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Editorial

General and comparative endocrinology: Special issue on insect neuroendocrinology and neurobiology

Insects comprise the most abundant and diverse group of animals on Earth and are often employed as small animal models in studies of fundamental and applied research. Insect neuropeptides and other endocrine factors are plentiful and many have structural and/or functional homologs in other animals, including humans. The study of insect endocrinology was pioneered nearly a century ago by Stefan Kopeć, who conducted a series of surgical experiments on the gypsy moth, *Lymantria dispar*, which led to the conclusion that pupation (and metamorphosis) is induced by a circulating substance that originates from the brain in the anterior portion of the animal which Kopeć termed as "head factor" (Kopeć, 1922). Soon after, using the kissing bug *Rhodnius prolixus*, Sir Vincent Wigglesworth decapitated early instars and fused the headless animals to late instars demonstrating that hormones from the final instar could induce metamorphosis in the earlier instar resulting in mini adults (Wigglesworth, 1934). Since these pioneering studies that provided some of the earliest documented evidence that humoral factors released into the circulatory system can control processes such as molting and metamorphosis, with the latter being a result of stage-specific differences in the hormonal composition of haemolymph, countless studies have contributed towards the advancement of insect endocrinology. In common with most other animals, the effects of neuropeptides along with biogenic amines are often mediated as hormones, regulating an array of behaviours and physiological processes including (to name a few) diapause, metabolism, water and ion homeostasis, chill tolerance and recovery, moulting and metamorphosis, innate immunity and reproductive biology.

This special issue in General and Comparative Endocrinology focuses on neuropeptides, biogenic amines, steroid hormones along with their cognate receptors and includes contributions from a number of leading insect biologists, biochemists and physiologists, whose research in one form or another is focusing on the neuroendocrinology and neurobiology of this diverse clade of arthropods, which represents the majority of animal species on the Earth.

In this issue, Jan Veenstra reports on an *in silico* analysis of the genomes of two phasmid insects (commonly known as stick insects) identifying neuropeptide genes along with several predicted receptor sequences (Veenstra, 2018).

Working on the cabbage looper moth *Trichoplusia ni*, Kolosov and O'Donnell report on the effects of helicokinin, a lepidopteran member of the kinin peptide family, demonstrating that this peptide alters fluid secretion rate and ion transport. Specifically, helicokinin inhibited fluid secretion by the Malpighian tubules and decreased K^+ secretion by principal cells while reducing Na^+ reabsorption by the secondary cells, which led to a reduction in the $[Na^+]/[K^+]$ ratio in the secreted fluid (Kolosov and O'Donnell, 2018). These findings greatly advance our understanding of the highly complex excretory system in this lepidopteran species.

Vafopoulou et al. report on their examination of the functional relationship between neuropeptides and serotonin in the circuitry associated with the circadian clock in the kissing bug, *Rhodnius prolixus*. In this study, these authors mapped allatostatin-A, crustacean cardioactive peptide, FMRFamide and serotonin analyzing their distribution within cell bodies and neuronal projections in relation to the primary circadian brain clock cells inferring integration with the clock including entrainment and the output leading to possible regulation of various brain neurochemicals (Vafopoulou et al., 2018).

Aside from their importance as disease vectors second only to mosquitoes, ticks are also important organisms for studies of comparative endocrinology and neurobiology since they share a number of conserved systems including neuropeptides and biogenic amines, along with their receptors. Kim et al. overview recent discoveries in relation to the neural and endocrine control of tick osmoregulatory organs, which are unique and differentially regulated in comparison to insects and are critical for coping with their haematophagous feeding strategies. Furthermore, these osmoregulatory organs also heavily contribute towards survival during the extended periods between blood meals, which often necessitates overcoming harsh environmental conditions (Kim et al., 2018).

A study by Bell et al. focused on the peptidergic regulation of the crop in the adult cabbage root fly, *Delia radicum*, which is an important agricultural pest of cruciferous vegetables in Europe. This study demonstrated that the decapeptide myosuppressin is present within innervation of the crop and through bioassay confirmed that this peptide acts to inhibit spontaneous contractions with potency in the nanomolar range. Moreover, while oral or injection delivery of the peptide had no detrimental activity on the adult cabbage root fly, feeding a non-peptide myosuppressin agonist increased mortality and decreased the rate of feeding of adult insects, an observation that will guide future studies in developing novel molecules useful as insecticides targeting pest species (Bell et al., 2018).

