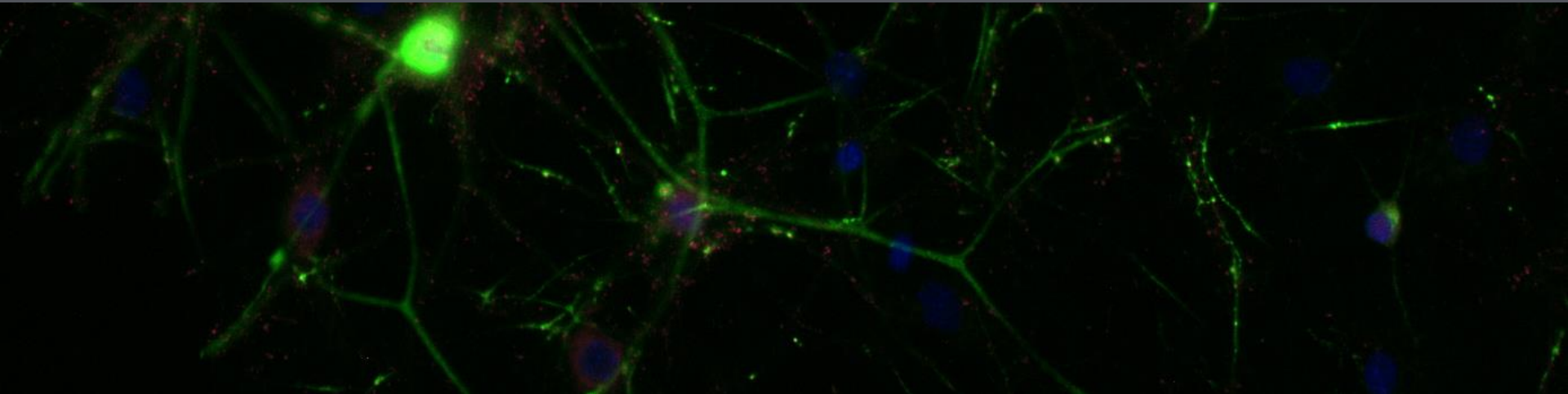


MODULATION OF VOLTAGE-GATED CALCIUM CHANNELS IN DISEASE



Gary Stephens¹ & Sumiko Mochida²

¹University of Reading and ²Tokyo Medical University

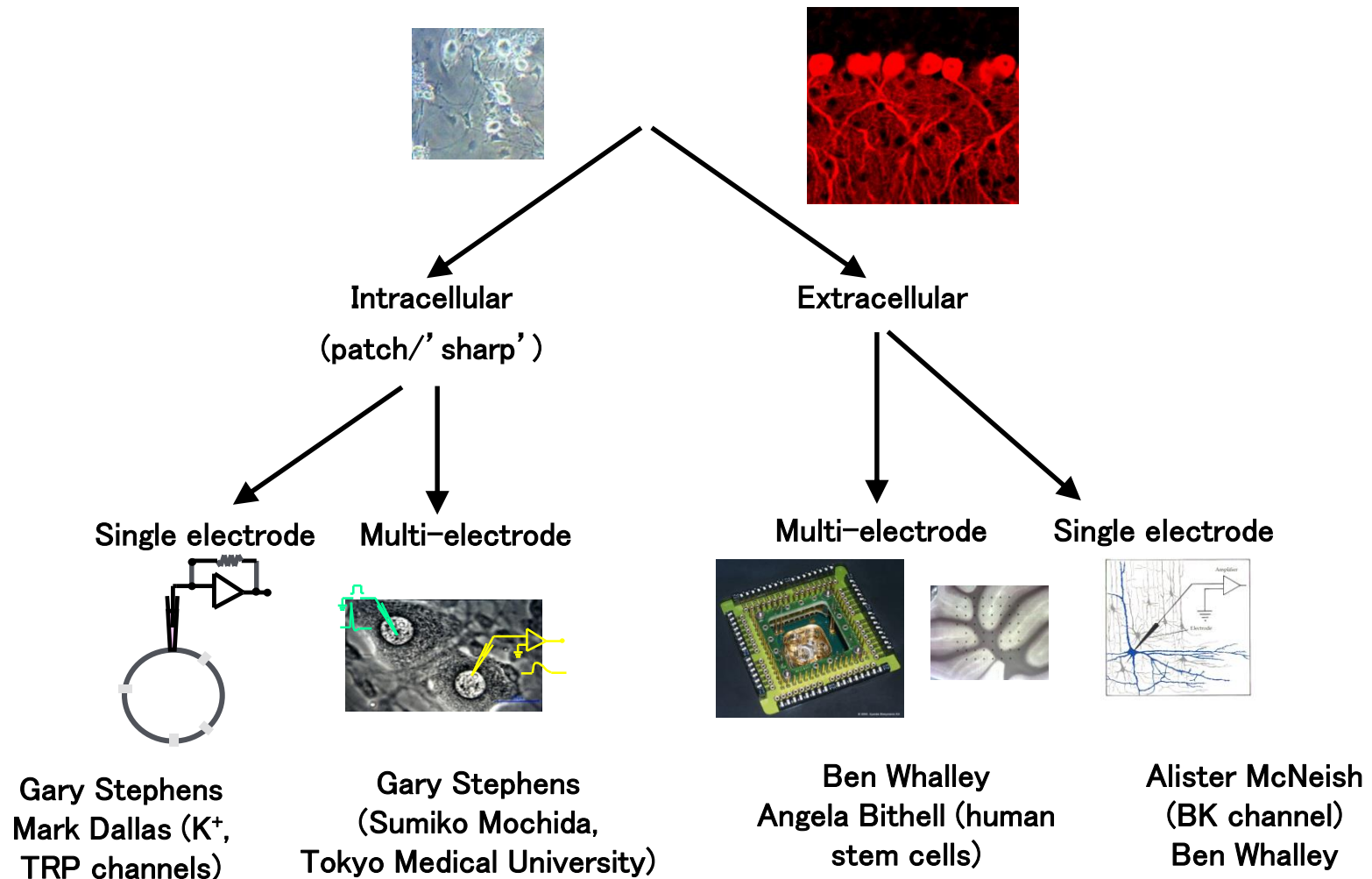
g.j.stephens@reading.ac.uk; mochida@tokyo-med.ac.jp

