SONIC HEDGEHOG SIGNALING IN BRAIN DEVELOPMENT AND DISEASES

By

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To my parents and wife

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The most beautiful scenes are not at the top of the mountain, they are every step that we took, every fall that we made, and every encouraging smile our loved ones gave us during the climbing. I want to thank them all.

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what is sympathy and what is love. She also takes whole care of our lives, thinking of every possible way to make a meal delicious, to make every day a happy one. I love her.

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LIST OF ABBREVIATIONS

Shh	Sonic hedgehog
FB	forebrain
MB	midbrain
HB	hindbrain
NPT	nasal pit
LGE	lateral ganglionic eminence
MGE	medial ganglionic eminence
ChP	choroid plexus
DSHB	developmental study hybridoma bank
hChP	hindbrain choroid plexus
hChPe	hindbrain choroid plexus epithelium
hChPm	hindbrain choroid plexus mesenchyme
HPE	holoprosencephaly
HP	hippocampus
ST	striatum
tCP	telencephalic choroid plexus
Hh	hedgehog
HC	hippocampus
FP	floor plate
MN	motor neuron
MIH	middle interhemispheric holoprosencephaly

psp	presphenoid bone
Ttr	transthyretin
N	notochord
NCX	neocortex
zli	zona limitans intrathalamica
CLP	cleft palate
CSF	cerebrospinal fluid
Ptch1	pacthed1
AQP1	aquaporin1
LRL	lower rhombic lip
Smo	Smoothened
RP	roof plate
V	vermis
H	hemisphere
M	molecular layer
P	Purkinje neuron
G	granule neuron layer
Tuj1	Class III neuronal Tubulin
LDL	low density lipoprotein
HSPG	heparan sulfate proteoglycans
Hip	Hedgehog-interacting protein

CELL AND DEVELOPMENTAL BIOLOGY

SONIC HEDGEHOG SIGNALING IN BRAIN DEVELOPMENT AND DISEASES

XI HUANG

Dissertation under the direction of Professor Chin Chiang

Sonic hedgehog (Shh) signaling regulates important biological processes during embryogenesis and adult homeostasis. Deregulation of this essential signaling pathway can lead to congenital defects and tumorigenesis. In this dissertation I explored the functional role of the cholesterol modification on Shh protein during central nervous system (CNS) patterning, determined previously unappreciated regulation of Shh pathway on hindbrain choroid plexus and cerebellum development, and established a novel mouse model for cerebellar tumor, medulloblastoma. These findings provide us new knowledge of how Shh signaling regulates various CNS organ development, as well as novel insights into the oncogenic processes in Shh-dependent brain tumor.

Approved by Professor Chin Chiang