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Department of Biomedical Sciences

Persistence of Ciguatera Fish Poisoning and its Associated Neurological Manifestations in Mice

Dr. Eddie C. H. Ma

City University of Hong Kong

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Ciguatoxin reduces regenerative capacity of axotomized peripheral neurons and delays functional recovery in pre-exposed mice after peripheral nerve injury

Ngan Pan Bennett Au[1,*], Gajendra Kumar[1,*], Pallavi Asthana[1], Chung Tin[2,3], Yim Ling Mak[4,5], Leo Lai Chan[1,4,5], Paul Kwan Sing Lam[4,5,6] & Chi Him Eddie Ma[1,3,4]

Mol Neurobiol
DOI 10.1007/s12035-016-0093-y

CrossMark

Acute Exposure to Pacific Ciguatoxin Reduces Electroencephalogram Activity and Disrupts Neurotransmitter Metabolic Pathways in Motor Cortex

Gajendra Kumar[1] · Ngan Pan Bennett Au[1] · Elva Ngai Yu Lei[2] · Yim Ling Mak[3,4] · Leanne Lai Hang Chan[5,6] · Michael Hon Wah Lam[2] · Leo Lai Chan[1,3,4] · Paul Kwan Sing Lam[2,3,4] · Chi Him Eddie Ma[1,3,6]

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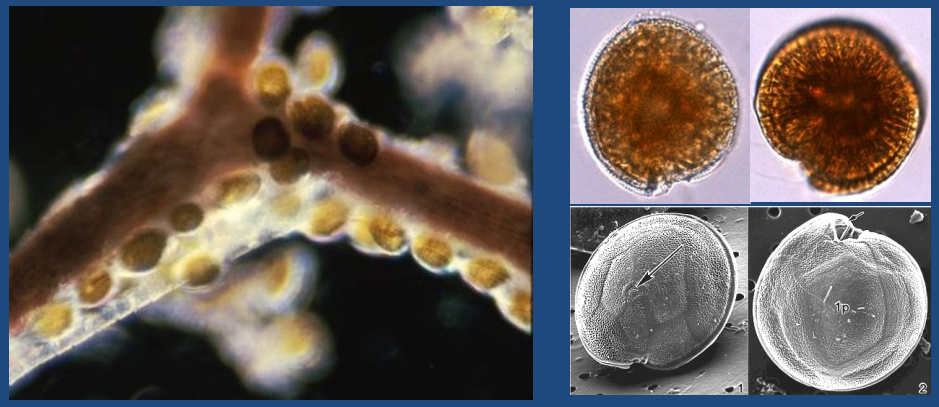
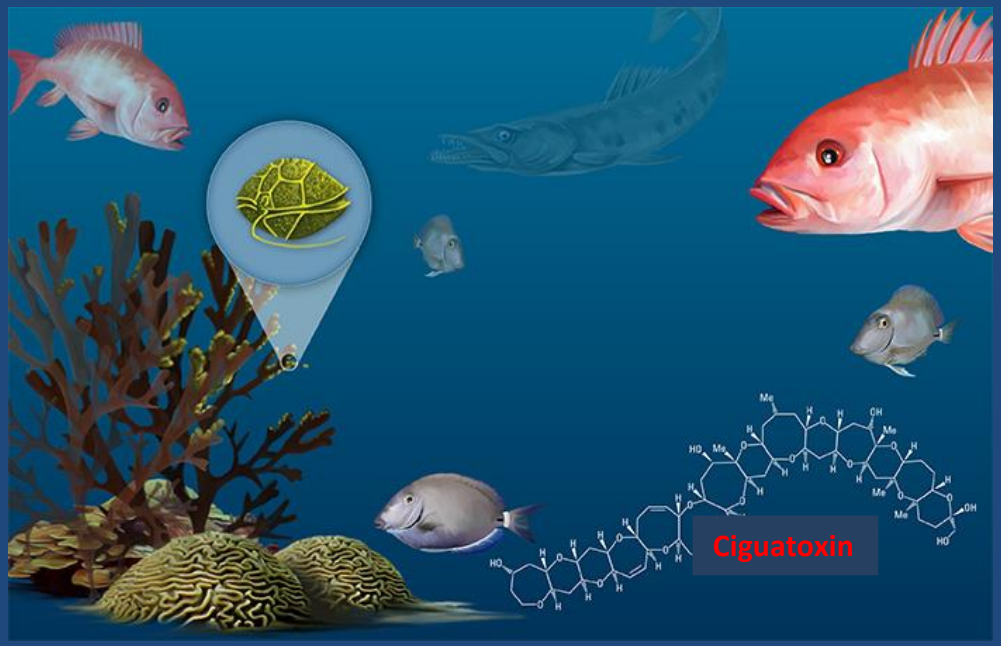
What is Ciguatera Fish Poisoning (CFP)?

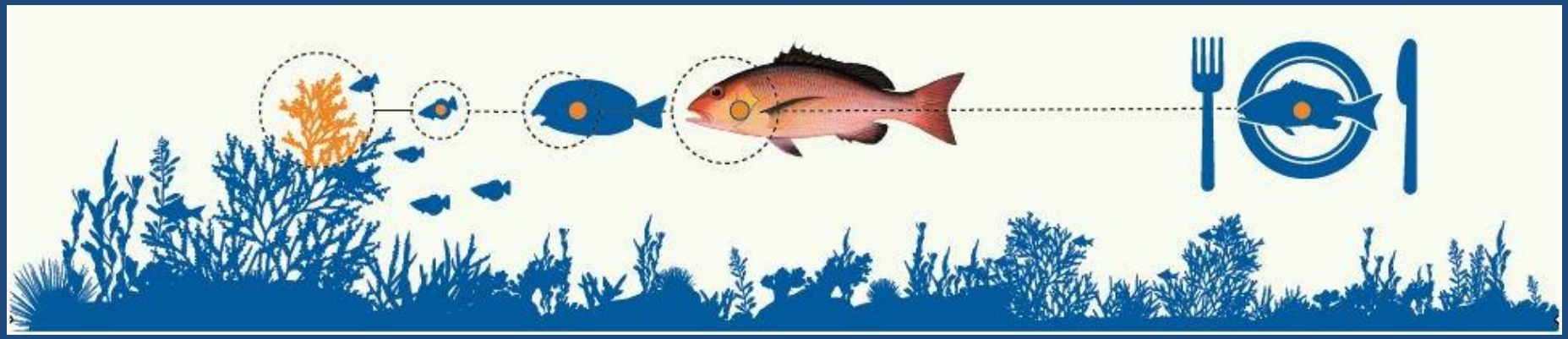
- CFP is a food-borne illness caused by the presence of ciguatoxins (CTXs) in the flesh and organs of tropical and subtropical coral reef fishes
- CTX is produced by dinoflagellates that are usually attached to dead coral surfaces in the sea, especially in tropical areas
- Heat/cold resistant, and lipophilic



Gambierdiscus spp.

How do we get Ciguatera Fish Poisoning (CFP)?





Over 100 cases reported affecting > 230 people in the past 10 years

即時新聞 2017年04月01日 請選擇

連續兩日有市民食魚後疑雪卡毒 大埔55歲男子中招

13,308

讚 7

遠立時間 (HKT): 0401 18:57

A A (蘋果日報)

衞生防護中心連續兩日接獲懷疑雪卡毒中毒個案。最新一宗個案患者是55歲男子，他周五在家午膳期間吃過魚頭及喝酒，兩小時後出現舌頭和口部麻痺及四肢乏力，到大埔那打素醫院急症室求醫，期間出現低血壓和心律下跌，同日入院接受治療。中心指病人的情況一直穩定。

初步調查顯示，病人曾進食的魚類是深海紅魚，該條魚是他在前日（3月30日）下午在大埔大元街市一魚檔購買，但他記不起是哪一檔魚檔，中心已將事件通知食物環境生署。

中心表示，雪卡毒素食物中毒在熱帶地方並不罕見，主要與進食大珊瑚魚有關。這類大魚會吃珊瑚礁海域的小魚，而小魚則吃有毒海藻，故毒素積聚在大珊瑚魚體內，特別是內臟。衞生防護中心錄得前日有4名市民進食購自藍田德田街市一魚檔買的魚後懷疑出現雪卡毒中毒，但患者記不起進食的魚類及購自哪個魚檔。

3000斤疑雪卡毒魚銷毀

本報訊】汕頭有市民進食由本港一家魚的老虎斑後中雪卡毒，食環署已聯絡批發商，據悉批發商銷毀約三千斤魚信流出市面的海產不多。另外，有消近期懷疑有人從曾爆發雪卡毒的南太國基里巴斯購買一批珊瑚魚後，運往以小型魚船轉運，聲稱魚類來自其他售，業內人士將會與食環署商討如何類事件。

生福利及食物局常任秘書長尤曾家麗昨日在一公開場合表示，衞生署在過去兩周並無收到有市民涉及雪卡毒的食物中毒個案，但由於內地汕頭有市民進食老虎斑後中雪卡毒，而該些老虎斑是經本港入口商英洋投資有限公司入口，同批部份珊瑚魚已售給本港一家批發商吳明記，故在港展開追查。

追查珊瑚魚下落

當局表示，批發商已同意銷毀有關魚類，並協助追查已出售珊瑚魚的下落，但食環署方面昨日未有正式銷毀數據。

據香港仔漁業海鮮商會主席陳富明表示，有關批發商吳明記位於東龍島，經由入口商購買了約三千斤老虎斑及杉斑等海產，前天已銷毀約一千斤，昨日銷毀約二千斤。

另外，香港海鮮業聯合總會發言人陳少華則表示，近期懷疑有人由南太平洋基里巴斯購入一批珊瑚魚，卻先運到越南，再由越南轉用較小型的魚船運往本港，聲稱海產來自東帝汶。

■部份深海珊瑚魚含有雪卡毒。 資料圖片

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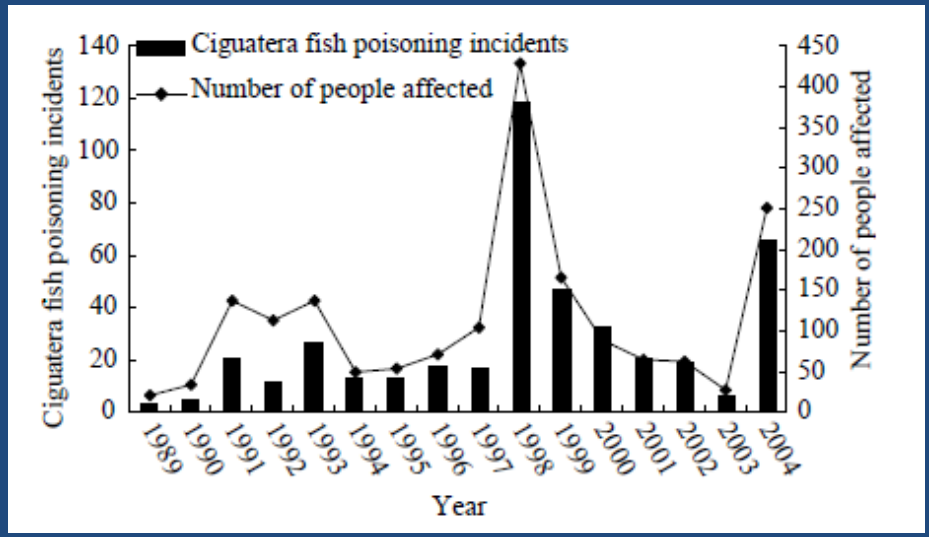
Two prominent outbreaks in 1998 and 2004

more than 100 cases, affecting > 550 people



Wong et al., Toxicon 2005

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Common coral reef fish for consumption in HK

Plectropomus leopardus (leopard coral grouper)

