INTERNATIONAL PEST CONTROL

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nEUROSTRESSPEP: Novel biocontrol agents for insect pests from neuroendocrinology

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Insect pests, left: Pine bark beetle, Hylobius abietis; right: Desert locust, Schistocerca gregaria

Seventy-five percent of food crop species are dependent on insect pollination, although insect pests cause enormous social, health and economic costs via crop, post-harvest and storage damage. In addition to direct plant or storage damage, insect vectors frequently transmit pathogens including bacteria and viruses. All this results in yield and/or quality losses and without pesticide use, it is estimated that global food production would drop by 40% (European Crop Protection Association). Moreover, new threats from invasive alien insect species have also arisen from the increased global movement of people and goods (Food and Agricultural Organisation of the United Nations) and threaten agriculture, horticulture and forests.

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There is thus a global dependence on pesticides, although there is insect resistance to current insecticides, and very few new insecticides have come to market in the last decade. Moreover, the challenge for insect pest control is dynamic, as pests adapt and new pests emerge, as climate change has already resulted in the emergence of non-native insect crop and forestry pests across the globe, reflecting a trend from the equator to the poles[1]. In addition, environmental concerns including reduction of conventional insecticide use and implementation of environmentally friendly, integrated and sustainable pest management approaches including pollinator protection and reduced residues, pose challenges for the insecticide industry. Moreover, consumer perceptions towards pesticides also drive innovation in development of plant protection strategies, e.g., 31% of EU residents list chemical residues from pesticides as major concerns (Special Eurobarometer, Food-related Risks, 2010). Altogether, this suggests that development and availability of novel biopesticides for control of specific insect pests is extremely timely, and meets a significant and growing market need, as the global biopesticides market is projected to exceed $6.9B by 2019 (BCC research).

Spotted wing fruit fly, Drosophila suzukii

A current European Commission H2020 programme, nEUROSTRESSPEP (EC project no. 634361, 2015-2019, nEUROSTRESSPEP.eu) is developing novel biopesticides based on insect neuropeptides. Neuropeptides regulate insect physiology and development, including water and ion balance, ecdysis, environmental stress tolerance, feeding, growth and metabolism, and reproductive behaviour[2] and so are crucial to insect survival. Understanding and disrupting these pathways via peptide 'mimetics' or analogues thus affords new ways of targeting insects to reduce their survival, via distinct modes of action from conventional insecticides[3-6].

Peptide-based insect control agents have many advantages as follows: they are not categorized as known or potential toxic compounds, and importantly do not have human counterparts. They can be designed as 'insect pest-specific' compounds and so reduce impact on non-target insects including pollinators, and can be applied like conventional pesticides. They are rapidly excreted and so reduce cumulative risk, and are degradable with a controlled half-life, and thus less likely to engender insect resistance due to degradation and reduced accumulation in the environ-

ment. Finally, rationally designed small peptides can form a basis for low-residue or residue-free products; and will meet increasing consumer demand for low- or no-residue, fresh, unprocessed produce.

The nEUROSTRESSPEP consortium, comprising 14 partners drawn from European and international research organisations, agencies, advisors and companies, is deploying research- and market-led strategies towards innovative peptide-based biopesticides for the agricultural, horticultural and forestry sectors. Research-based expertise and activities include insect genetics/genomics, insect neuropeptide identification and function, environmental/metabolic stress survival, insect toxicology, cutting-edge 'omics' technologies, imaging technologies, high throughput screening, development and use of analogues, compound formulation, plant protection, pest and disease monitoring, integrated pest (and forest) management, field trials and demonstrations and genetic pest management.

There are numerous insect neuropeptide families that modulate a range of physiological responses over a vast number of insect species[2], so to deliver the work programme, a targeted approach for selection of neuropeptide families and specific insect species has been undertaken. This is based on end-user need, prior art (data, techniques, field trials), and potential for intervention by genetic means or novel mimetic analogues. Target insects include key beetle, moth, aphid and fly pests e.g., *Drosophila suzukii*, of agriculture and horticulture; and the forestry pest, the pine bark beetle. nEUROSTRESSPEP is also working on targeted disruption of locust survival, specifically *Locusta migratoria* and *Schistocerca gregaria* which are swarming agricultural pests of the Southern Mediterranean, Middle East, Asia and Africa. nEUROSTRESSPEP is also tackling invasive, emerging pest species by using 'omics' technologies that include deciphering the complete genome of these insects to identify 'weak' points in their armoury.

The consortium has developed mimetic agonist and antagonist analogues of a number of insect neuropeptide classes with enhanced bio-stability and bioavailability. nEUROSTRESSPEP has now demonstrated success with several bio-stable peptide analogues, which reduce insect fitness and/or disrupt critical life processes in laboratory trials. Work is also continuing with trials on beneficial insects, and in other areas leading to trials outside the laboratory. The nEUROSTRESSPEP project will also deliver new platform technologies for novel insect biocontrol agents applicable to a range of insect species and habitats based on peptide hormone analogues and insect synthetic biology for genetic pest management.

Current control of insects is reliant on chemical approaches, with attendant issues of legislation, protection of beneficial insects, insecticide resistance, and environmental sustainability - and so requires novel tools. For the first time, 'Beyond the State-of-the-Art' approaches in neuroendocrinology are being utilised to develop biocontrol agents for multiple insect pest species across agriculture, horticulture and forestry.

Insect pests, from top: Bordered straw moth, Heliothis peltigera, Peach potato aphid, Myzus persicae; gregaria; Red flour beetle, Triblolium castaneum

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