred to as”

Page 18, line 6: “controversial that whether” to “controversial whether”

Page 18, line 9: “is not incorporated in” to “is not incorporated into”

Page 18, line 23: “with diminished AP spanning as progressing dorsally” to “with diminishing AP spanning towards the dorsal domain”

Page 18, line 30: “In cooperation of” to “In cooperation with”

Page 18, line 31: “within diencephalon” to “within the diencephalon”

Page 19, line 3: “Division along AP” to “Division along the AP”

Page 19, line 4: “composing” to “comprised”

Page 20, line 20: “present at” to “present in”

Page 21, line 1” “inner cell mast” to “inner cell mass”

Page 22, line 8: “a role of” to “a role for”

Page 24, line 7: “portion” to “proportion”

Page 24, line 29: “pharyngeal arches” to “pharyngeal arch”

Page 25, line 5: “(Minoux and Rijli)” to “(Minoux and Rijli, 2010)”

Page 25, line 20: “Together, these” to “Together, these studies”

Page 26, line 1: “describes” to “describe”

Page 26, line 2: “the discussion *Sox3*” to “the discussion of *Sox3*”

Page 26, line 21: “there lack any” to “there is lack of any”

Page 26, line 30: “transcription regulation” to “the transcriptional regulation”

Page 27, line 2: “this study” to “the study in Zhang et al. (2004)”

Page 27, line 4: “secrets” to “secretes”

Page 27, line 16: “throughout CNS” to “throughout the CNS”

Page 27, line 23-24: “when both ectopically expressed, *xSox3* counteracted *POU class V protein oct-91 (xOct91)* neuralising” to “when both *xSox3* and *POU class V protein oct-91 (xOct91)* are ectopically expressed, *xSox3* counteracted *xOct91* neuralising”

Page 27, line 26: “function” to “functions”

Page 29, line 13: “A requirement of” to “A requirement for”

Page 29, line 17: “resulting in the loss” to “resulted in the loss”

Page 30, line 22: “xenopus” to “*Xenopus*”

Page 31, line 20: “a effect” to “an effect”

Page 31, line 24: “heavily implicated the” to “heavily implicated in the”

Page 32, line 29: “also promote gliogenesis” to “also promoting gliogenesis”

Page 33, line 15: “capable to induce” to “capable of inducing”

Page 33, line 19: “identity” to “identify”

Page 34, line 2: “150kp” to “150kb”

Page 34, line 12: “capable to driving” to “capable of driving”

Page 34, line 28: “further strengthen by” to “further strengthened by”

Page 35, line 17: “NC cells migration defect towards the” to “NC cell migration defect towards”

Page 36, line 1: “activate” to “activates”

Page 37, line 10: “neural during” to “neural identity during”

Page 40, line 6: “functional compromisation” to “functional compromise”

Page 40, title 1: “1.5.3 The subcommisural organ” to “1.5.3 The subcommissural organ”

Page 40, line 10: “differentiated from” to “differentiate from”

Page 40, line 12: “fenestrated wall” to “fenestrated walls”

Page 40, line 17: “aspect of SCO” to “aspect of the SCO”

Page 41, line 10: “SCO is” to “the SCO is”

Page 42, line 8: “SCO primordium” to “the SCO primordium”

Page 43, line 5: “poses” to “pose”

Page 43, line 9: “neuroepithelium” to “neuroepithelial”

Page 44, line 19: “possess a thrombospondin type I repeats and a low density lipoprotein receptor” to “posses thrombospondin type I repeats and low density lipoprotein receptor”

Page 44, line 20: “extracellular matrix” to “extracellular matrix proteins”

Page 44, line 28: “function SCO” to “functional SCO”

Page 45, line 7: “islet of cuboidal cells was no present although remanent of SCO ependymal cells” to “islets of cuboidal cells was no longer present although a remanent of SCO ependymal cells”

Page 45, line 24: “author” to “authors”

Page 45, line 28: “as evident” to “as evidenced”

Page 46, line 4: “damages” to “damage”

Page 46, line 17-18: “individuals contracting mumps encephalitis led to damages to the CNS ventricular ependymal lining and hence causing non-communicating hydrocephalus” to “contraction of mumps encephalitis can cause damage to the ventricular ependymal lining, which may lead to the development of non-communicating hydrocephalus within affected individuals”

Page 46, line 22: “evidence from” to “evidence from a”

Page 46, line 26: “characteristic to” to “characteristic of”

Page 46, line 27: “the presence of dome-shaped cranium” to “the presence of a dome-shaped cranium”

Page 46, line 29: “SCO defect” to “SCO defects”

Page 47, line 12: “suffered” to “suffering”

Page 47, line 25: “which is the followed” to “which is followed”

Page 48, line 8: “the SCO development” to “SCO development”

Page 48, line 10: “Recent study” to “A recent study”