Cromileptes altivelis (humpback grouper)

Cheilinus undulaus (humphead wrasse)

Plectropomus areolatus (areolated coral grouper)

Epinephelus polyphekadion (camouflage grouper)

Lutjanus bohar (two-spot red snapper)

Epinephelus fuscoguttatus (Brown-marbled grouper)

Gymnothorax spp. (moray eel)

Variola louti (yellow-edged lyretail)

Epinephelus lanceolatus (giant grouper)

Lutjanus argentimaculatus (mangrove red snapper)

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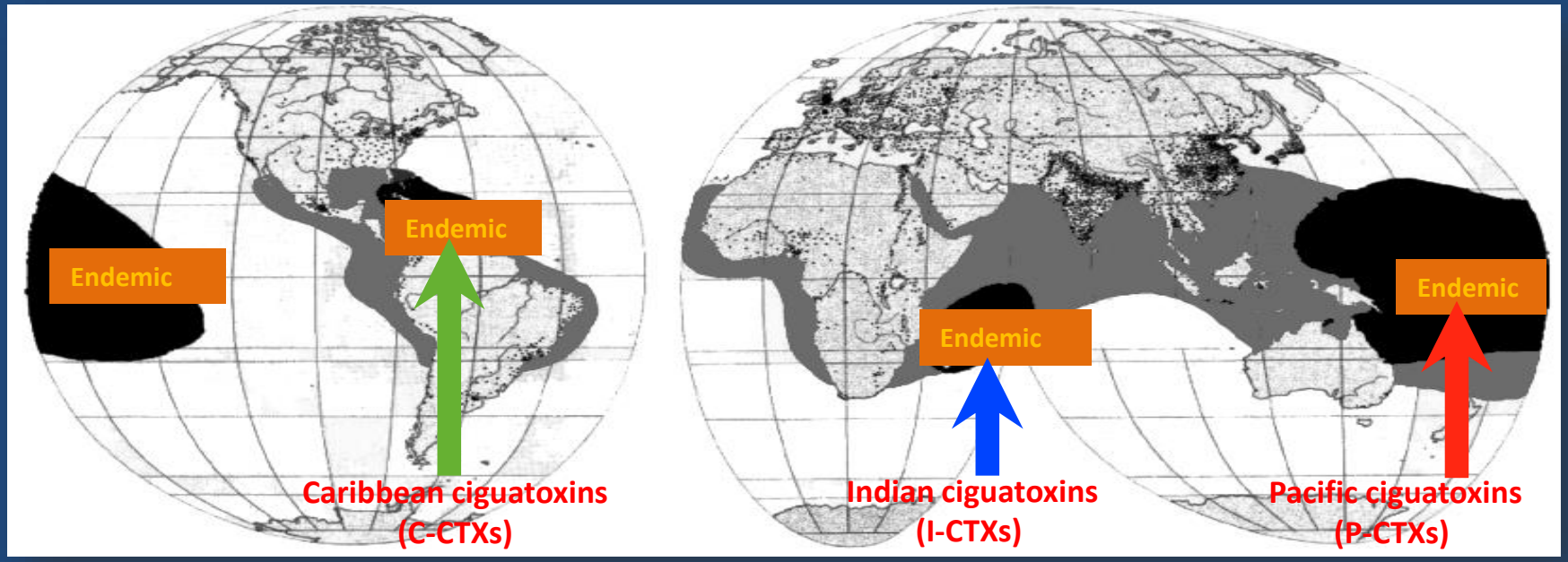
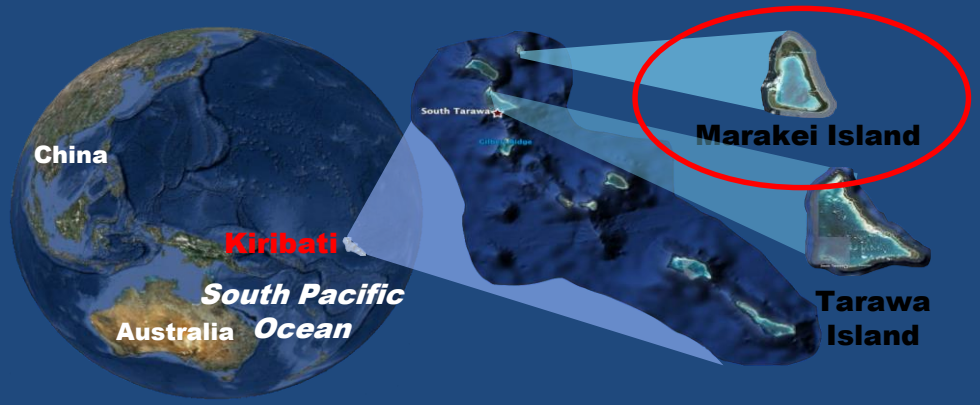
Classification of Ciguatoxins





Gymnothorax javanicus
(Giant moray eel)

Chan et al., Chemosphere 2011

Toxicon 86 (2014) 96–106

Contents lists available at ScienceDirect

Toxicon

journal homepage: www.elsevier.com/locate/toxicon

Ciguatera fish poisoning in Hong Kong—A 10-year perspective on the class of ciguatoxins

Chun-Kwan Wong, Patricia Hung, Janice Y.C. Lo*

Public Health Laboratory Services Branch, Centre for Health Protection, Department of Health, 382 Nam Cheong St., Shek Kip Mei, Kowloon, Hong Kong, China

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ABSTRACT

The present study used liquid chromatography-tandem mass spectrometry (LC-MS/MS) to investigate retrospectively ciguatoxin (CTX)-positive samples as determined by mouse bioassay (MBA) in the past 10 years in Hong Kong. The results showed that Pacific CTXs (P-CTX-1, -2 and -3) were the most commonly observed toxins found in the samples, indicating Pacific Ocean areas as the most important origin of ciguatera fish poisoning. Clinical diagnosis from ciguatera patients also revealed the predominance of neurological illnesses in most cases, supporting intoxication of Pacific origin. This study demonstrated the ability of laboratory analysis to identify and quantify Pacific CTXs in suspected fish samples, so as to support the clinical diagnosis of ciguatera. Comparative analysis (Student's *t*-test and Spearman's rank correlation analysis) on the two CTX detection methods showed approximate linearity for overall P-CTXs (P-CTX-1, -2 and -3)/P-CTX-1 alone as derived by LC-MS/MS and total toxicity levels (P-CTX-1 equivalent) as determined by MBA. The LC-MS/MS method coupled with the rapid extraction method could allow the detection of trace amount of CTXs at levels below the clinically relevant limit, 0.1 ppb P-CTX-1 in fish flesh. For practical application, the adoption of a two-tiered approach for testing, chemical analysis by LC-MS/MS for toxic fish screening, coupled with biological assay by MBA for final toxicity confirmation, was proposed for first-line screening of CTX in potentially contaminated fish samples in the market, with an aim to minimizing the use of laboratory mice and at the same time providing reasonably effective means for routine analysis.

Clinical Symptoms

Gastrointestinal disorders:

Abdominal pain, vomiting, nausea and diarrhea

Neurological disorders:

Muscle weakness, limb paraesthesia, reversal of hot and cold sensation, numbness, tingling, and nerve damage

Cardiovascular disorders:

Irregular pulse, decreased blood pressure, bradycardia, dizziness

->CFP affects >50,000 people worldwide annually with 0.5% of mortality rate

->Under-reporting are common

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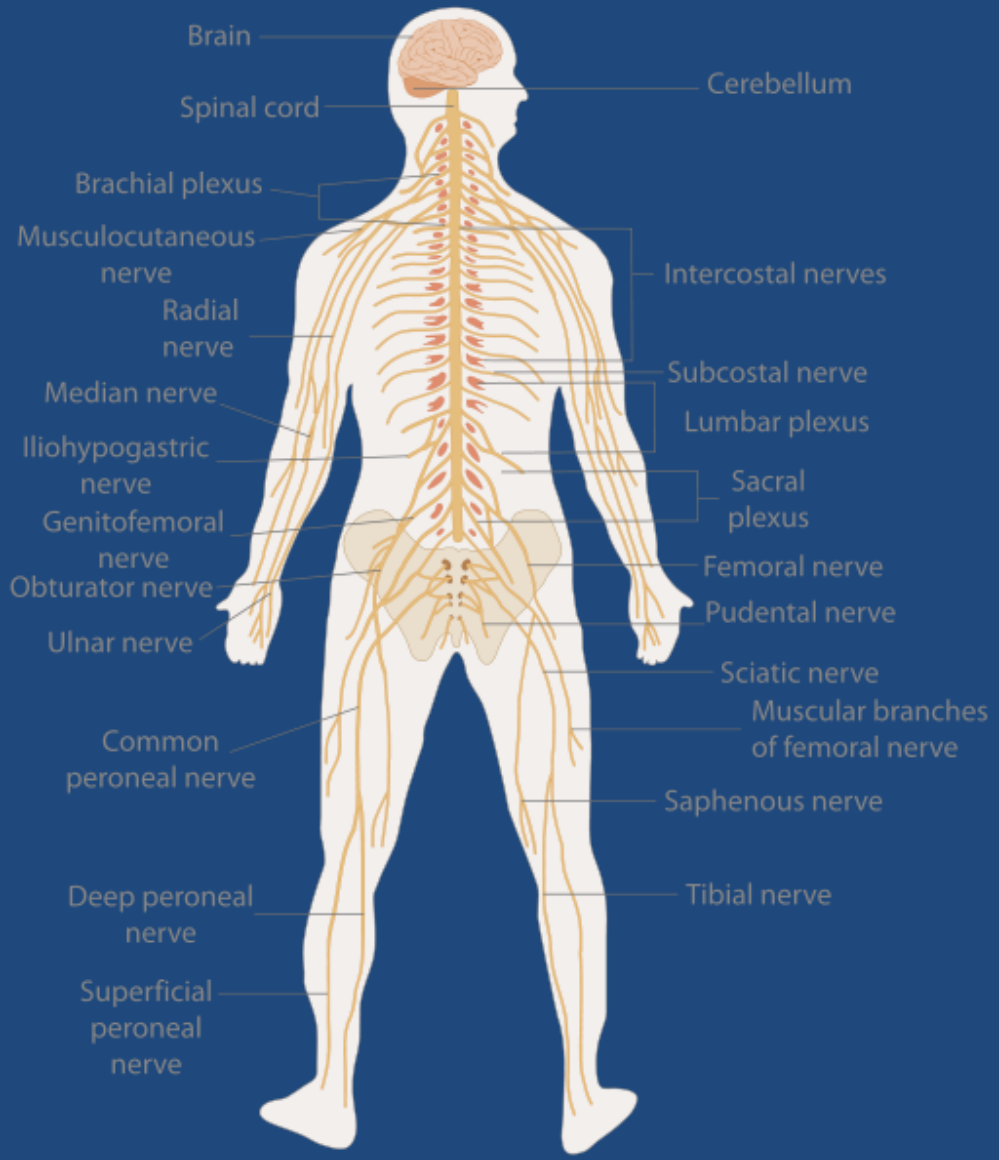
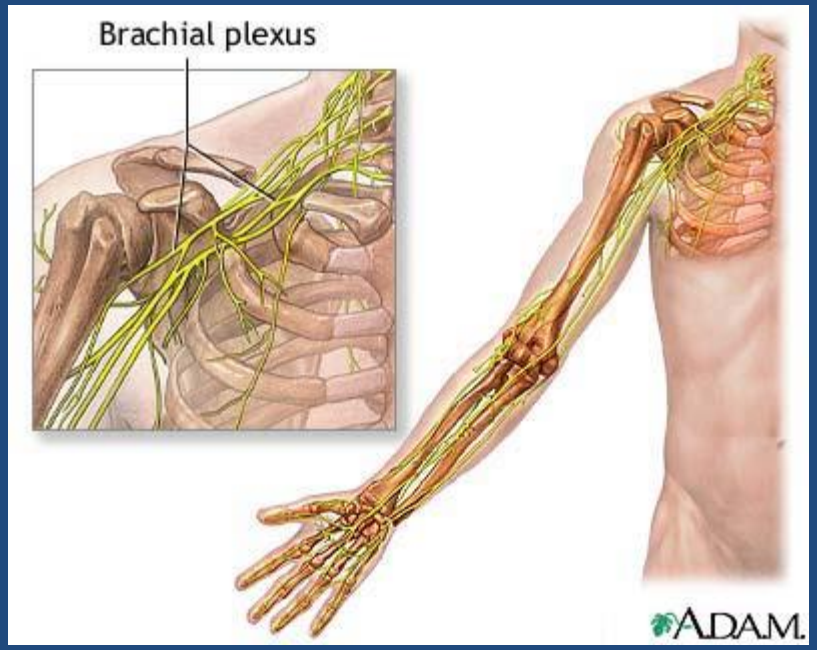
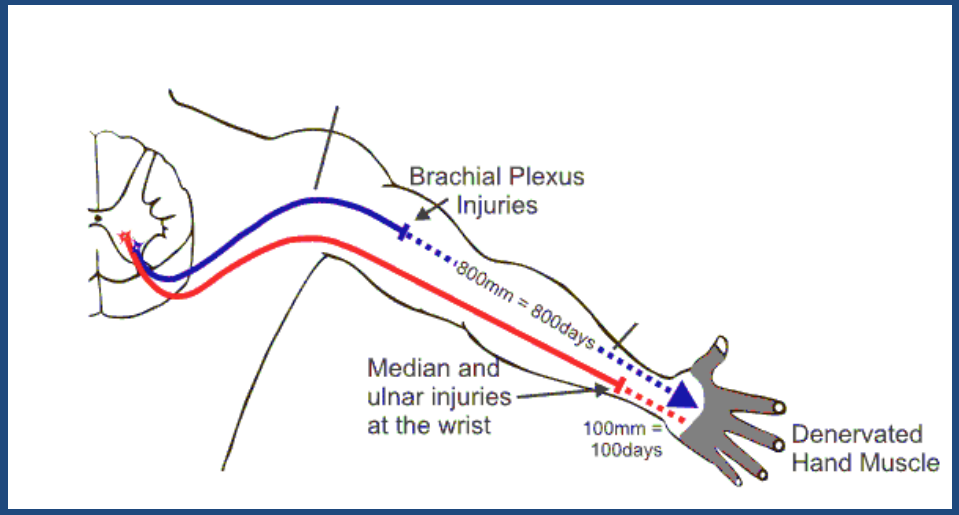
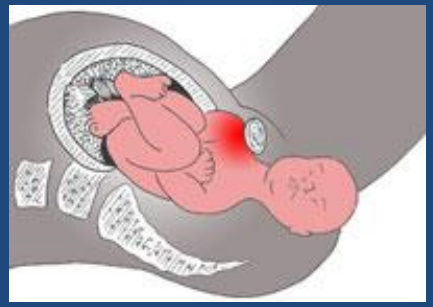
Human Nervous System



