

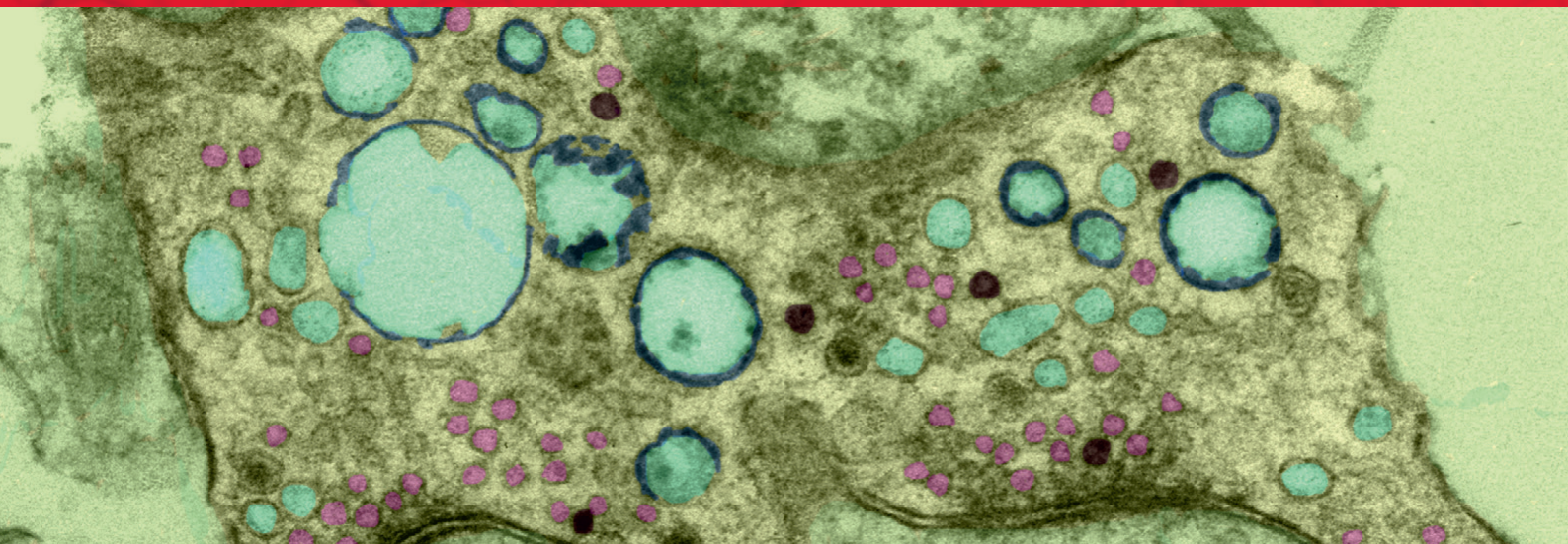
JNC

The Official Journal of the International
Society for Neurochemistry



Journal of Neurochemistry

VOLUME 150 | SUPPLEMENT 1 | JULY 2019



ISN-ASN 2019 Meeting
Montreal, Canada
4th-8th August 2019

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Aims & Scope

Journal of Neurochemistry focuses on molecular, cellular and biochemical aspects of the nervous system, the pathogenesis of neurological disorders and the development of disease specific biomarkers. It is devoted to the prompt publication of original findings of the highest scientific priority and value that provide novel mechanistic insights, represent a clear advance over previous studies and have the potential to generate exciting future research.

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Front cover

Image content: The false colour image shows two presynaptic nerve terminals after a train of neuronal activity which triggered neurotransmitter release followed by both clathrin-mediated endocytosis (CME) and activity-dependent bulk endocytosis (ADBE). In addition to existing synaptic vesicles (pink) and endosomes (light blue) new organelles generated by both CME (purple synaptic vesicles) and by ADBE (dark blue endosomes) are displayed. Image modified from original version in Clayton et al (2010) *Nature Neuroscience* 13: 845–851.