Page 48, line 15: “In addition of” to “In addition to”

Page 50, line 13: “junction” to “junctions”

Page 51, line 21: “epithelial” to “epithelia”

Page 51, line 30: “the *Spag6*” to “*Spag6*”

Page 52, line 15: “precedes the ependymal” to “precedes ependymal”

Page 52, line 16: “by the defective ependymal” to “by defective ependymal”

Page 52, line 20: “associated to” to “associated with”

Page 53, line 6: “signalling event” to “signalling events”

Page 53, line 18: “regulation the” to “regulation of the”

Page 53, line 27: “indicating the *Msx1* is only indispensable for the development of RP” to “indicating that *Msx1* is only indispensable for development of the RP”

Page 53, line 29: “null mutant” to “null mutants”

Page 54, line 30: “known function to” to “known function for”

Page 56, line 16: “6-8 of” to “6-8 weeks of”

## **Chapter 2: Materials and methods**

Page 62, line 13: “50mg/kg” to “50 mg/kg”

Page 62, line 13: “10mg/ml” to “10 mg/ml”

## **Chapter 3: Characterisation of CH in *Sox3* transgenic mouse model**

Page 74, line 9: “the possibility a defective” to “the possibility of a defective”

Page 75, line 24: “no evident” to “no evidence”

Page 77, line 18: “accounted for this” to “accounted for in this”

Page 77, line 22: “*Sr* and *Nr Sox3* transgene” to “*Sr* and *Nr Sox3* transgenes”

Page 78, line 18: “Haemorrhage” to “Haemorrhage”

Page 79, line 20: “recapitulated this” to “recapitulated *Sox3* endogenous”

Page 80, line 2: “SCO primordium” to “The SCO primordium”

Page 83, line 16: “assoiction” to “association”

Page 84, title 1: “in other area of dorsal” to “in other areas of the dorsal”

Page 85, line 27: “inhibitor or” to “inhibitor of”

Page 85, line 30: “study the” to “study of the”

Page 86, line 8: “*Sox3* transgene has” to “the *Sox3* transgene has”

Page 86, line 10: “integration induced” to “integration-induced”

Page 86, line 20: “inhibits conformational change” to “inhibits the conformational change”

Page 86, line 22: “The lack of poly-A tail” to “The lack of a poly-A tail”

Page 87, line 20: “brought by” to “brought about by”

Page 88, line 14: “telencephalic transgenic expression” to “telencephalic transgene expression”

Page 88, line 26-29: “both the *Sr/+* and *Nr/+* embryos lack telencephalic *Sox3* transgene expression at 10.5 to 12.5 dpc (N. Rogers, unpublished data) arguing against the case of a positional effect despite this explanation is still reserved.” to “both *Sr/+* and *Nr/+* embryos lack telencephalic *Sox3* transgene expression from 10.5 to 12.5 dpc (N. Rogers, unpublished data), which argues against positional effect as an explanation for this observation.”

Page 89, line 17-18: “there cannot rule out the possibility of a positional effect whereby integration site residing transcription enhancing element might act on the transgene and upregulate its expression.” to “it is possible that local transcription enhancing element at the integration site might act on the transgene and upregulate its expression.”

Page 90, line 5: “with identical” to “with an identical”

Page 90, line 28: “spatial domain, and the” to “spatial domain and the”

Page 91, line 17: “these indicate” to “these observations indicate”

Page 93, line 5: “To further this” to “To further investigate this”

Page 93, line 6: “proliferation study” to “a proliferation study”

Page 93, line 6: “demonstrated that adult rat SCO” to “demonstrated that the adult rat SCO”

Page 93, line 7: “the SCO is one of all” to “the SCO is the only”

Page 93, line 7: “express” to “expresses”

Page 93, line 11: “When transplanted *in vivo*” to “When transplanted in mouse *in vivo*”

## **Chapter 4: Analysis of SOC development in *Sox3* transgenic mice**

Page 95, line 13: “As shown in prevous chapter” to “As shown in the previous chapter”

Page 95, line 18: “ependymals” to “ependymal”

Page 95, line 25: “ventriculear” to “ventricular”

Page 95, line 30: “basal localisation” to “basal nuclear localisation”

Page 96, line 14: “invaginated SCO” to “the invaginated SCO”

Page 96, title 2: “SCO dyspalsia” to “SCO dysplasia”

Page 93, title 1: “functioally” to “functionally”

Page 98, line 13: “dysplasic” to “dysplastic”

Page 98, line 16: “by which the SCO” to “by which time the SCO”

Page 98, line 20: “indicate” to “indicates”

Page 98, line 28: “exercebated” to “exacerbated”

Page 99, line 8: “Habenuclar” to “Habenular”

Page 100, line 17: “using on alternative technique” to “using alternative techniques”

Page 102, line 8: “previous study” to “a previous study”

Page 102, line 18: “proliferative” to “the proliferative”