Proximal peripheral nerve injury







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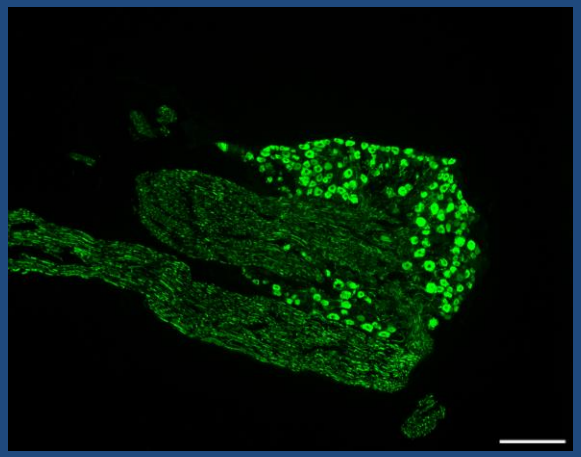
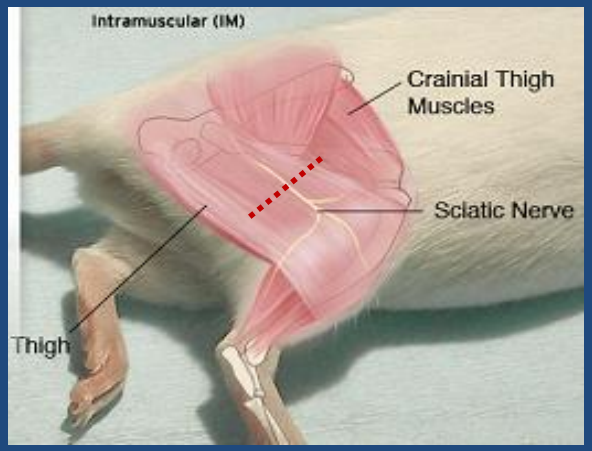
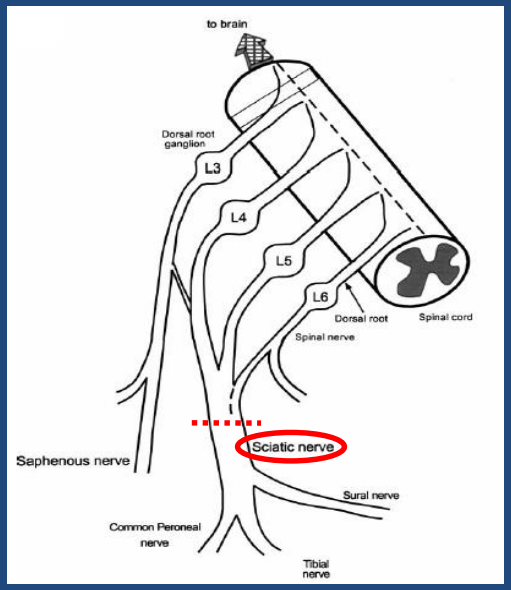
Peripheral nervous system regeneration







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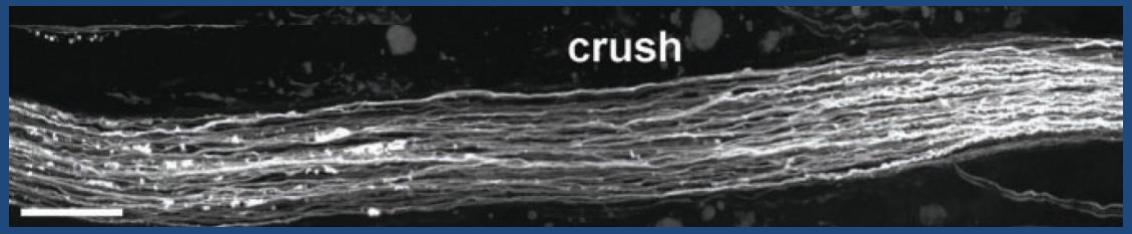

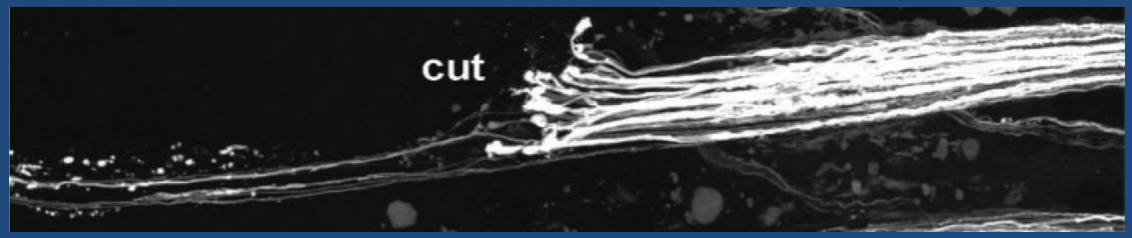

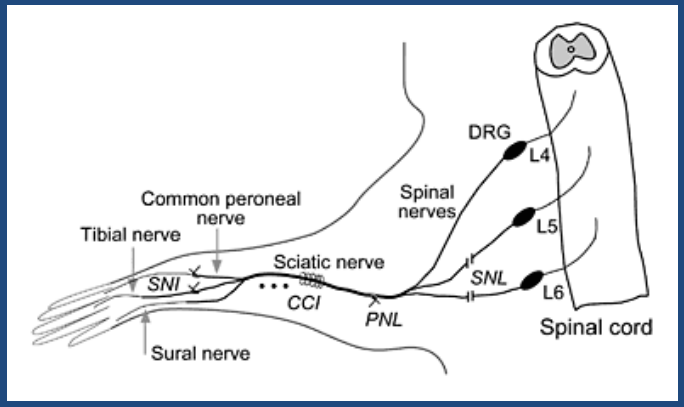

Pan YA et al., J. Neurosci. 2003

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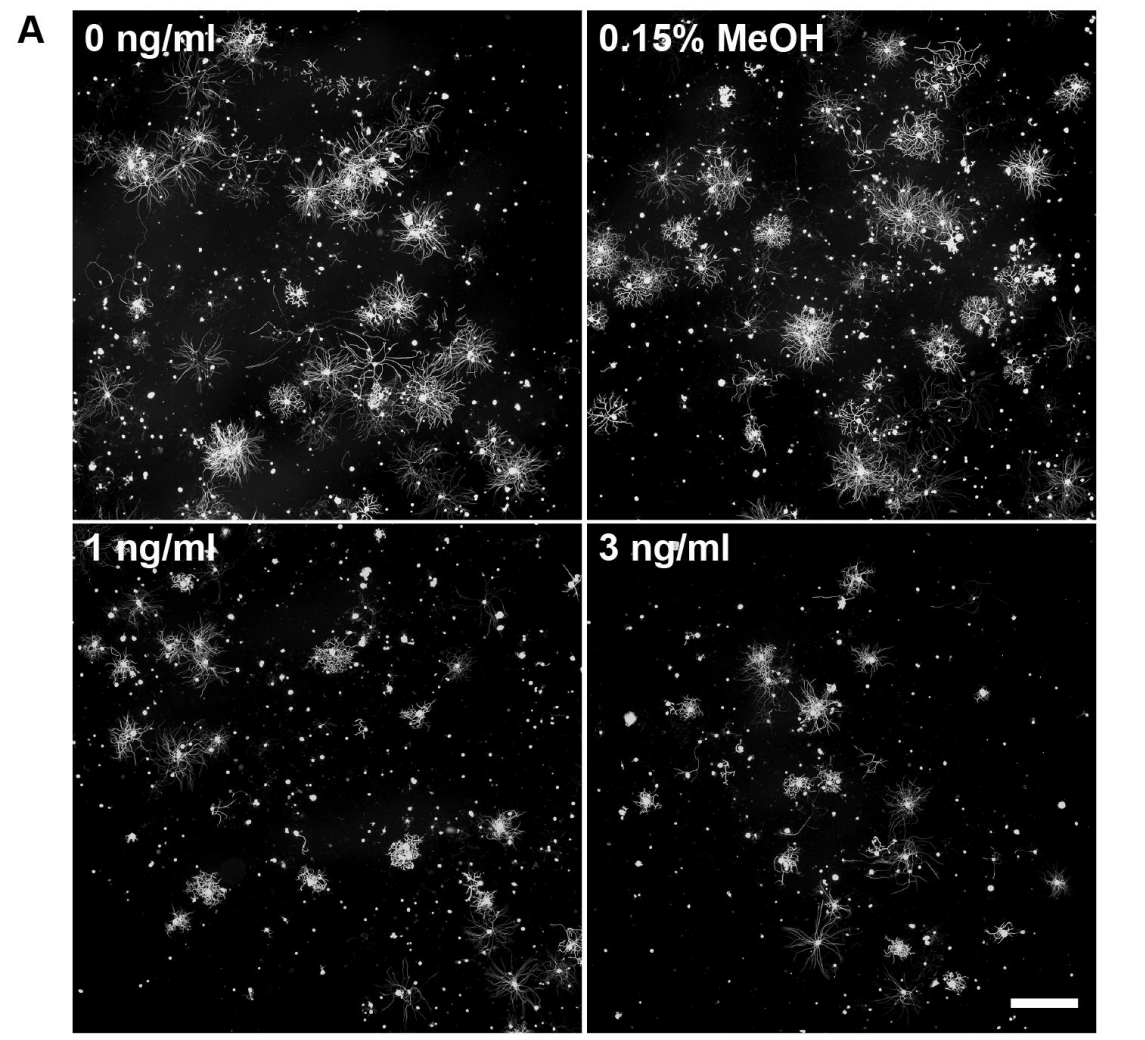
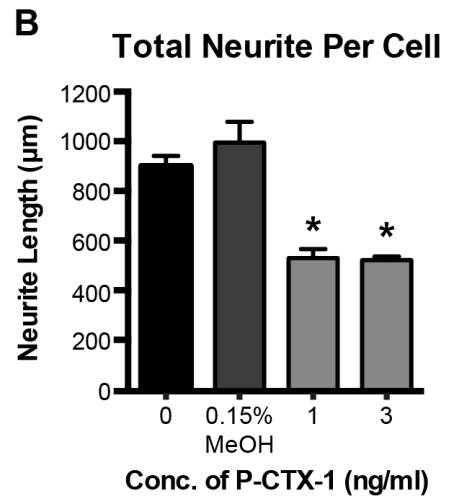
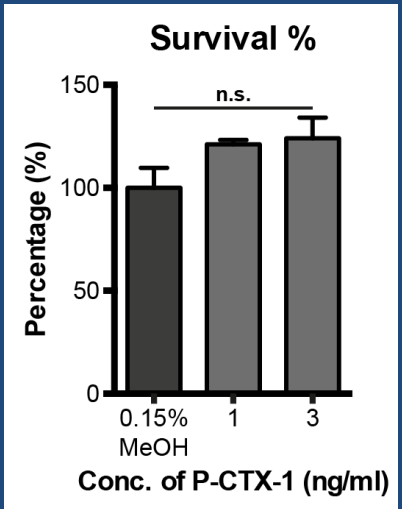
P-CTX-1 reduces neurite outgrowth in peripheral neurons