Advice on visiting Japan.....

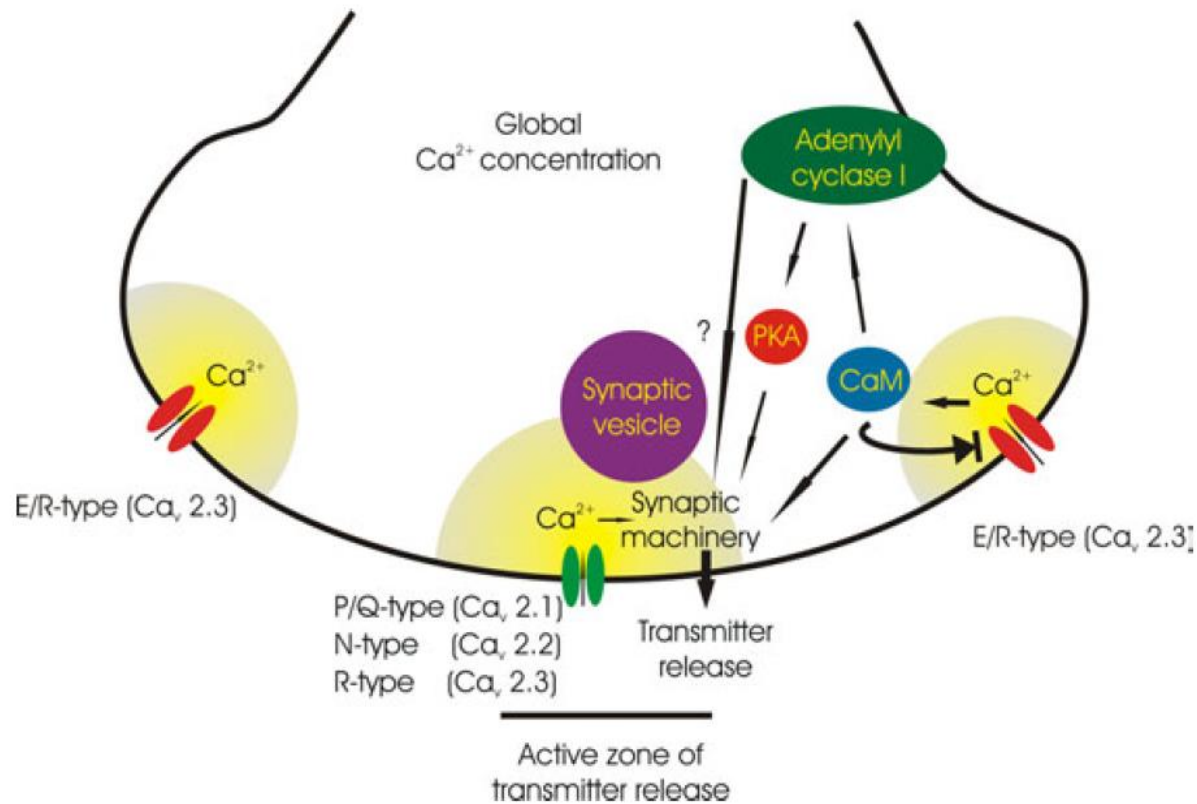
I first visited Japan in 1990 by ‘accident’