Page 102, line 19: “The VZ” to “the VZ”

Page 103, line 25: “but also in the” to “but is also found in the”

Page 104, line 4: “intense and was patchy” to “intense and patchy”

Page 104, line 6: “at its neighbouring section” to “in a neighbouring section”

Page 104, line 15: “dysplasic” to “dysplastic”

Page 106, line 12-13: “was present at the LV ChP was detected from WT” to “was present in the LV ChP of WT”

Page 106, line 16: “EGFP indicative” to “EGFP, indicative”

Page 107, line 22: “apparent in those of the diencephalon.” to “apparent in the VZ of diencephalon”

Page 108, line 18: “causative role of defective ChP” to “causative role for defective ChP”

Page 109, line 10: “transformed” to “transform”

Page 109, line 24: “accompanied the” to “accompanied by the”

Page 109, line 25: “neuroepithelial cell” to “neuroepithelial cells”

Page 109, title 1: “sepcific” to “specific”

Page 110, line 8: “projected” to “projecting”

Page 111, line 13: “mediodorsally” to “mediodorsal”

Page 111, line 16: “embryos are in contrast” to “embryos is in contrast”

Page 112, line 1: “dysplasic” to “dysplastic”

Page 112, line 29: “transgene” to “transgenes”

Page 113, line 5: “levels *Sox3*” to “levels of *Sox3*”

Page 113, line 7: “response” to “respond”

Page 113, line 9: “In addition to the diencephalon” to “In addition to the diencephalic RP,”

Page 113, line 11: “Fasciculation of corpus callosum” to “Fasciculation of the corpus callosum”

Page 113, line 13: “corpus callosum” to “a corpus callosum”

Page 113, line 23: “in the RP development” to “in RP development”

Page 114, line 31: “at 12.5 dpc” to “in the 12.5 dpc”

Page 115, line 18: “fails RP development” to “fails to develop RP”

Page 115, line 23: “a *Sox3* dosage” to “*Sox3* dosage”

Page 115, line 30: “to be an indirect” to “to be indirect”

## **Chapter 5: Molecular function of *Sox3* in SCO development**

Page 118, line 4: “atlas” to “analysis”

Page 120, line 4: “statistically” to “statistical”

Page 120, line 16: “(assumed most gene expressions did not change between samples)” to “(assuming most gene expressions did not change between samples)”

Page 120, line 22: “but the other” to “but absent from the other”

Page 121, line 15: “analysed” to “analysis”

Page 121, line 22: “the direction for future investigation” to “the direction of future investigation”

Page 125, line 12: “might due” to “might be due”

Page 126, line 20-21: “In contrast, *Sr/+; Nr/+* SCO *Dab2* expression had a 1.25-fold decrease from the two microarray samples. This did not correlate with the microarray, which indicated a 3-fold decrease in expression.” to “On the other hand, the microarray experiment detected a 3-fold decrease of *Dab2* expression in *Sr/+; Nr/+* SCO . However, qRT-PCR analysis using identical SCO samples as the microarray indicated that *Dab2* expression has only downregulated for 1.25-fold.”

Page 129, line 10: “accuratly” to “accurately”

Page 129, title 1: “5.4.1” to “5.4.2”

Page 129, line 27: “SMAD complex” to “the SMAD complex”

Page 131, line 10: “*in vitro* study” to “an *in vitro* study”

Page 133, title 1: “5.4.2” to “5.4.3”

Page 134, line 1: “expressed at” to “expressed in”

Page 134, line 3: “these prompt” to “these observations prompt”

Page 134, line 16: “encode a protein that is” to “encode proteins that are”

Page 134, title 1: “5.4.3” to “5.4.4”

Page 135, title 1: “5.4.4” to “5.4.5”

Page 135, line 20: “to implicate in” to “to be implicated in”

Page 136, line 7: “similar to” to “similar function to”

Page 136, line 11: “Perkinje” to “Purkinje”

Page 136, line 12: “GABAnergic” to “GABAergic”

Page 138, title 1: “5.4.5” to “5.4.6”

Page 139, line 3: “rhombencephalon an anteriorly” to “rhombencephalon anteriorly”

Page 139, line 12: “by an prior defect” to “by a prior defect”

## **Chapter 6: Discussion**

Page 141, line 9: “mild defect was” to “mild defects were”

Page 142, line 1: “within the dorsal neural developing RP” to “within the developing dorsal neural RP”

Page 142, line 5: “unlikely due to” to “unlikely to be due to”

Page 142, line 12: “These suggest” to “These observations suggest”

Page 142, line 13: “functional redundant with *Sox2* such that the function of *Sox3* is substituted by *Sox2* in *Sox3* null embryos” to “functionally redundant with *Sox2*”

Page 143, line 20: “these indicate” to “these data indicate”

Page 143, line 23: “SOX3 expression difference were found” to “SOX3 expression were found”