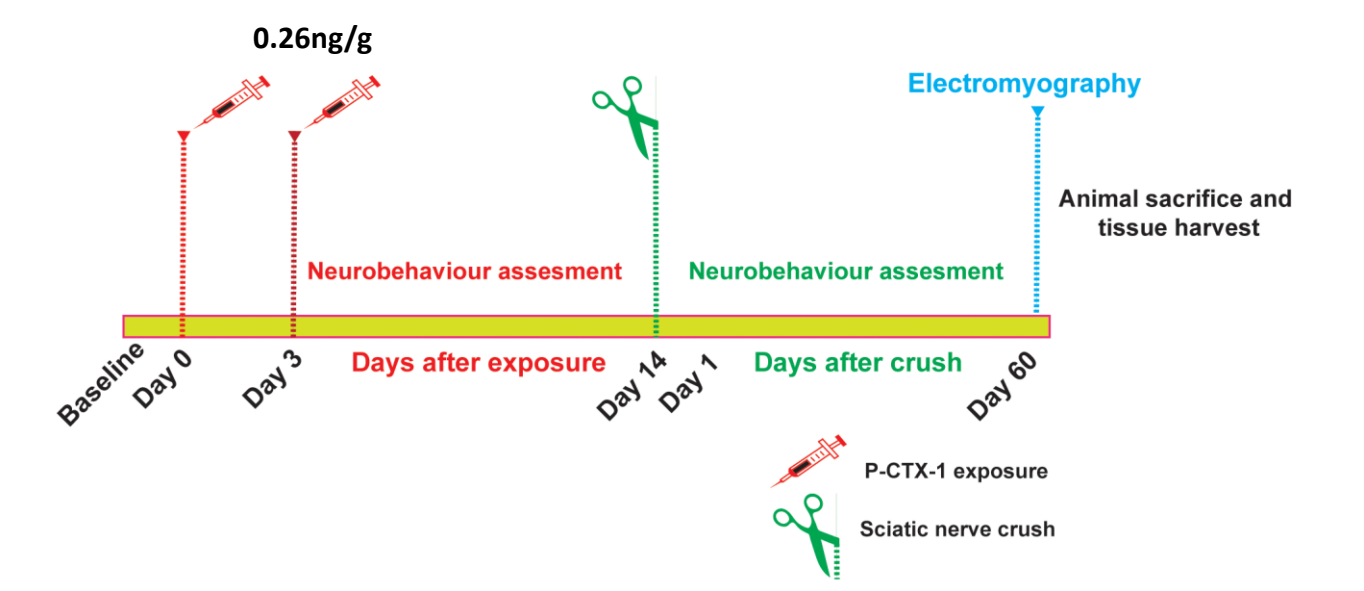






Au et al., Scientific Report 2016

Experimental Paradigm



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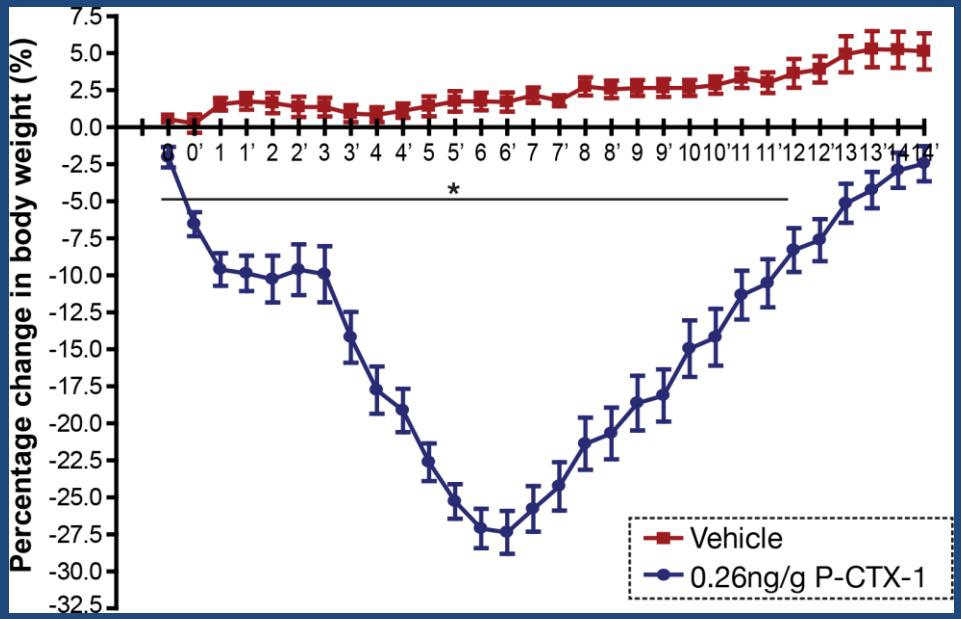
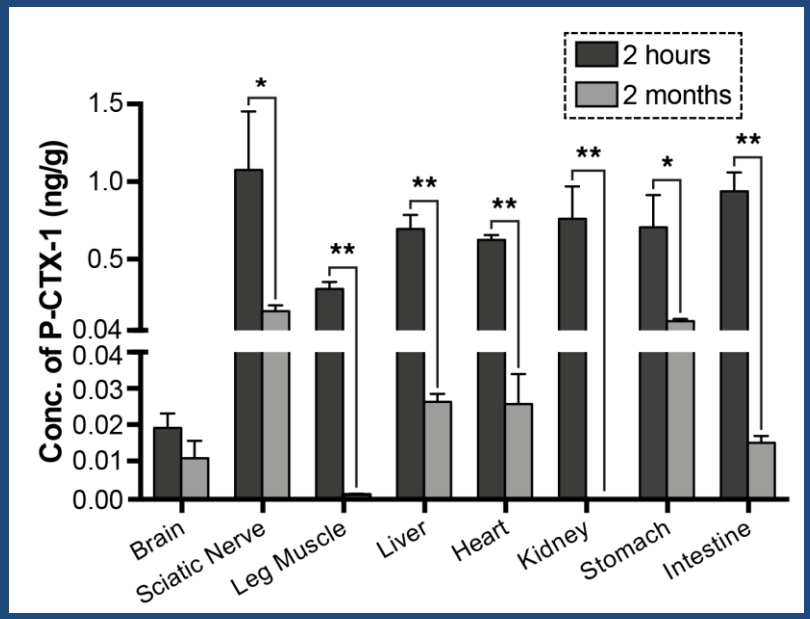
P-CTX-1 levels in various tissue organs in mice





Au et al., Scientific Report 2016

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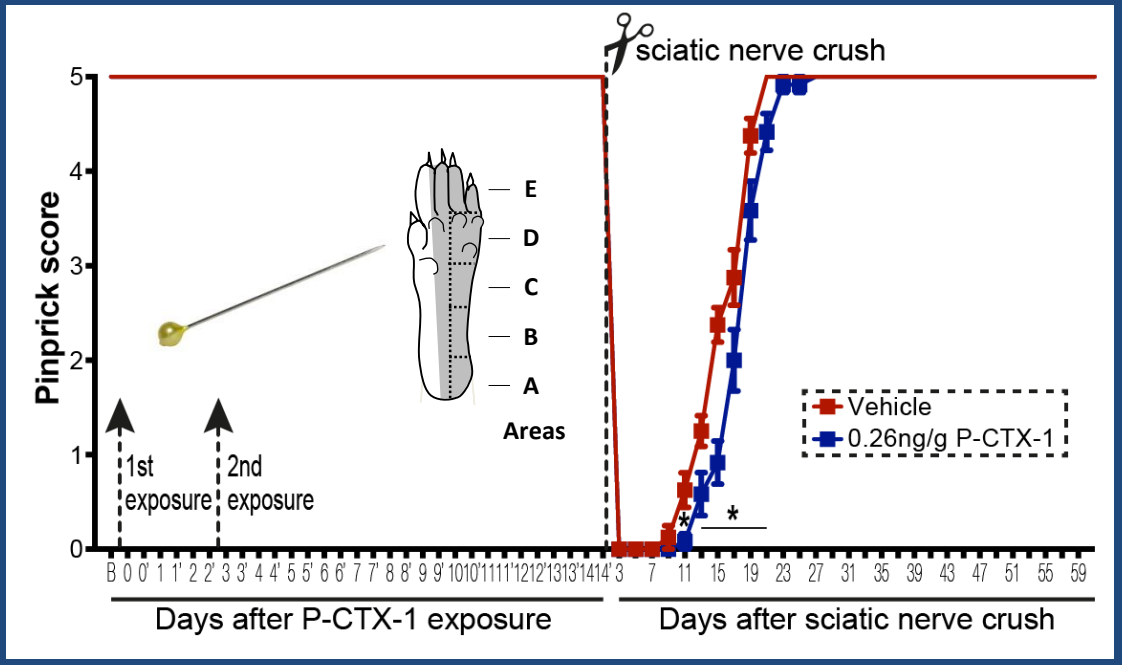
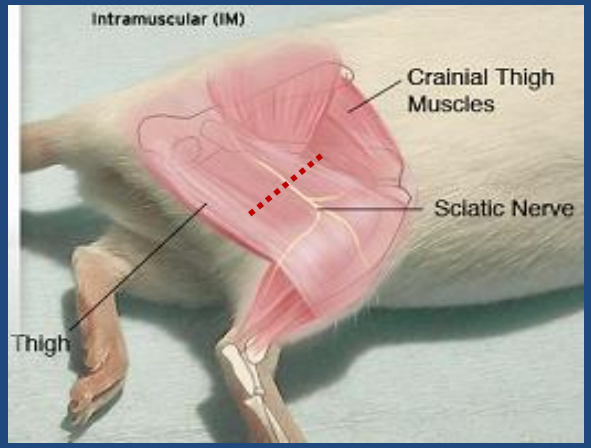
P-CTX-1 exposure delays sensory function recovery (Pinprick assay)