Employing heterologous expression of two arthropod kinin receptors to test a series of kinin analogs designed for increased biostability and bioavailability, Xiong *et al.* discovered a number of kinin mimetics that demonstrated high potency which may serve as candidate compounds for development of environmentally benign and selective agents for use against arthropods pests, including disease vectors such as ticks and mosquitoes (Xiong et al., 2018).

The next contribution involved another important agricultural pest, the cotton earworm, *Helicoverpa zea*. It focused on elucidating if three chemically distinct compounds that terminate pupal diapause each

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elicited a common response to the expression of a number of miRNAs, as well as transcripts that encode components of ecdysone signalling. The study's findings were quite interesting since, while all three agents resulted in similar effects in a subset of examined miRNA's and ecdysone signalling transcripts, this was not a universal phenomenon with certain diapause terminating agents eliciting distinct responses to miRNA and mRNA targets. These findings bring forward the notion that chemically distinct endocrine factors may elicit the termination of diapause in *H. zea* through unique signalling mechanisms (Reynolds et al., 2018).

While ecdysis triggering hormone and its receptor are chiefly known in controlling the normal behavioural sequence necessary for shedding of the cuticle during molting, Deshpande et al. report in their study an examination of the ecdysis triggering hormone receptor (ETHR) in the adult fruit fly, *Drosophila melanogaster*, demonstrating its involvement in courtship behaviour. Specifically, silencing ETHR in a subset of brain neurons, including local interneurons of the antennal lobes and *fruitless* neurons, resulted in pronounced incidence of male-male courtship behaviour. Furthermore, the authors utilized RNAseq to examine the potential molecular underpinnings of this observation. They identified changes in the expression of genes related to axonal guidance, chemosensation and courtship behaviour. Together, this study supports that ETHR plays a key role in antennal lobe chemosensory processing with an influence on courtship behaviour in *D. melanogaster* (Deshpande et al., 2018).

Calkins et al. provide an update on the first publication of the draft genome of the red imported fire ant, *Solenopsis invicta*, expanding our knowledge of G protein-coupled receptors (GPCRs) in this highly invasive social insect. Through this extensive data mining effort, the authors provide an organized and curated resource for GPCRs and related G protein subunit genes in this social hymenopteran insect, since previous to this current work only an estimate of the number of genes encoding GPCRs was documented. Importantly, these authors also investigated the potential involvement of differentially expressed GPCRs and G proteins in the brain transcriptomes of different castes, including workers, mated queens and alate virgin queens. This revealed that a number of GPCRs and G proteins are indeed differentially expressed in the brain transcriptomes of queens and workers, indicating that these transcripts may be involved in the extreme division of labour in this species (Calkins et al., 2018).

Finally, the concluding manuscript in this special issue reviews the evolutionary origins of insect seminal fluid proteins (SFPs), which are examples of intraspecific influential proteins since they can affect the behaviour and physiology of conspecifics, particularly individuals of the opposite sex. Here, Laura Sirot discusses the production of insect SFPs in specialized reproductive organs, the possible origins of SFPs from an evolutionary perspective as well as the regulatory mechanisms, which include hormonal factors such as juvenile hormone and ecdysteroids, acting upon the specialized glands that synthesize SFPs. Furthermore, the author also discusses the possibility of evolutionary co-option of novel factors acting as SFPs discussing adipokinetic hormone as an example, whose expression is most largely documented in neurosecretory cells of the corpus cardiacum in insects, but which has been shown to be expressed in the male reproductive tract of *Aedes* mosquitoes and is believed to be transferred to females during mating (Sirot, 2019).

We would like to sign off by thanking all the authors who contributed towards this special issue, as well as all the expert reviewers who critiqued and provided important insight to improve the submitted manuscripts. Lastly, thanks to Editor-in-Chief, Dr. Deborah Power, for the invitation and opportunity to serve as guest editors of this special issue.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygcen.2019.05.002.

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