Page 143, line 25: “intensity that those” to “intensity than those”

Page 144, line 1: “progneitor” to “progenitor”

Page 144, line 4: “stem cells” to “stem cell”

Page 144, line 25: “upregulate” to “upregulates”

Page 145, line 7: “in consistent” to “consistent”

Page 145, line 12: “effect” to “effects”

Page 145, line 14: “is due its dynamic function in different” to “is due to its dynamic function in different”

Page 145, line 15: “context” to “contexts”

Page 145, line 18: “*Sox3* direct targets” to “direct *Sox3* targets”

Page 146, line 4: “Since the RP is an organising centre” to “The RP is an organising centre”

Page 146, line 16: “recently study” to “a recent study”

Page 146, line 18: “the transcription activity of *Hes1*, which *Hes1* then acts” to “the transcription activity of *Hes1*. In return, *Hes1* then acts”

Page 146, line 30: “repressing” to “repression”

Page 148, line 25: “leaving the dorsal NT with cells making up the definitive RP” to “and only cells that give rise to the definitive RP are left at the dorsal NT”

Page 149, line 15: “understanding this defect” to “understanding of this defect”

Page 149, line 16: “Cranial NC cells” to “Cranial NC cell”

Page 149, line 17: “begin migrate” to “begin to migrate”

Page 149, line 23: “were observed” to “was observed”

Page 151, line 1: “due the functional redundancy” to “due to the functional redundancy”

Page 152, line 10: “lethally” to “lethality”

Page 152, line 24: “immuneprecipitation” to “immunoprecipitation”

## **Figures**

Figure 1.18, legend, line 3: “trasngenic” to “transgenic”

Figure 1.6, legend, line 1: “within an developing” to “within a developing”

Figure 3.5 A, the note at the bottom of the figure, line 1: “frequecny” to “frequency”

Figure 3.14, the figure at the top right corner is labelled as (K)

Figure 4.1, legend, line 7: “ependymals” to “ependymal”

Figure 4.15, legend, line 1: “at a varing low level” to “at varying low levels”

Figure 4.16, bottom of the figure: “12.5 dpc” to “15.5 dpc”

<b>CHAPTER 1: INTRODUCTION.....</b>	<b>1</b>
1.1 The central nervous system .....	1
1.2 <i>SOX3</i> – a member of the <i>SOX</i> transcription factor family .....	3
1.2.1 <i>Sox3</i> belongs to <i>SOXB1</i> subgroup .....	3
1.2.2 <i>SOX</i> transcription factor interact with partnering proteins to achieve specificity in transcription regulation.....	4
1.3 An overview of CNS development .....	7
1.3.1 Axes formation and patterning of the developing CNS domains.....	7
1.3.2 Neural induction .....	8
The development of early embryos.....	8
Anterior organisers protect the default neural fate of the epiblast.....	9
<i>AVE</i> and its role in early neural development.....	9
<i>GO</i> and its derivative (the node) are critical for neural development.....	10
Summary .....	11
1.3.2 Neurulation and dorsal midline maintenance .....	11
NT closure.....	11
Dorsal NT development and NC migration .....	13
Summary .....	14
1.3.3 RP formation and its role in dorsal CNS development .....	14
The molecular regulatory network of RP development.....	15
<i>Bmp</i> and <i>Wnt</i> signalling are required for both NC cells and definitive RP development .....	16
Other genes that lead to RP dysgenesis within the diencephalon.....	17
Summary .....	17
1.3.4 Patterning of forebrain – diencephalon .....	17
1.4 <i>SOX3</i> in the developing CNS .....	20

1.4.1	<i>SOXB1</i> expression during neural development .....	20
	<i>SOXB1</i> expression during anterior neural development in mouse.....	20
	<i>SOX3</i> expression during anterior neural development in other vertebrates .....	21
	Summary .....	22
1.4.2	<i>SOX3</i> and human disease – X-linked hypopituitarism .....	22
1.4.3	<i>Sox3</i> null mouse model.....	24
1.4.4	<i>SOX3</i> has an important role in early and neural development .....	25
	<i>SOX3</i> in early embryonic development .....	26
	<i>SOX3</i> in neural plate determination .....	27
	<i>SOX3</i> and neurogenesis in CNS.....	28
	Other <i>SoxB1</i> members have also been implicated in early embryonic and neural development in CNS .....	29
	Genetic interactions of <i>SOX3</i> in neural development .....	31
	Summary .....	32
1.4.6	<i>SOX3</i> in sex determination .....	33
1.4.7	Regulation of <i>SOX3</i> expression.....	33
1.4.8	Functional redundancy between <i>SoxB1</i> subgroup members.....	35
1.5	Cerebrospinal fluid, hydrocephalus and the subcommissural organ.....	38
1.5.1	CSF production and circulation.....	38
1.5.2	CNS barriers and CSF homeostasis.....	39
1.5.3	The Subcommissural organ .....	40
1.5.4	Origin and development of mouse SCO.....	41
1.5.5	SCO and its role in RF production .....	43
1.5.6	Human SCO.....	44
1.5.7	Hydrocephalus – Congenital hydrocephalus .....	45
	Relationship between SCO and CH.....	46
1.5.8	CH in human – <i>LICAM</i> .....	47