Au et al., Scientific Report 2016

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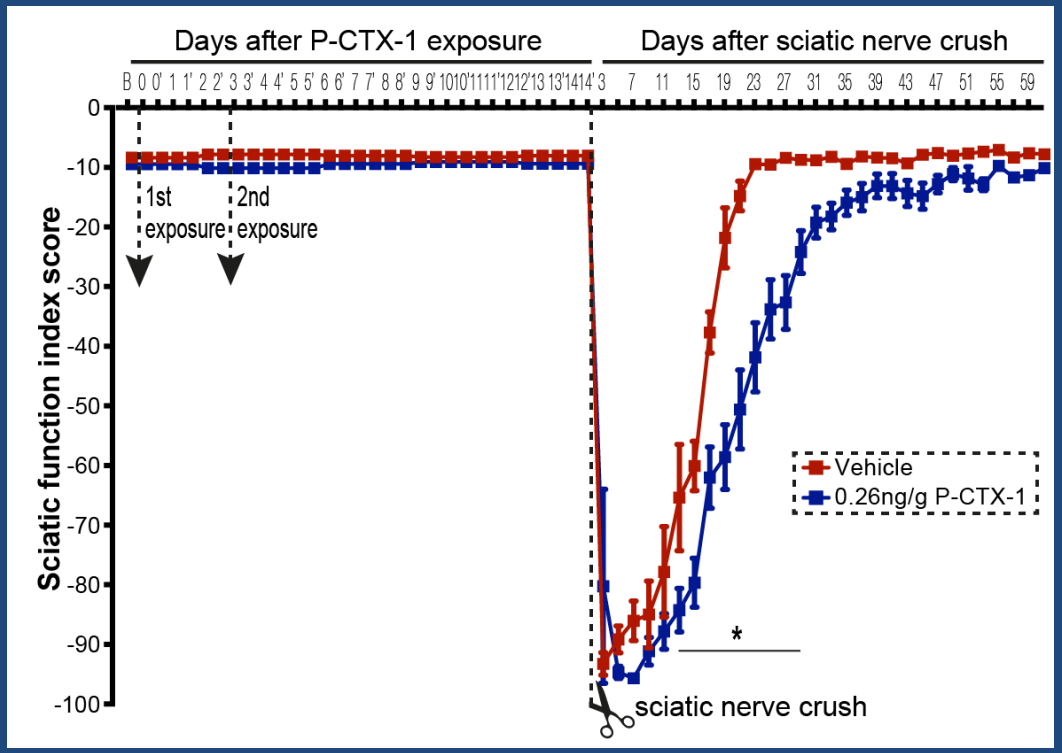
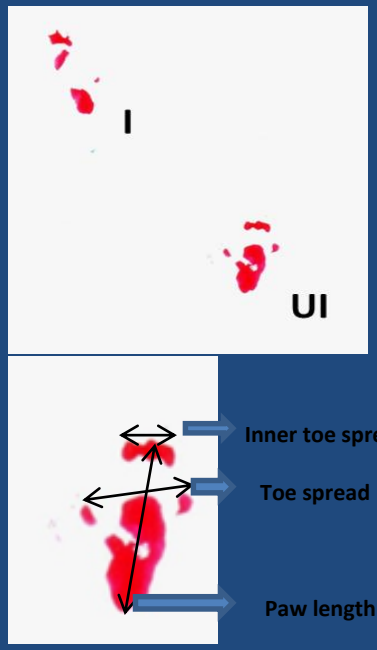
P-CTX-1 exposure delays motor function recovery (Sciatic Function Index)





Au et al., Scientific Report 2016

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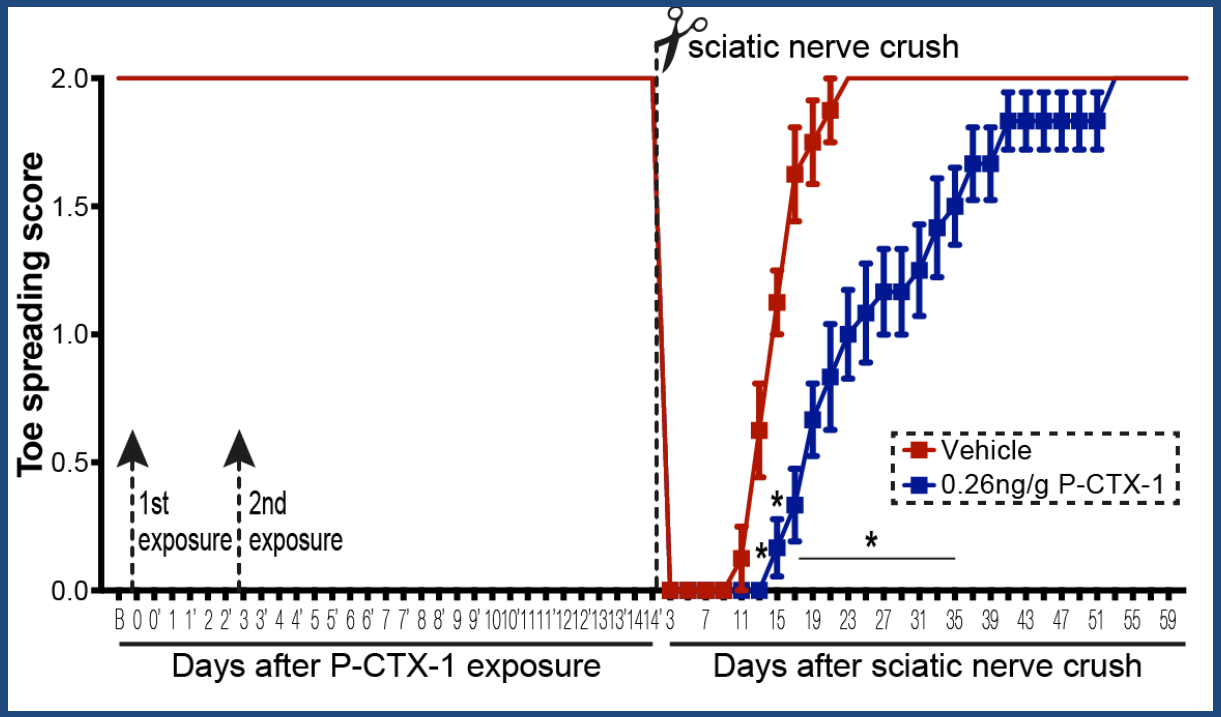
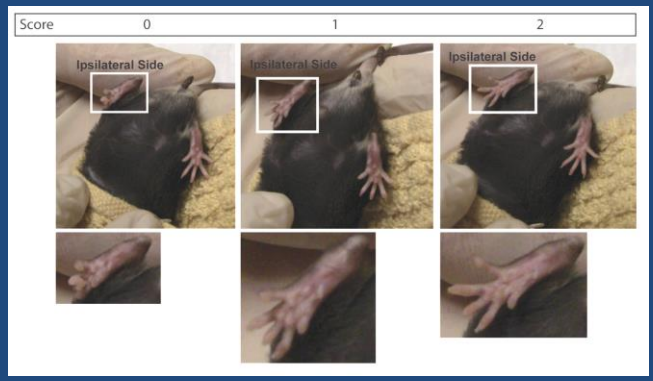
P-CTX-1 exposure delays motor function recovery (Toe Spreading)





Au et al., Scientific Report 2016

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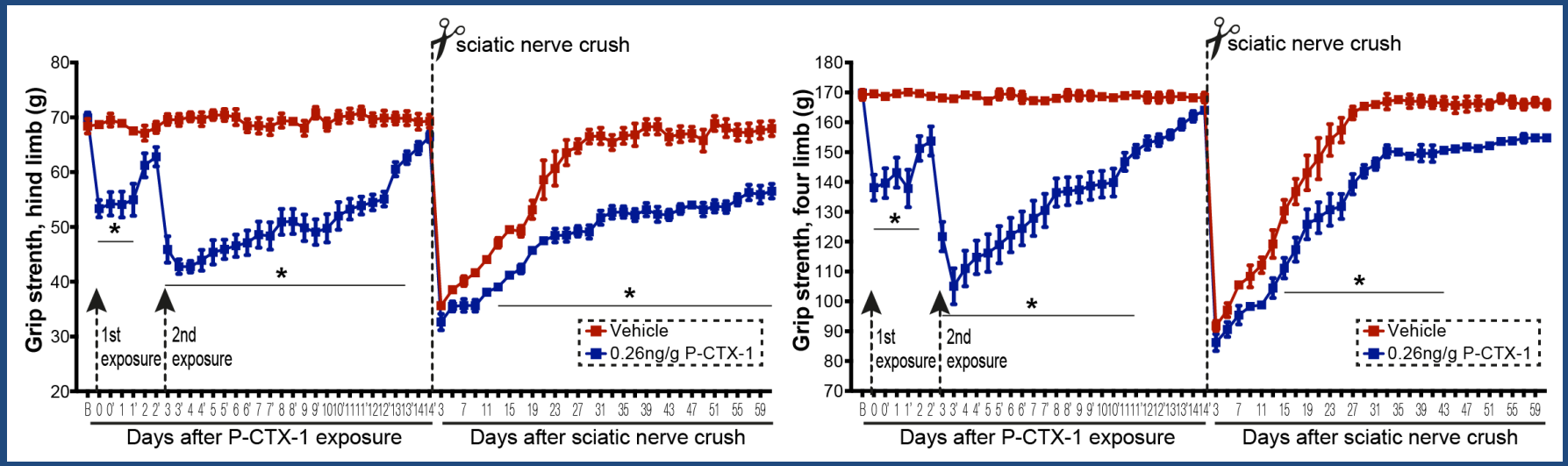
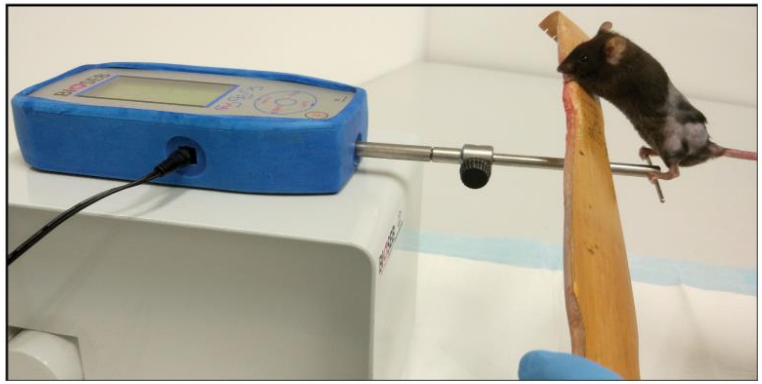
P-CTX-1 exposure delays motor function recovery (Grip Strength)