- Learn a few key Japanese phrases
- Be respectful of differences in culture
- A little thought (and common sense) largely negates these ‘differences’

Electrophysiology at Reading

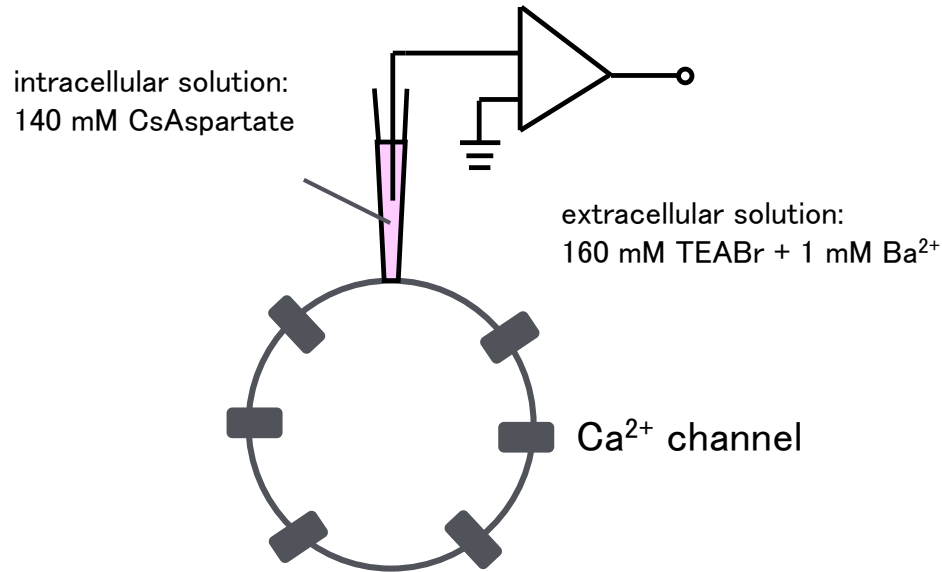


Voltage-gated Ca^{2+} channel synaptic function

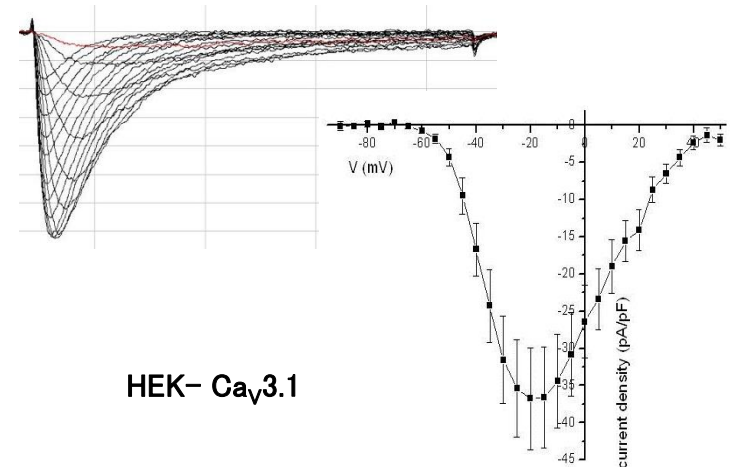
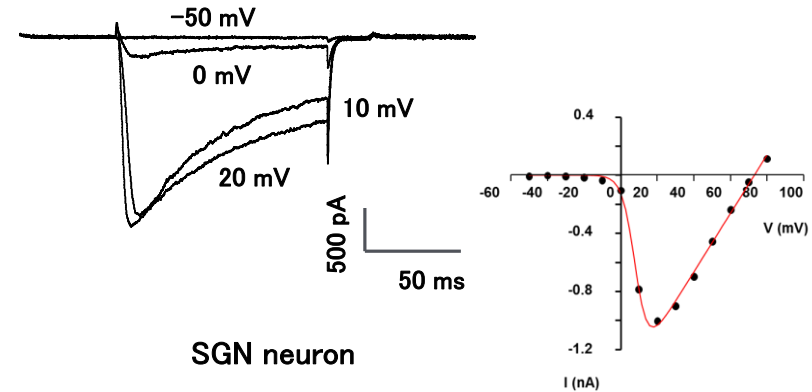


