(Revised 07/09)

RGC Ref.: N_HKBU213/11 NSFC Ref. : 81161160571
(please insert ref. above)

NSFC/RGC Joint Research Scheme
Joint Completion Report

(Please attach a copy of the completion report submitted to the NSFC by the Mainland researcher)

Part A: The Project and Investigator(s)

1. Project Title

Functional analysis of Corynoxine B in promoting autophagy and protecting neurons
（柯诺辛碱B促进细胞自噬和保护神经细胞的功能研究）

2. Investigator(s) and Academic Department/Units Involved

	Hong Kong Team	Mainland Team
Name of Principal Investigator *(with title)*	Prof. LI Min	Prof. MA Long
Post	Professor	Professor
Unit / Department / Institution	School of Chinese Medicine , Hong Kong Baptist University	State Key Lab. of Medical Genetics of China, Central South University
Co-investigator(s) *(with title)*	Dr. Chan Ho-Yin, Edwin Associate Professor, Biochemistry Department, Life Science Faculty, The Chinese University of Hong Kong.	

3. Project Duration

	Original	Revised	Date of RGC/ Institution Approval *(must be quoted)*
Project Start date	01/12/2011	01/01/2012	No approval required
Project Completion date	30/11/2014	31/12/2014	Tally with the scheme's rule
Duration *(in month)*	36	36	

Part B: The Completion Report

5. Project Objectives

5.1 Objectives as per original application

1. To understand the effects of IRY on autophagy and neuroprotection using animal models based on phenotypic analysis;
2. To examine the role of Beclin-1 complex in the IRY-induced autophagy;
3. To identify the molecular targets of IRY and novel genes mediating the effects of IRY.

5.2 Revised Objectives

Date of approval from the RGC: 27 Nov., 2012

Reasons for the change: Change the chemical name from "Isorhychophylline" to "Corynoxine B".
Revised title: Functional Analysis of **Corynoxine B** in Promoting Autophagy and Protecting Neurons

1. To understand the effects of **Corynoxine B** (Cory B) on autophagy and neuroprotection using animal models based on phenotypic analysis;
2. To examine the role of Beclin-1 complex in the Cory B-induced autophagy;
3. To identify the molecular targets of Cory B and novel genes mediating the effects of Cory B.

6. Research Outcome

Major findings and research outcome

(maximum 1 page; please make reference to Part C where necessary)

1. Neuroprotective effect of Cory B on transgenic and rotenone-intoxicated Drosophila models (Attachment 1, Unpublished data).
2. Effects of Cory B on transgenic C. elegans (Attachment_ NSFC final report).
3. Acute toxicity, autophagic actions, and neuroprotective effects of Cory B in mice and rats (Attachment 2, Unpublished data).
4. The role of HMGB1- Beclin-1 interaction in Cory B -induced autophagy and neuroprotection (Attachment 3_autophagy paper, Attachment 4_poster).
5. Corynoxine, the isomer of cory B, induces autophagy and promotes the degradation of alpha-synuclein in a mTOR-dependent manner (Attachment 5_ J Neuroimmune Pharmacol paper, Attachment 6_poster).
6. Phosphoproteomic analysis reveals the involvement of cyclin-dependent kinases in Corynoxine-induced autophagy (Attachment 7_poster)
7. HMGB1 as a direct molecular target of Cory B (Attachment 8, Unpublished data)

Potential for further development of the research and the proposed course of action

(maximum half a page)

In this project, we have systematically evaluated the autophagy-enhancing and neuroprotective effects of a natural compound corynoxine B from the Chinese herbal medicine Gouteng and found its direct molecular target. These important data will facilitate our next step drug development. We propose to perform structure-activity relationship analysis to optimize the autophagy-enhancing and neuroprotective effects using cory B as a lead compound and then collaborate with pharmaceutical companies to develop new drugs.

7. The Layman's Summary

(describe in layman's language the nature, significance and value of the research project, in no more than 200 words)

Autophagy is a highly conserved process for cellular degradation of cytosolic contents including protein aggregates. Targeting the autophagic pathway in the neuronal cells for the degradation of pathogenic protein aggregates has emerged as a novel therapeutic strategy for neurodegenerative diseases including Parkinson's disease. Previously we identified a natural compound named corynoxine B which can induce autophagy and protect neurons. In this project, we evaluated the in vivo effects of cory B on autophagy and neuroprotection and identified its molecular target. These preclinical data are important for further drug development of autophagy enhancers and neuroprotective agents for the treatment of neurodegenerative diseases.

Part C: Research Output

8. Peer-reviewed journal publication(s) arising directly from this research project

(Please attach a copy of each publication and/or the letter of acceptance if not yet submitted in the previous progress report(s). All listed publications must acknowledge RGC's funding support by quoting the specific grant reference.))

The Latest Status of Publications				Author(s)	Title and	Submitted	Attached	Acknowledged
Year of publication	Year of Acceptance *(For paper accepted but not yet published)*	Under Review	Under Preparation *(optional)*	***(bold** the authors belonging to the project teams and denote the corresponding author with an asterisk*)*	Journal/Book *(with the volume, pages and other necessary publishing details specified)*	to RGC *(indicate the year ending of the relevant progress report)*	to this report *(Yes or No)*	the support of this Joint Research Scheme *(Yes or No)*

2014	N/A	N/A	N/A	**Song JX, Lu JH, Liu LF, Chen LL, Durairajan SS**, Yue Z, Zhang HQ*, **Li M***.	HMGB1 is involved in autophagy inhibition caused by SNCA/α-synuclein overexpression : a process modulated by the natural autophagy inducer corynoxine B. **Autophagy**. 2014 Jan;10(1):144-54.	Yes	Yes	Yes
2014	N/A	N/A	N/A	**Chen LL, Song JX, Lu JH, Yuan ZW, Liu LF, Durairajan SS, Li M***.	Corynoxine, a natural autophagy enhancer, promotes the clearance of alpha-synuclein via Akt/mTOR pathway.	No	Yes	Yes

9. Recognized International conference(s) in which paper(s) related to this research project was/were delivered *(Please attach a copy of each delivered paper)*

Month/Year/ Place	Title	Conference Name	Submitted to RGC *(indicate the year ending of the relevant progress report)*	Attached to this report *(Yes or No)*	Acknowledged the support of this Joint Research Scheme *(Yes or No)*
Huangshan, China, 19-23 March, 2015	Phosphoproteomic analysis reveals the involvement of cyclin-dependent kinases in Corynoxine-induced autophagy	7th International Symposium on Autophagy (7th ISA)	No	Yes	Yes
Austin, Texas, USA, 23-28 May, 2014	Corynoxine, a Chinese herbal compound, induces autophagy via Akt/mTOR pathway and promotes the clearance of alpha-synuclein	Keystone Symposia on Autophagy: Fundamentals to Disease (E2)	No	Yes	Yes

Miami, USA, 26-29 Jan., 2014	Corynoxine B restores autophagy through inhibiting alpha-synuclein-HMGB1 interaction in cell models of Parkinson's disease	Miami 2014 Winter Symposium: the Molecular Basis of Brain Disorders	No	Yes	Yes

10. Student(s) trained *(Please attach a copy of the title page of the thesis.)*

Name	Degree registered for	Date of registration	Date of thesis submission/ graduation
N/A	N/A	N/A	N/A

11. Other impact *(e.g. award of patents or prizes, collaboration with other research institutions, technology transfer, etc.)*

N/A