1.5.9	Genetic and molecular etiology of CH in mouse models.....	48
	Cell adhesion defects .....	49
	Cilia structure/function defects .....	50
	Signal transduction defects .....	52
	Developmental defects.....	53
	Proposed model for the developmental regulation of prosomere 1 RF and SCO.....	55
	Summary .....	55
1.6	Thesis aims and approaches .....	56
1.6.1	Aim: To understand the molecular mechanism of <i>Sox3</i> overdosage that underlies the physiological pathogenesis of CH. ....	56
1.6.2	Approach 1: Identification and characterisation of the morphological and cellular defect within the CNS that is responsible for CH related phenotype.....	57
1.6.3	Approach 2: Understanding the molecular role of <i>Sox3</i> in SCO development through identification of its downstream effectors.....	57
<b>CHAPTER 2: MATERIALS AND METHODS .....</b>		<b>58</b>
2.1	General Solution(s).....	58
2.2	Animal husbandry .....	58
2.3	Mouse embryos generation and tissue collection.....	58
2.4	Genotyping of animals .....	59
2.4.1	<i>Sox3</i> transgene genotyping .....	59
2.4.2	<i>Sr</i> transgene specific genotyping.....	59
2.4.3	<i>Nr</i> transgene specific genotyping.....	60
2.5	Genome walking.....	60
2.6	H & E stains.....	61
2.7	Nissl stains.....	61
2.8	qPCR for <i>Sox3</i> transgene copy number analysis.....	61

2.6	Immunofluorescence .....	62
2.7	BrdU analysis .....	62
2.8	TUNEL assay .....	63
2.9	<i>In Situ</i> Hybridisation.....	63
2.9.1	Template plasmid production .....	63
2.9.1	Riboprobe synthesis.....	64
2.9.2	Section <i>in situ</i> hybridisation .....	64
2.9.3	Whole mount <i>in situ</i> hybridisation .....	64
2.10	SCO microdissection and RNA extraction.....	64
2.11	Microarray data processing .....	65
2.12	qRT-PCR analysis for microarray validation.....	65
2.13	Image analysis .....	66
2.14	Primers table .....	67
2.15	Plasmids table .....	73

## **CHAPTER 3: CHARACTERISATION OF CH IN *SOX3* TRANSGENIC**

### **MOUSE MODEL.....74**

3.1	Introduction .....	74
3.2	Results .....	75
3.2.1	<i>Sox3</i> transgene integration site in <i>Nr</i> mouse model .....	75
3.2.2	The <i>Sox3</i> transgene is not expressed in the developing dorsal telencephalon of <i>Nr/+</i> embryos .....	76
3.2.3	CH is dosage dependent on <i>Sox3</i> .....	77
3.2.4	CNS morphology of <i>Nr/+</i> and <i>Sr/+</i> mice suggested non-communicating hydrocephalus.....	78
3.2.5	Endogenous and transgenic <i>Sox3</i> expression in the SCO .....	78

3.2.6	Lower level of SOX3 expression in prosomere 1 RP.....	81
3.2.7	Dysmorphic SCO in post-weaning <i>Nr/+</i> and <i>Sr/+</i> mice .....	82
3.2.8	Endogenous and transgenic <i>Sox3</i> expressions in other area of dorsal diencephalon .....	84
	Endogenous and transgenic <i>Sox3</i> expression in 12.5 dpc dorsal diencephalon.....	84
	Endogenous and transgenic <i>Sox3</i> expression at 15.5 dpc dorsal diencephalon .....	85
3.3	Discussion.....	86
3.3.1	<i>Sox3</i> transgene integration site in <i>Nr</i> mouse line .....	86
3.3.2	Transgene incorporated <i>Sox3</i> regulatory sequences were insufficient for complete recapitulation of endogenous telencephalic expression.....	87
3.3.3	Transgenic <i>Sox3</i> expression in the diencephalon .....	89
3.3.4	<i>Sox3</i> has a role in SCO development .....	90
3.3.5	<i>Sox3</i> overexpression leads to defective SCO development and CH .....	91
3.3.6	Proper <i>Sox3</i> dosage regulation is important during SCO development .....	91
3.3.7	The role of endogenous SOX3 in mature SCO .....	92