Kamp et al. EJM 2005; 21, 1617–1625

Patch clamp recording of Ca^{2+} currents



Transiently or stably transfected HEK cell/DRG/SCG neuron/brain slice neuron



Previous JPSP funded collaborations



Tokyo Medical University

東京医科大学

Since 1916

Previous JPSP funded collaborations



Tokyo (Shinjuku) and Mt. Fuji

Previous JPSP funded collaborations



Michinori Mori Sumiko Mochida Michikata Hayashida
Shota Tanifuji Huan Ma



Professor Sumiko Mochida
1999 Saruhashi Prize (猿橋賞)
(awarded to a Japanese female
researcher in the natural sciences.
Prize recognises accomplishments
in research as well as the
mentoring of other women
scientists)

Previous JPSP funded collaborations



The conveners of the gender equality seminar at the **Japan Neuroscience Society** meeting on July 20, 2016: Dr. Mami Noda (Kyushu University), Prof. Sumiko Mochida (Tokyo Medical University), Prof. Noriko Osumi (Tohoku University) with speaker Prof. Carol Mason (Columbia University)

Speaker at **WiSe UP** (Women in science forum founded at RIKEN)

Previous JPSP funded collaborations

1. **JSPS Postdoctoral Fellowship Program:** early career researcher in Prof. Stephens' laboratory, Christian Vogl, award to visit Prof. Mochida at Tokyo Medical University in Oct–Nov 2012.

Outputs: a poster presentation at the Biophysical Society meeting, San Francisco, Feb 2014 and a peer-reviewed publication:

Christian Vogl, Shota Tanifuji, Benedicte Danis, Veronique Daniels, Patrik Foerch, Christian Wolff, Benjamin J Whalley, Sumiko Mochida & Gary J Stephens “[Synaptic vesicle glycoprotein 2A modulates vesicular release and calcium channel function at peripheral sympathetic synapses.](#)” European Journal of Neuroscience (2015) 41:398–409

Previous JPSP funded collaborations

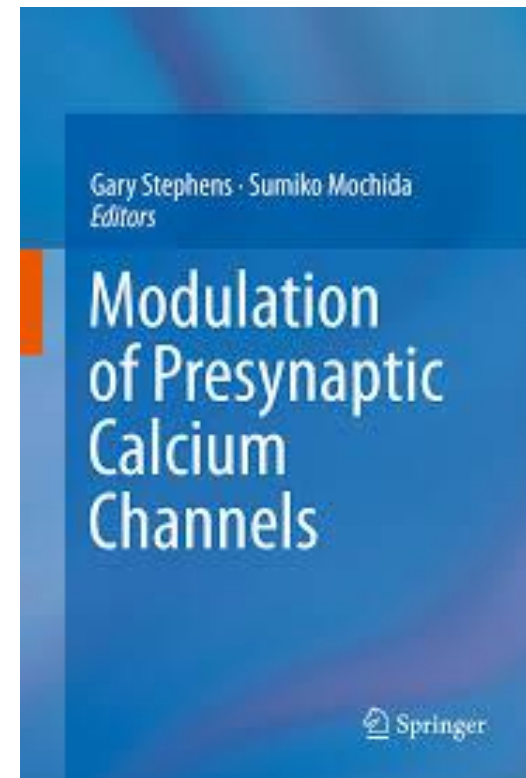
2. **JSPS Joint Research Project award** to Prof. Sumiko Mochida (Dept. of Physiology, Tokyo Medical University) with Prof. Stephens was the UK counterpart (see report: http://www.jsps.org/case_studies/2014/04/dr-gary-stephens-reading-university.html).