Read the full article '*Dynamin 1 phosphorylation by GSK3 controls activity-dependent bulk endocytosis of synaptic vesicles*' by Emma L Clayton, Nancy Sue, Karen J Smillie, Timothy O'Leary, Nicolai Bache, Giselle Cheung, Adam R Cole, David J Wyllie, Calum Sutherland, Phillip J Robinson & Michael A Cousin (*Nature Neuroscience* volume 13, pages 845 -851 (2010)) on doi: 10.1038/nn.2571

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MTU14-01

Expression of FMRFamide and GFSKLYFamide peptides in holothuria scabra: Implication for the neuroendocrine system

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Neuropeptides are key mediators of physiological processes in animals and a considerable amount of information has been accumulated on their diversity and functions across phyla. FMRFamide-related peptides are a large collection of neuropeptides found in invertebrates and vertebrates. They are identified by the possession of a C-terminal -RFamide amino acid sequence and are often coded for by multiple genes. Echinoderms are of phylogenetic importance to chordates in that they are deuterostomes. The sea cucumber, *Holothuria scabra* is a high-premium tropical echinoderm species that is overexploited globally and may be in imminent danger of extinction in some areas. Conservation of this species and its amenability to culture is however hampered by our limited knowledge of its biology, including the neurohormonal system. In this study, FMRFamide peptide, a cardioactive neuropeptide first isolated in a mollusk and GFSKLYFamide peptide, an Echinoderm SALMFamide were investigated for their presence in *H. scabra*. We used indirect immunofluorescence technique with confocal microscope and dot immunoblot assay utilizing polyclonal antisera raised against FMRFamide and GFSKLYFamide peptides. Both FMRFamide- and GFSKLYFamide-immunoreactivity were demonstrated to be widely distributed in *H. scabra* tissues, such as the radial nerve cord, body wall, intestines and coelomic fluid. This underscores the potential physiological roles of these peptides, which might be working as neurotransmitters and neuromodulators in this species.

MTU14-02

Promoting endogenous photoreceptor regeneration in the mammalian retina

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Regenerating the retina using endogenous stem cells is a promising therapy for vision restoration. While fish Müller glial cells (MG) can regenerate the retina, this natural ability was lost in mammals. Recently, however, some genetic manipulations in mouse MG were found to trigger neuron production, but it remains unknown whether MG can generate cone photoreceptors, which are essential for high acuity vision. Interestingly, MG have a similar gene expression profile to late-stage retinal progenitors, and our previous work identified temporal identity factors that can reprogram late progenitors to produce early-born cones. We hence hypothesized that these factors might reprogram MG into cone-producing progenitors. We co-electroporated Cre-dependent

constructs into GlastCre^{ERT};RosaYFP^{fl/fl} retinal explants, which express Cre^{ERT} specifically in MG, allowing expression of genes of interest and cell lineage tracing with the YFP reporter. Of the 21 combinations tested, one was able to reprogram MG into immature cones. MG-derived cells migrated to where cones normally reside, downregulated glial markers, started expressing the cone marker RxRg and adopted a cone-like morphology. These factors were also sufficient to reprogram MG to immature cones *in vivo* in the adult mouse retina, and into more mature cones under certain culture conditions. It remains to be determined whether these cells are functional, but this work suggests that stimulating cone production from endogenous glia might represent a new therapeutic opportunity for retinal degeneration.

MTU14-03

Inner hair cell and neuron degeneration contribute to hearing loss in a DFNA2-like mouse model

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DFNA2 is a progressive deafness caused by mutations in the voltage-activated potassium channel KCNQ4. Hearing loss develops with age from a mild increase in hearing threshold to profound deafness. The first phase starts around 10-15 years old, progressing to the last phase by the age of 70. Studies using transgenic mice for *Kcnq4* expressed in a mixed background demonstrated the implication of outer hair cells (OHCs) at the initial phase. However, it could not explain the last phase mechanisms of the disease. Genetic backgrounds are known to influence disease expressivity. To unmask the cause of profound deafness phenotype, we backcrossed *Kcnq4* knock-out allele to the inbred strain C3H/HeJ and investigated inner and outer hair cell and spiral ganglion neuron (SGN) degeneration across lifespan. In addition to the already reported OHC death, C3H/HeJ strain also exhibited inner hair cell (IHC) and SGN death. We tracked the spatiotemporal survival of cochlear cells by plotting cytochrome c oxidase (COX) and neuronal counts at different ages. Cell loss progressed from basal to apical turns with age for both hair cells. Interestingly, the time-course of cell degeneration was different for each cell-type. While for OHCs it was already present by week 3, IHC and neuronal loss started 30 weeks later. We established that OHC loss kinetics slowed down from basal to apical regions correlating with KCNQ4 expression pattern determined in wild-type mice. Our findings indicate that KCNQ4 plays differential roles in each cochlear cell-type impacting in their survival ability. IHC and SGN neuron death generates severe hearing loss that could be associated to the last phase of DFNA2.