## **CHAPTER4: ANALYSIS OF SCO DEVELOPMENT IN SOX3**

	<b>TRANSGENIC MICE.....</b>	<b>94</b>
4.1	Introduction .....	94
4.2	Results .....	94
4.2.1	LV expansion and SCO aplasia in 18.5 dpc <i>Sr/+; Nr/+</i> embryos.....	95
4.2.2	Normal morphology of the SCO at 12.5 dpc <i>Sr/+; Nr/+</i> embryos .....	96
4.2.3	SCO dyspalsia from 13.5 dpc in <i>Sr/+; Nr/+</i> embryos .....	96
4.2.4	Morphologically and functionally defective SCO from 15.5 dpc <i>Sr/+; Nr</i> embryos .....	97
4.2.5	Developmental defects in the diencephalon of <i>Sr/+; Nr/+</i> embryos are restricted to the RP .....	99
4.2.6	Absence of apoptosis in SCO from WT and <i>Sr/+; Nr/+</i> embryos.....	99

4.2.7	Overproliferation of the SCO primordium of 12.5 dpc <i>Sr/+; Nr/+</i> embryos ....	101
4.2.8	Loss of SCO progenitors from 12.5 dpc in <i>Sr/+; Nr/+</i> embryos .....	103
4.2.9	Downregulation of diencephalic midline markers in 12.5 dpc <i>Sr/+; Nr/+</i> embryos .....	104
4.2.10	Characterisation of ChP in <i>Sox3</i> transgenic mice.....	105
4.3	Discussion.....	107
4.3.1	Defective SCO development is the primary cause of CH .....	107
4.3.3	SCO dysplasia was a consequence of loss of SCO cellular identity .....	108
4.3.2	Morphological defect was not restricted to SCO but was RP sepcific.....	109
	Loss of PC.....	110
	HbC failed to cross midline .....	111
	Absence of PG development.....	111
	General RP defect .....	112
4.3.4	<i>Sox3</i> regulates <i>Msx1</i> and <i>Wnt1</i> for RP development.....	113

## **CHAPTER 5: MOLECULAR FUNCTION OF SOX3 IN SCO**

	<b>DEVELOPMENT .....</b>	<b>117</b>
5.1	Introduction .....	117
5.2	The design of microarray experiment .....	117
5.3	Results .....	119
5.3.1	Microarray data processing and quality control .....	119
5.3.2	Microarray statistical analysis .....	120
5.3.3	Candidate genes selection.....	121
5.3.4	Validation of transcriptional profiles in microarray through qRT-PCR.....	124
	Category 1: genes with high fold-change .....	125
	Category 2: Genes implicated in Wnt and Bmp6 signalling pathways .....	125
	Category 3: Genes with SCO specific expression .....	126

5.3.5	The expression domains of pretectal markers are expanded .....	127
5.3.6	Low penetrance of exencephaly observed in <i>Sr/+</i> and <i>Sr/+; Nr/+</i> embryos .....	128
5.4	Discussion.....	128
5.4.1	Some candidate genes displayed variable fold-changes between the microarray and qRT-PCR experiments .....	128
5.4.1	Bmp and Wnt RP expression was diminished transgenic embryos.....	129
	Bmp ligands .....	131
	Wnt ligands .....	131
5.4.2	<i>Fmo1</i> , <i>Adamts3</i> , <i>Hmgcs2</i> – a possible function in the synthesis of SCO secretions .....	133
5.4.3	<i>Fibcd1</i> – a possible endocytic activity in SCO development.....	134
5.4.4	Disrupted dorsal diencephalic patterning due to defective RP development .....	135
5.4.5	Failure of cranial NT fusion might be associated with disrupted dorsal NT tube patterning.....	138

**CHAPTER 6: DISCUSSION .....141**

6.1	The knowledge of <i>Sox3</i> function in mammalian CNS development was limited.....	141
6.2	Diencephalic RP development was sensitive to overdosage but not underdosage of <i>Sox3</i> .....	142
6.3	<i>Sox3</i> dosage regulation is important for proper RP specification .....	142
6.4	<i>Sox3</i> activity was repressed to upregulate Bmp and Wnt expression in RP development.....	144
6.5	<i>Hes1</i> – a direct target of <i>Sox3</i> in RP development? .....	145
6.6	The role of <i>Sox3</i> in RP neural differentiation .....	147
6.7	<i>Sox3</i> in earlier dorsal NT development .....	148
6.7.1	Dorsal NT induction .....	148