The funding allowed Prof. Mochida and three Japanese PhD students (Shoto Tanifuji, Michinori Mori and Michikata Hayashida) to make two research visits to University of Reading in July 2012 and Aug 2013 including attending a JSPS event at the London headquarters.

Previous JPSP funded collaborations

2. JSPS Joint Research Project award

Prof. Stephens and Prof. Mochida were supported in writing manuscripts and also acted as joint Editors on a book '*Modulation of Presynaptic Calcium Channels*' published by Springer in 2013 during this Joint Research Project.



Previous JPSP funded collaborations

3. **JSPS Short Term Fellowship award** to Prof. Stephens to visit Prof. Sumiko Mochida (Tokyo Medical University) (see report:

http://www.jsps.org/case_studies/files/alumni_activity_gary_stephens.pdf).

Outputs: work submitted as a communication at the forthcoming 37th National Meeting of the Spanish Society of Pharmacology in Barcelona June 2017

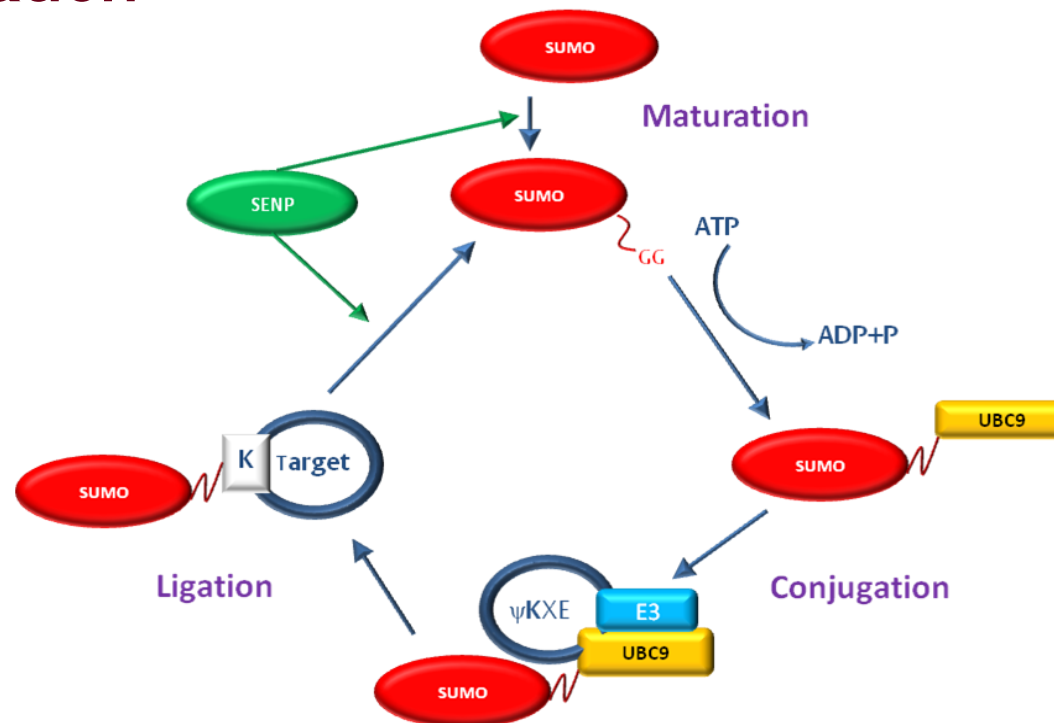
JPSP applications

JSPS BRIDGE application to visit Prof. Sumiko Mochida (Tokyo Medical University) in progress

Scheme for past fellows of JSPS programmes to revisit Japan to create, sustain and/or strengthen collaborative linkages with the Japanese academic community.