Hind limb grip strength test

Four limb grip strength test

Au et al., Scientific Report 2016

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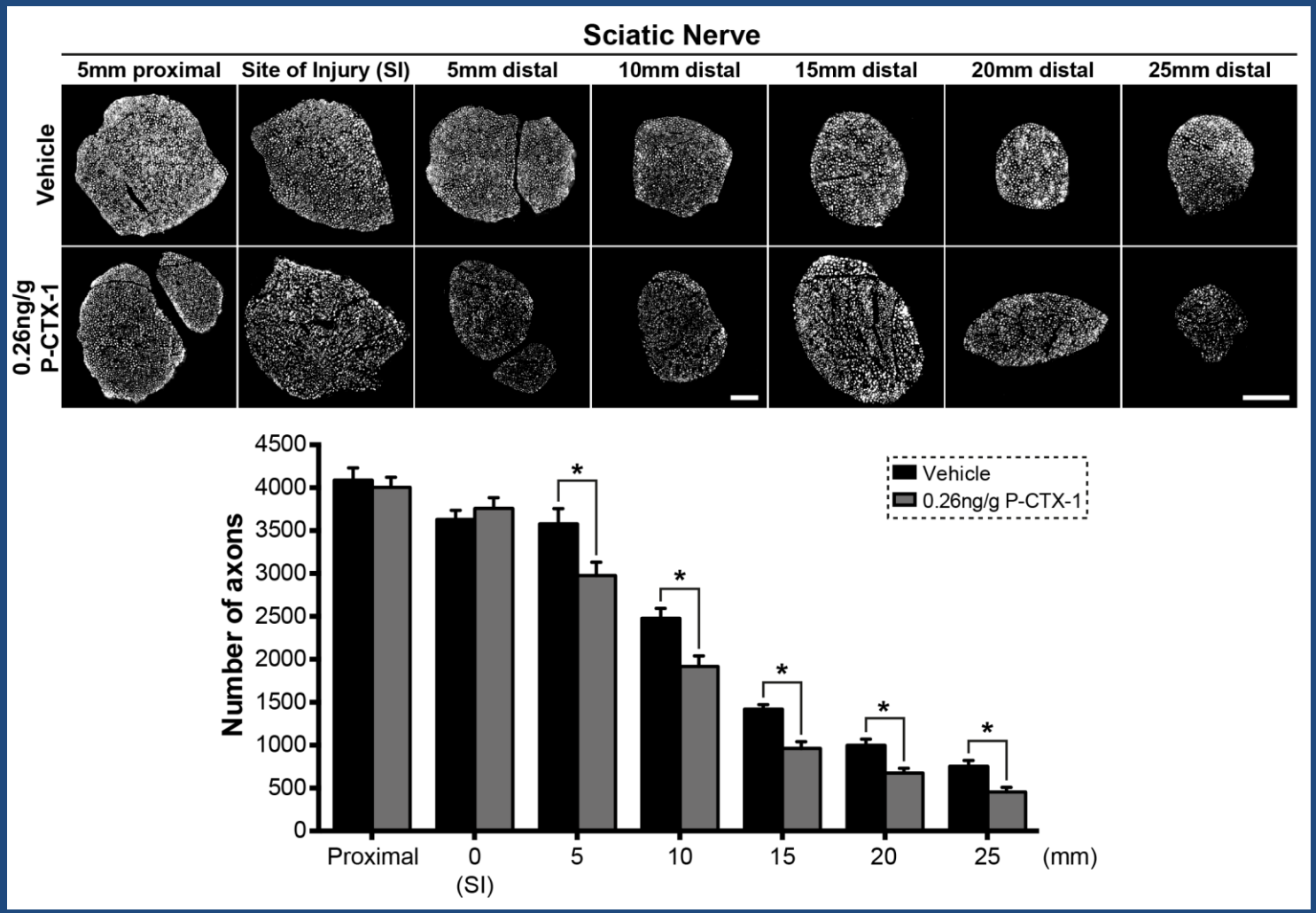
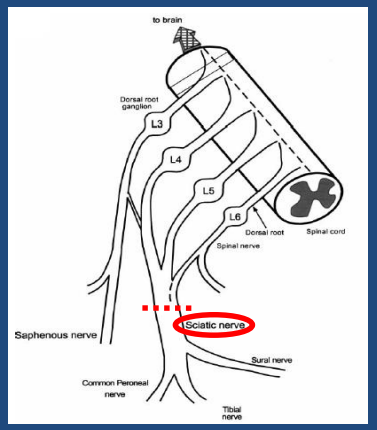
P-CTX-1 reduces the number of regenerating axons





Au et al., Scientific Report 2016

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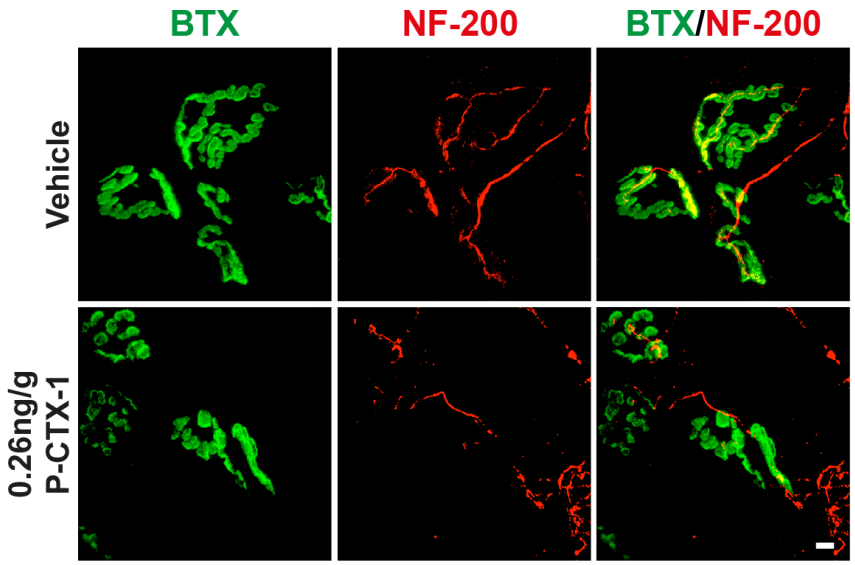
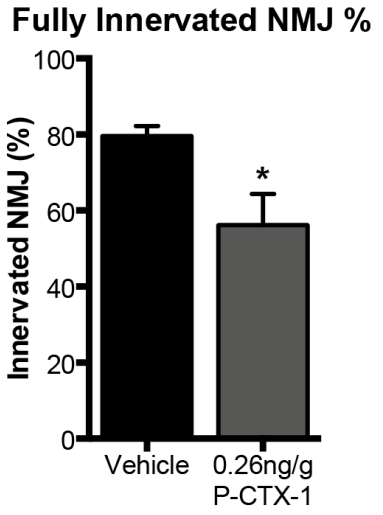
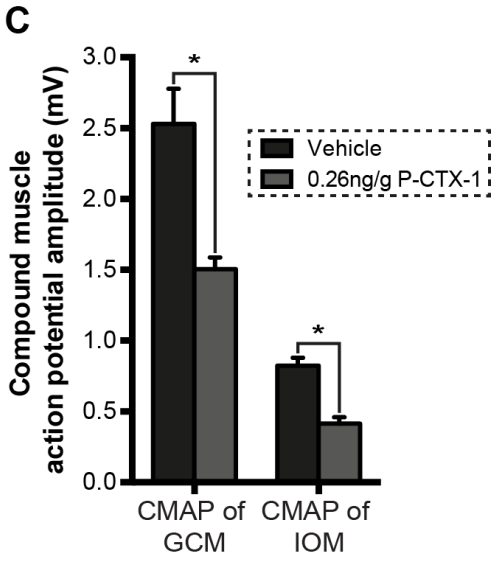
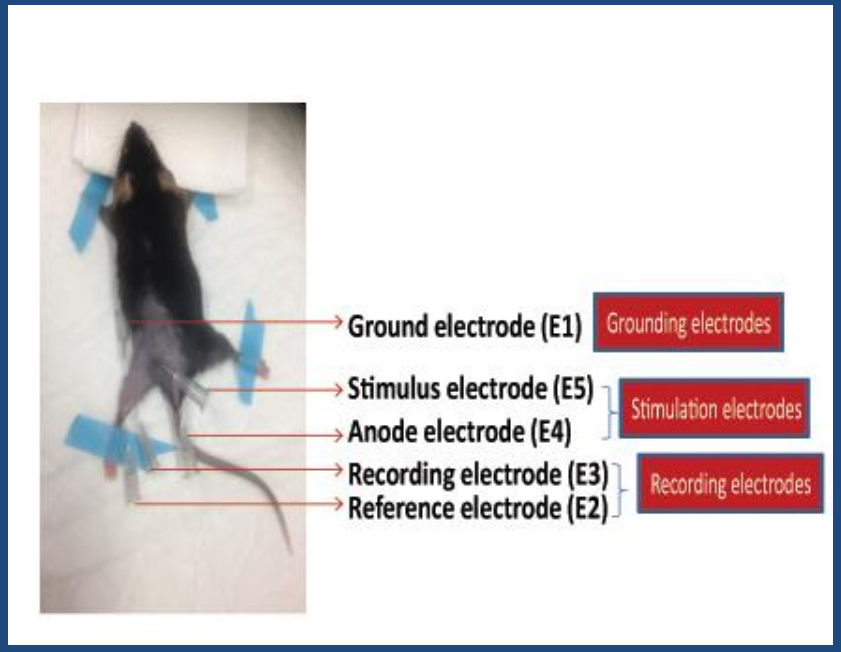
P-CTX-1 inhibits neuromuscular junction formation









Au et al., Scientific Report 2016

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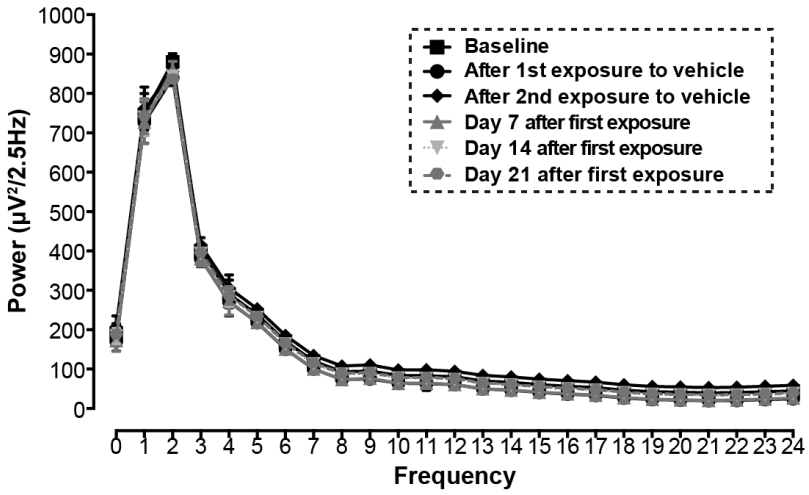
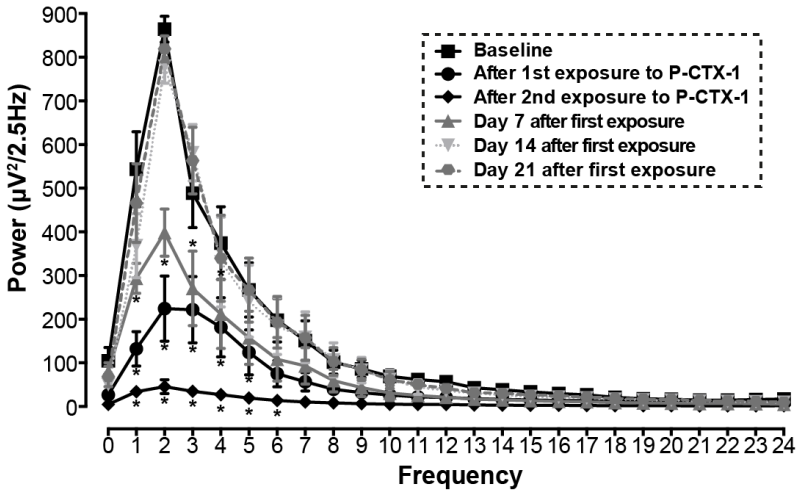
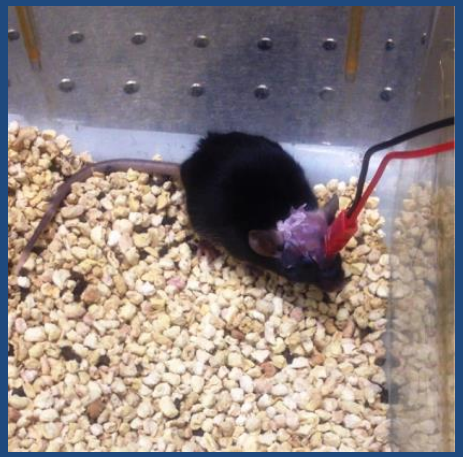
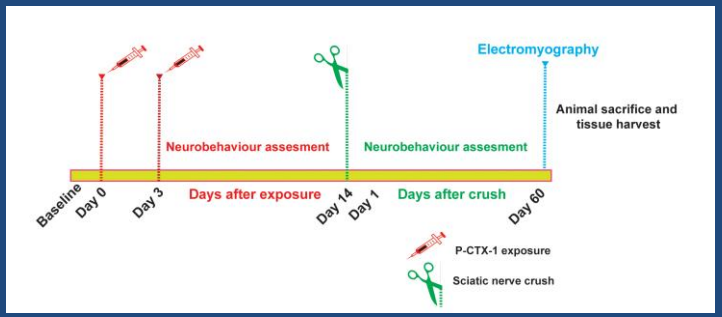
P-CTX-1 inhibits brain activity (electroencephalogram, EEG)