6.7.2	NT closure .....	149
6.7.3	Cranial NC development .....	149
6.8	Similarities and differences in overdosage of <i>Sox3</i> between mice and human .....	150
6.9	Normal SCO development and CSF homeostasis in human.....	151
6.10	Future directions .....	152
6.11	Concluding remarks.....	153
<b>APPENDIX I: THE SEQUENCES OF <i>BTBD11</i> LAST EXON.....</b>		<b>155</b>
<b>APPENDIX II: THE SEQUENCES OF THE <i>SOX3</i> TRANSGENE INTEGRATION SITE IN <i>NR</i> MOUSE MODEL .....</b>		<b>156</b>
<b>APPENDIX III: <i>SOX3</i> ANTIBODY SPECIFICITY .....</b>		<b>167</b>
<b>APPENDIX IV: AN OUTLINE OF THE MICROARRAY EXPERIEMNT .....</b>		<b>168</b>
<b>APPENDIX V: THE PAIRWISE MA PLOTS GENERATED FROM PARTEK® ANALYSIS .....</b>		<b>169</b>
<b>APPENDIX VI: MICROARRAY CEL FILES AND GENE LISTS.....</b>		<b>170</b>
<b>APPENDIX VII: MICROARRAY – A TABLE OF GENES WITH A FOLD-CHANGE IN MODULUS OF 2 OR ABOVE .....</b>		<b>171</b>
<b>APPENDIX VIII: PLASMID MAPS .....</b>		<b>176</b>
<b>REFERENCES.....</b>		<b>I</b>

# Summary

The central nervous system (CNS) is one of the most complicated organs in the body. Its development requires spatially and temporally dynamic but yet coordinated proliferation and differentiation of neural progenitors in order to allow the formation of the neural tube (NT) from a sheet-like neural plate, as well as the specification of different CNS domains from a homogeneous group of neural precursors. A number of genes have been identified to be important for the robust genetic and molecular regulation of the CNS development. One of these genes is *SOX3*, which encodes a *SOX* family transcription factor within a single exon. In humans, *SOX3* duplications and mutations have been implicated in X-linked hypopituitarism (XH) with variable mental retardation, suggesting that CNS development is sensitive to *SOX3* dosage. To recapitulate the condition in XH patients with *SOX3* duplications, a transgenic *Sox3* overexpression mouse model was generated in the Thomas laboratory. Two *Sox3* transgenic lines were established. Intriguingly, they presented not with XH associated phenotypes, but with hallmarks of hydrocephalus.

This thesis focuses on the characterisation of the hydrocephalus phenotype and the elucidation of the molecular pathogenesis that underlines the defect. Comprehensive morphological and expression analyses of single hemizygous and double hemizygous (mice with two transgene alleles, one from each *Sox3* transgenic line) *Sox3* transgenic mice demonstrated that the hydrocephalus has a congenital origin (congenital hydrocephalus, CH) and is associated with defective development of the subcommissural organ (SCO), a diencephalic roof plate (RP) derivative that has previously been implicated in CH. Moreover, both the CH and the SCO dysmorphology of *Sox3* transgenic mice are dependent on *Sox3* dosage. In addition to the SCO, defective development was also identified in other diencephalic RP derivatives in *Sox3* double hemizygous embryos. In fact, SCO maldevelopment appears to be the consequence of a general RP defect, in which the identity of the RP cells (or SCO precursors) is lost and is coupled with an elevation of cellular proliferation. Further molecular analysis of the SCO development supported that *Sox3* overexpression leads to the loss of RP cellular identity as the expression of genes implicated in both Bmp and Wnt signalling pathways, which are important for normal RP development, were significantly downregulated in *Sox3* transgenic embryos. In addition to its role as the precursor of RP derivatives, the RP is also essential to maintain dorsal identity for proper DV

patterning within the NT. Moreover, dorsal NT patterning was disrupted within the developing *Sox3* transgenic embryos. Together these suggest that the *Sox3* overdosage leads to the loss of RP identity and the failure of RP dependent processes.

In summary, this thesis indicates that, at least in the mouse, *Sox3* dosage regulation is important for proper RP development. In fact, a low level of *Sox3* is permissive for RP specification. It is not known what cellular identity is taken up by the RP cells in the *Sox3* double hemizygous embryos. However, given endogenous *Sox3* is highly expressed in the lateral tissue that flanks the RP, it is logical to propose that the RP cells of *Sox3* double hemizygous embryos may take on a cellular identity similar to their laterally neighbouring tissue. Interestingly, a CNS defect that may be due to RP dysfunction has been identified in some XH patients with *SOX3* duplications, suggesting that *SOX3* may have similar role in humans. CH is a heterogeneous disorder in which identification of its genetic basis in humans is difficult. This thesis proposes *SOX3* as a candidate gene for CH and other RP associated defects in humans, which may assist the development of relevant prognostic techniques for clinical application.

# Statement

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Signed: .....(Kristie Pan Yu Lee)

Date: .....