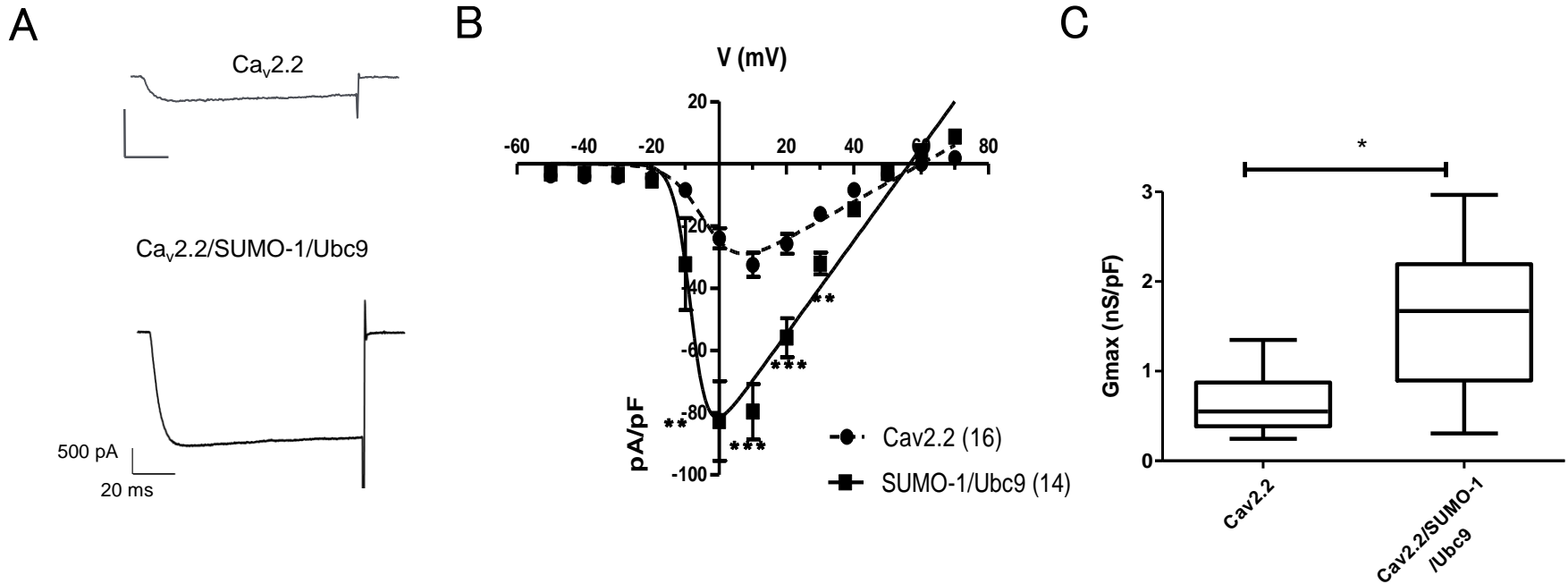


Modulation of voltage-gated Ca^{2+} channels by SUMOylation



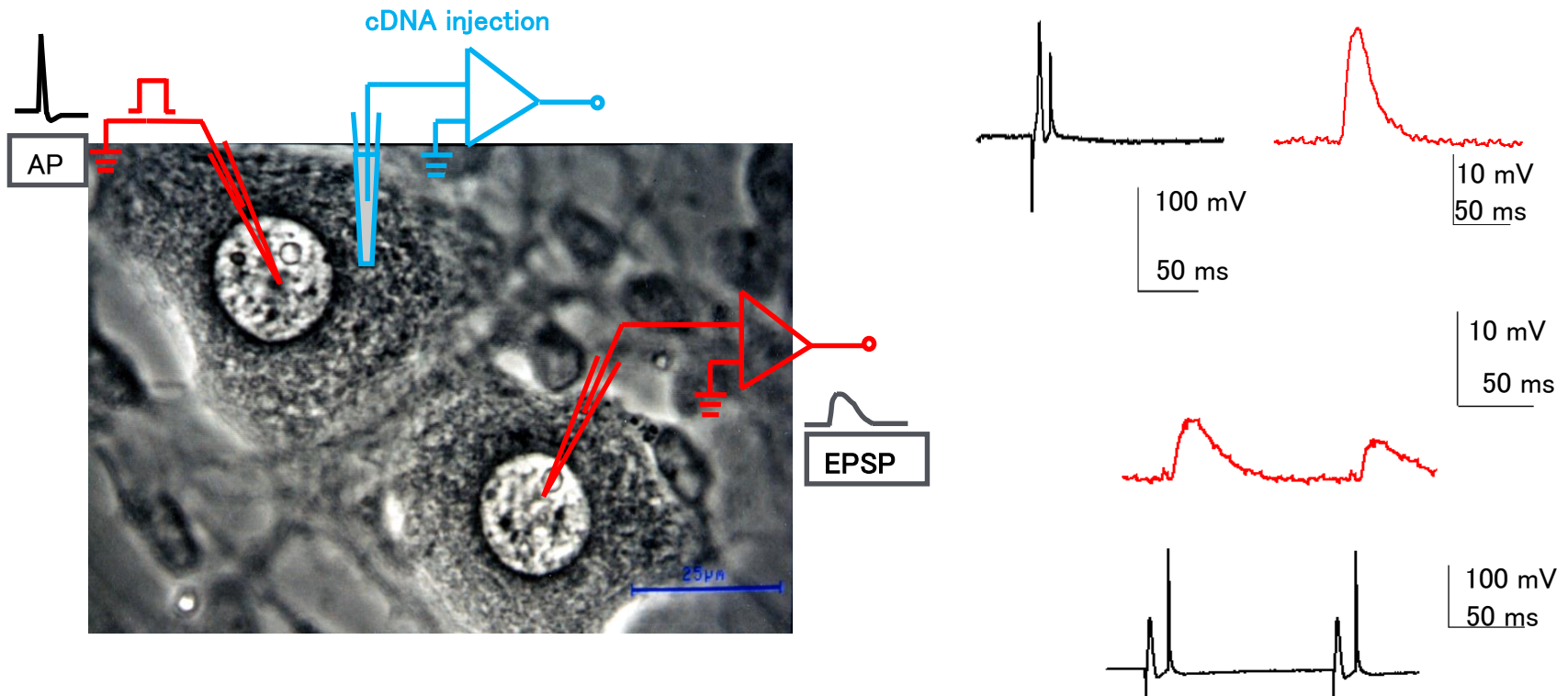
The SUMO-specific family of proteases, sentrin-specific proteases SENP, mature SUMO proteins revealing a double-glycine motif, which allows for SUMO to interact with target proteins. The conjugating enzyme Ubc9 facilitates this conjugation before the SENP family of proteases terminates the ligation.