Kumar et al., Molecular Neurobiology 2017

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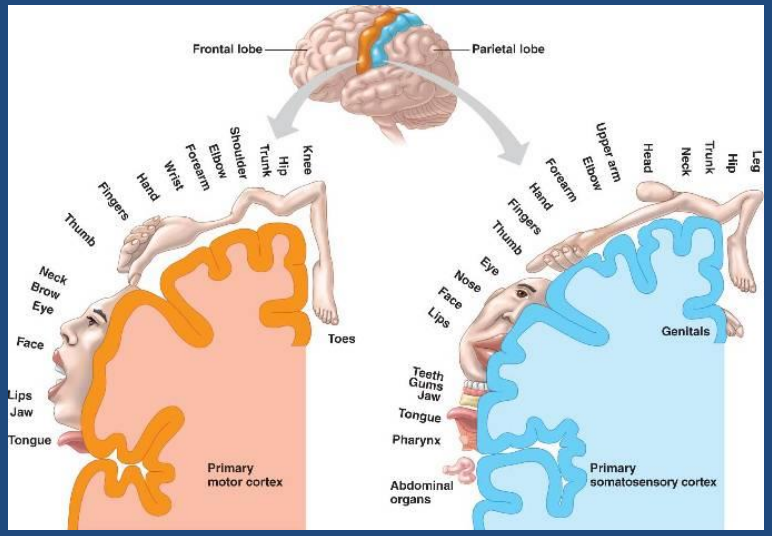
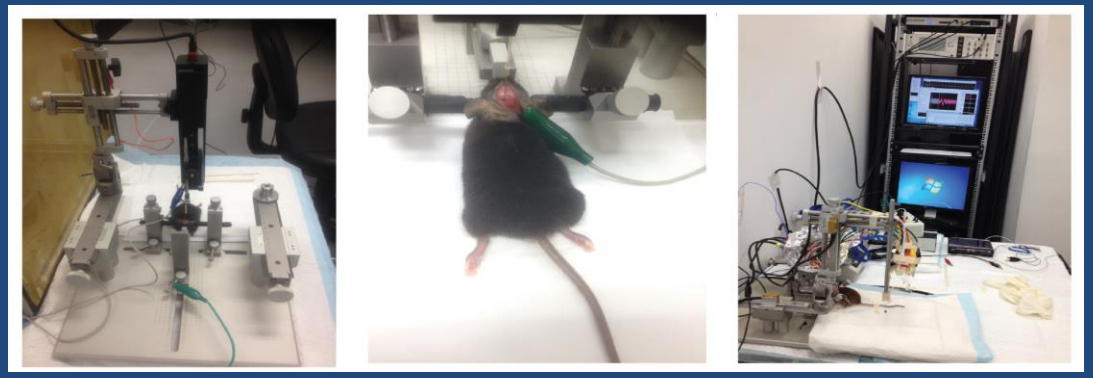
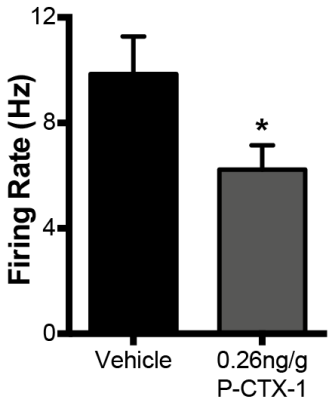
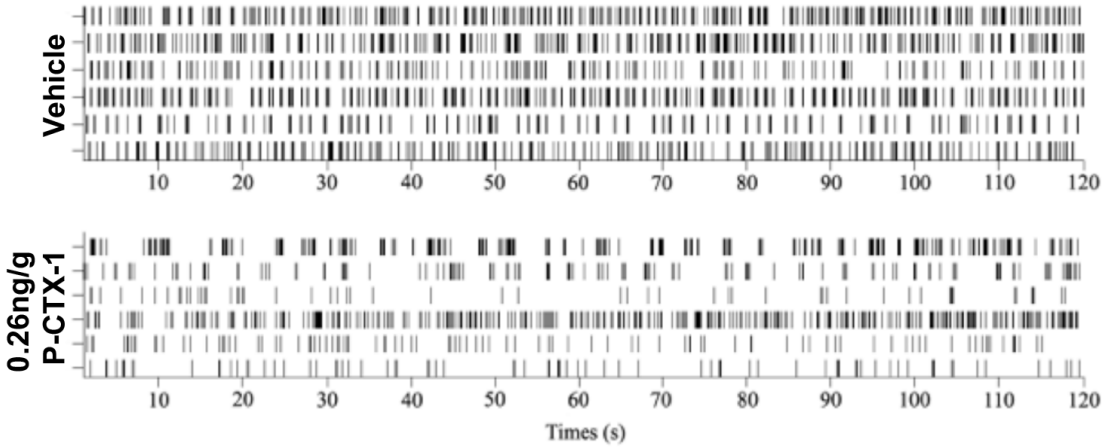
P-CTX-1 reduces spontaneous firing rates of single motor cortex neuron



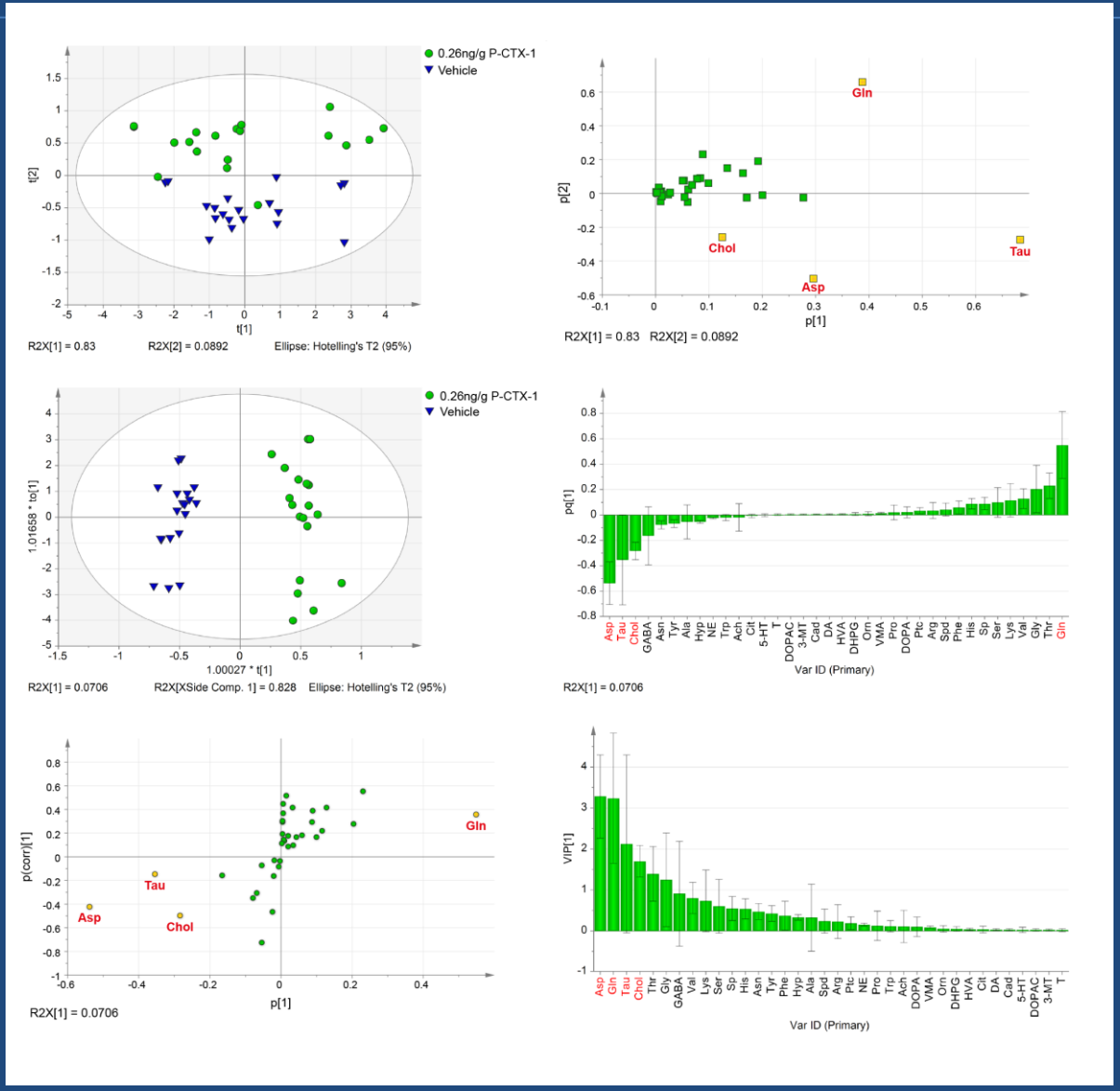






Kumar et al., Molecular Neurobiology 2017

Target neurotransmitter profiling in motor cortex



Aspartic Acid (Asp)
Taurine (Tau)
Glutamine (Gln)
Choline (Chol)

Kumar et al.,
Molecular Neurobiology 2017

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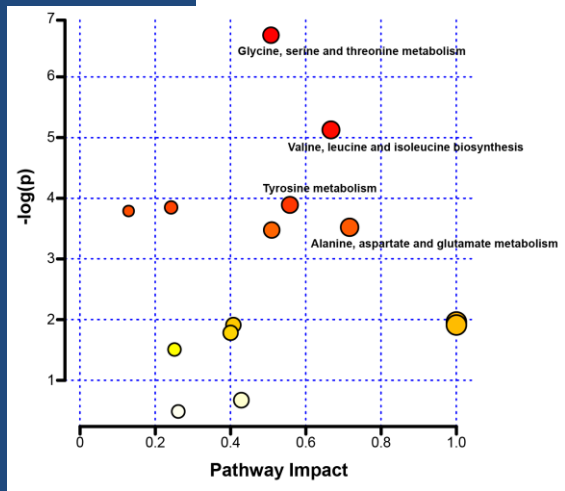
P-CTX-1 disrupts major signaling pathways inducing excitotoxicity?