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# Abbreviations Abbreviations

## Standard terms

%	percentage
°C	degree Celsius
cDNA	complementary deoxyribonucleic acid
DNA	deoxyribonucleic acid
g	gravitational force
kb	kilobase
kDa	kilodalton
kg	kilogram
RNA	ribonucleic acid
M	molar
mg	milligram
ml	millilitre
μl	microlitre
mm	millimetre
μm	micrometer (micron)
mM	millimolar
μM	micromolar
ms	millisecond

ng	nanogram
N	normality
w/v	weight per volume
v/v	volume per volume

### **Non-standard terms**

a.a.	amino acid
AH	acquired hydrocephalus
BAC	bacterial artificial chromosome
bp	base pair
CH	congenital hydrocephalus
dpc	days post coitum
ES	embryonic stem
HCNE(s)	highly conserved non-coding element(s)
IRES	internal ribosome entry site
NC	neural crest
ORF	open reading frame
P	postnatal
RF	Reissner's fibre
RIN	RNA integrity number
SCBE	SOX core binding sequence
UTR	untranslated region

WT	wildtype
XH	X-linked hypopituitarism

### **Mouse lines**

<i>Nr</i>	<i>Sox3 non-sex reversal line</i>
<i>Sr</i>	<i>Sox3 sex reversal line</i>

### **Materials and methods**

BrdU	bromodeoxyuridine
DIG	dioxigenin
EtOH	ethanol
gDNA	genomic DNA
H & E	haematoxylin and eosin staining
IgG	immunoglobulin G
MeOH	methanol
MQ	milliQ
NaAc	sodium acetate
OCT	optimal cutting temperature
O/N	overnight
PBS	phosphate buffered saline
PCR	polymerase chain reaction
PFA	paraformaldehyde

qPCR	quantitative polymerase chain reaction
qRT-PCR	quantitative real-time polymerase chain reaction
RT	room temperature
TUNEL	terminal deoxynucleotidyl transferase dUTP nick end labelling
U	unit

### **Statistical and bioinformatics terms**

ANOVA	analysis of variance
BLAST	Basic Local Alignment Search Tool
FDR	false discovery rate
Limma	linear models for microarray analysis
MGI	Mouse Genome Database
NCBI37	<i>mus musculus</i> genome assembly NCBI37

### **Anatomical terms**

3V	third ventricle
4V	fourth ventricle
AP	anterior-posterior
Aq	Sylvian aqueduct
AVE	anterior visceral endoderm
BBB	blood-brain barrier
BCSFB	blood-CSF barrier

CCx	cerebral cortex
Cer	cerebellum
ChP	choroid plexus
CNS	central nervous system
CSF	cerebrospinal fluid
CSFBB	CSF-brain barrier
CVO	circumventricular organs
DLHP	dorsolateral hinge point
DTh	dorsal thalamus
DV	dorsoventral
EpTh	epithalamus
FP	floor plate
GO	gastrula organiser
HbC	habenular commissure
Hpc	hippocampus
LGE	lateral ganglionic eminence
LV	lateral ventricles
MGE	medial ganglionic eminence
MHP	medial hinge point
MR	mesocoelic recess
MZ	mantel zone

NT	neural tube
PC	posterior commissure
PG	pineal gland
PR	pineal recess
PS	primitive streak
Pt	pretectum
RP	roof plate
SCO	subcommissural organ
TrG	trigeminal ganglia
VTh	ventral thalamus
VZ	ventricular zone
ZLI	zona limitans intrathalamica

### **Cell lines**

293T	human embryonic kidney 293 cells
HeLa	human cervical cancer cells
NTERA2	human embryo carcinoma cells

### **Protein families and protein domains**

<i>APC</i>	<i>adenomatous polyposis coli</i>
Bmp	bone morphogenic protein
Fgf	fibroblast growth factor

Gli	GLI-kruppel family member
GSK3	glycogen synthase kinase
HMG	high motility group
JAK	Janus family of tyrosine kinases
MAP	mitogen associated protein
mTOR	mammalian target of rapamycin
NICD	notch-intracellular domain
Shh	sonic hedgehog
SNARE	N-ethylmaleimide sensitive fusion attachment protein receptors
SOX	sry-related HMG box
STAT	signal transducers and activators of transcription
TA	transactivation
Tgf $\beta$	transforming growth factor beta
Wnt	wingless-related MMTV integration site

# Gene Nomenclature

## Human

**Gene:** italic, all capital, e.g. *SOX3*

**Protein:** non-italic, all capital, prefixed with 'h' indicative of human origin, e.g. hSOX3

## Mouse

**Gene:** italic, first letter capital, e.g. *Sox3*

**Protein:** non-italic, all capital, e.g. SOX3

## Other model organisms

**Gene:** italic, first letter capital, prefixed with a relevant letter indicative of animal origin, i.e. 'c' for chicken; 'z' for zebrafish; 'x' for *Xenopus*, e.g. *cSox3*, *zSox3*, *xSox3*

**Protein:** non-italic, first letter capital, prefixed with a relevant letter indicative of animal origin, i.e. 'c' for chicken; 'z' for zebrafish; 'x' for *Xenopus*, e.g. cSox3, zSox3, xSox3

**Note:** The nomenclature of the highest organism is used if describing a gene or protein from more than one model organisms.