SUMO-1 increases $Ca_v2.2$ Ca^{2+} current density

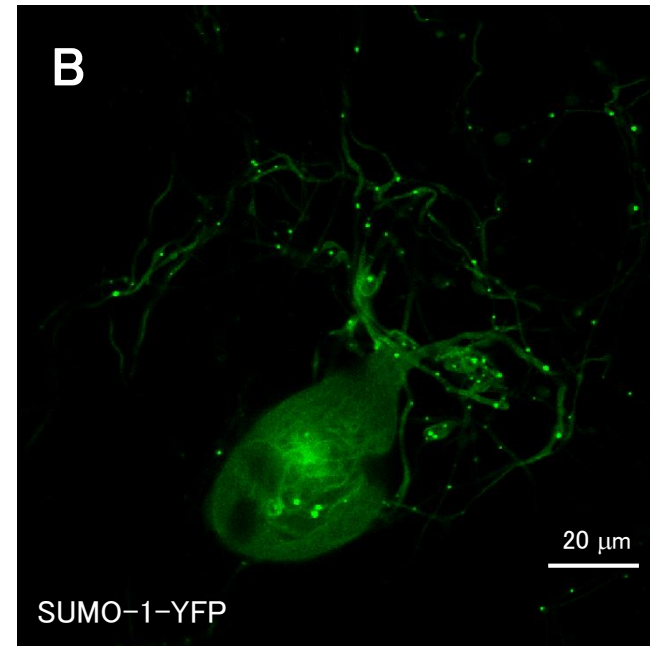
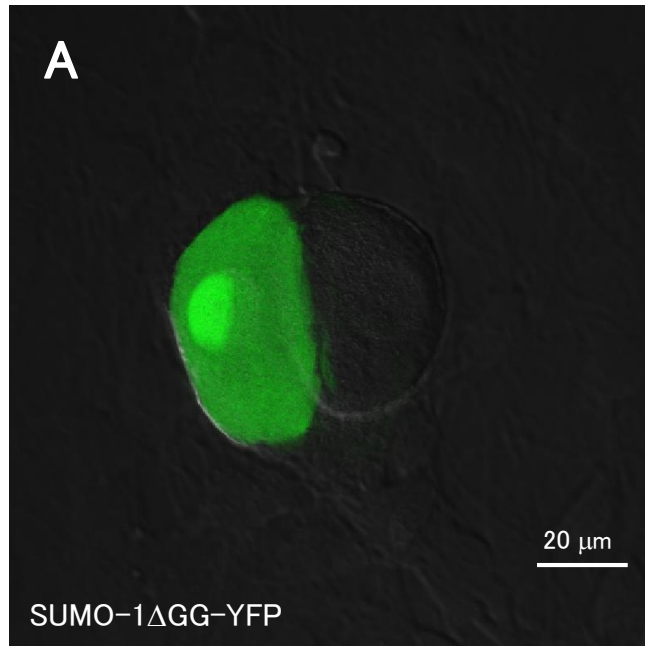