Kumar et al., Molecular Neurobiology 2017

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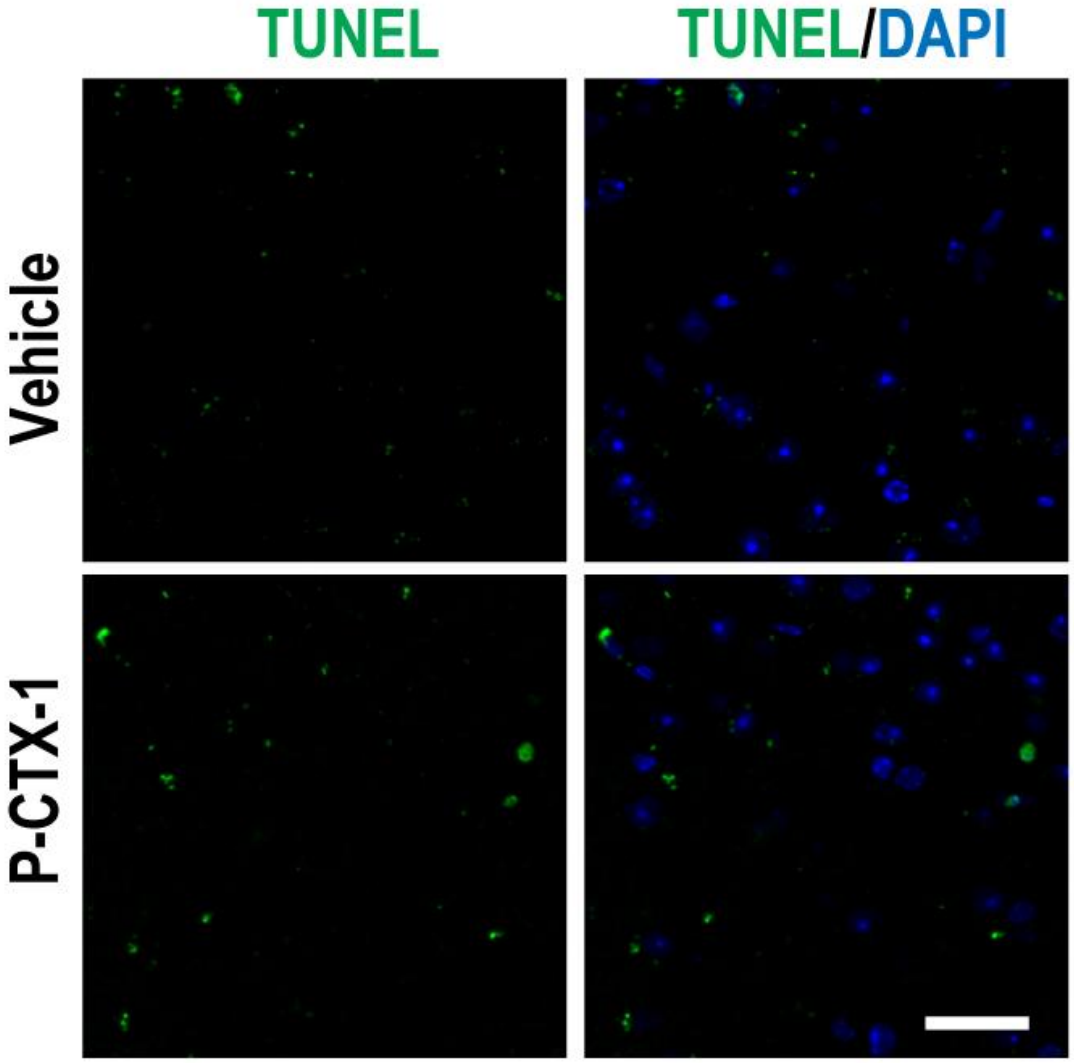
P-CTX-1 induces apoptotic cell death in the motor cortex



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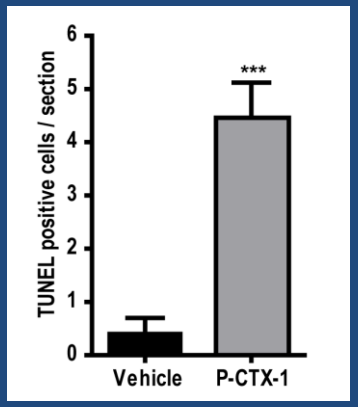

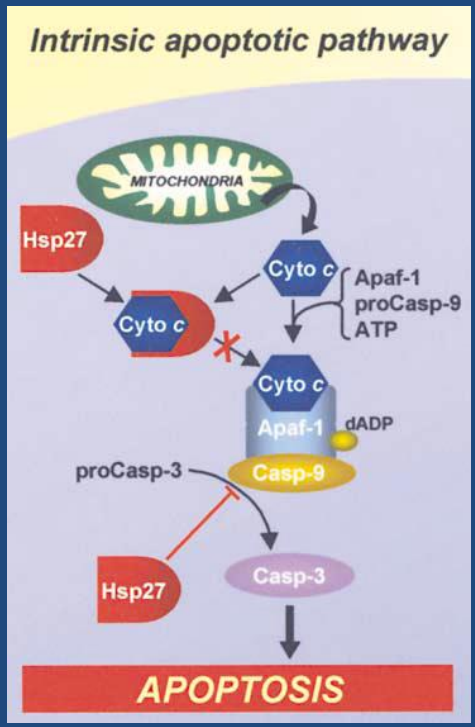

Benn et al., Neuron 2002

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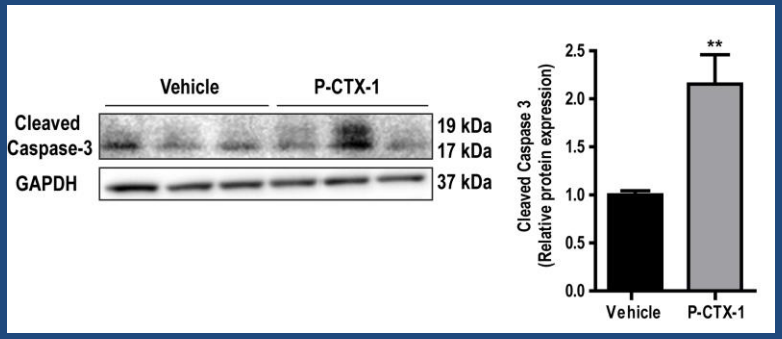
P-CTX-1 induces apoptotic cell death via Caspase-3 activation



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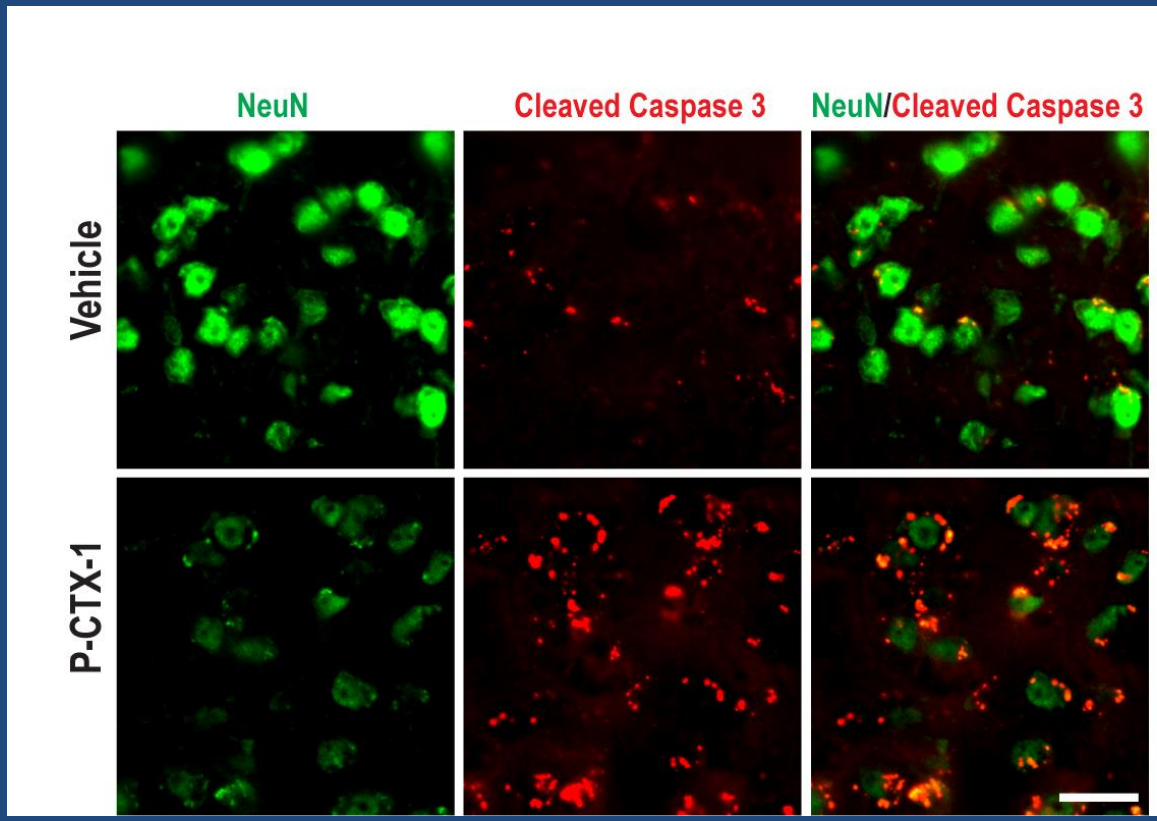

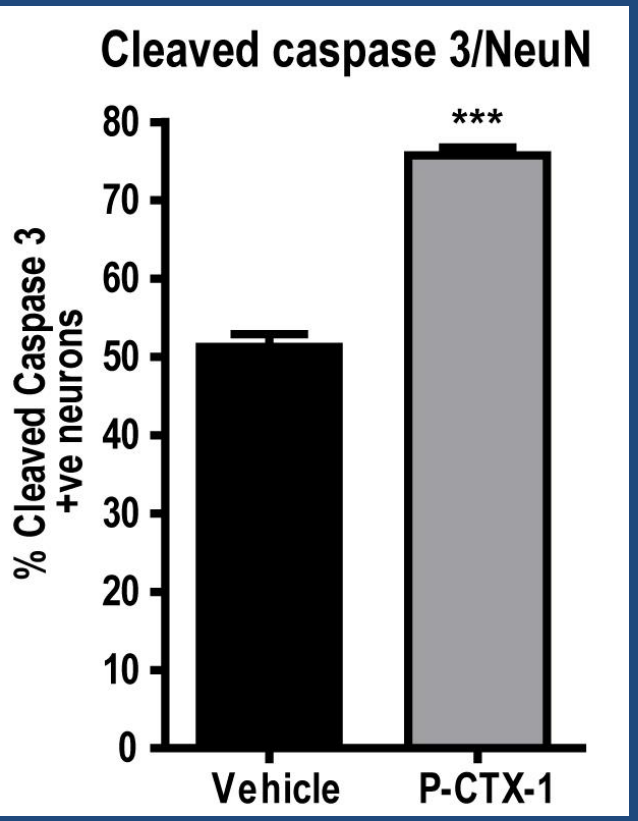

City University of Hong Kong
Department of Biomedical Sciences

Lab Members:

Bennett Au
Dr Gajendra Kumar
Pallavi Asthana
Kunal Kumar Singh
Virendra Bhagawan Chine

Collaborators:

CityU

Prof. Paul Lam
Dr. Leo Chan
Dr. Maggie Mak
State Key Laboratory of Marine Pollution

Dr. Chung Tin
Mechanical and Biomedical Engineering

Dr. Leanne Chan
Electronic and Electrical Engineering

Prof. Michael Lam
Biology and Chemistry

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