Silveirinha et al

SUMOylation effects on synaptic transmission/plasticity in superior cervical ganglion (SCG) neurons

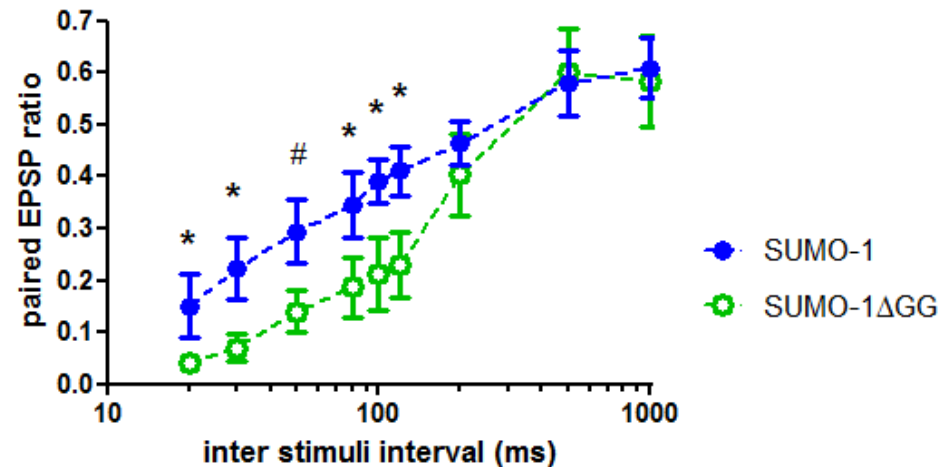
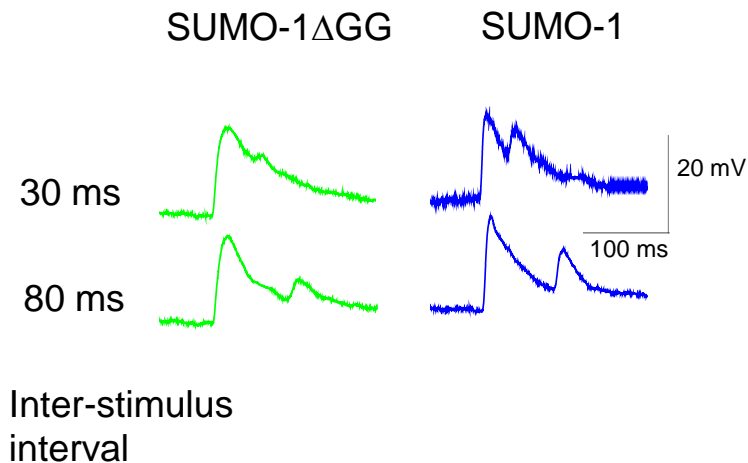


SUMO protein expression studies



Confocal images of SCG neurons 48 h after injection with
A) SUMO-1 Δ GG-YFP or B) SUMO-1-YFP constructs

SUMOylation effects on synaptic transmission/plasticity



SUMO-1 increases paired EPSP ratio in comparison to SUMO-1 Δ GG: data consistent with increased presynaptic Ca^{2+} levels facilitating vesicle release

Ca_v2.2 (N-type) voltage-gated calcium channels are activated by SUMO-1 protein

Ca_v2.2 (N-type) voltage-dependent calcium channels are targets for SUMOylation

Vasco C. Silveirinha¹, Hong Lin¹, Graeme S. Cottrell¹, Shota Tanifuji², Sumiko Mochida², Helena Cimarosti^{1,3} and Gary J. Stephens¹

¹School of Pharmacy, University of Reading

²Dept of Physiology, Tokyo Medical University, Japan

³Universidade Federal de Santa Catarina, Florianópolis, Brazil

To be presented at: 37th National Meeting of the Spanish Society of Pharmacology in Barcelona June 2017

Advice on visiting Japan

At work:

Hierarchy is important

Working patterns can be different to UK

After work:

Socializing can be an equally important way to learn about Japan and it's culture; enjoy the enkai.....

Pharmacology Group, Hopkins Building

