Biological and chemical approaches towards combating resistance in agriculture

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Securing food security for 9 billion people in 2050, addressing the realities of climate change and reduced resources such as land and water are the “Grand Challenges” facing feeding the world today¹. Over the past fifty years, very significant advances have been made in improving agricultural productivity; however, resistance issues are currently threatening some of these hard won gains. Successfully combating resistance will be an essential component of securing food security and protecting the food we have from pests such as insects, nematodes, fungi and weeds. If ignored, pest resistance will significantly reduce worldwide agricultural production at a time when crop yields have to increase in order to feed everyone healthily and equitably.

This special edition of the Journal of Chemical Biology highlights the role chemical biology plays in addressing the challenges associated with combating chemical resistance in agriculture. The articles are from a symposium entitled “Biological and Chemical Approaches Towards Combating Resistance in Agriculture” which was sponsored by the Biological and Medicinal Chemistry Sector and Chemical Biology Interface Division of the Royal Society of Chemistry, in partnership with the AGRI-net, Bayer CropScience, Syngenta and the Biochemical Society. The symposium was held at Imperial

College, London on the 26th of September 2013. Unusually, it brought together expert scientists from all three of the most important resistance areas, namely fungal, insect, and plant (weed) resistance.

The special edition features six papers from authors who participated in the London symposium. The articles exemplify the diversity of science needed to combat resistance, ranging from modelling and prediction (van Westen), metabolism (Parker *et al.*) and biochemistry (Hahn) to molecular characterisation of complex receptors (Crossthwaite *et al.*) and how herbicide resistance parallels can be drawn between insecticide and fungicide resistance mechanisms (Strek).

Chemical Biology is developing rapidly as a scientific discipline in agricultural research; it relies on the integration of a wide range of scientific disciplines and has been greatly facilitated by the creation of a BBSRC-funded network in agricultural chemical biology, the AGRI-Net, who co-hosted the symposium. It also relies on the availability of chemical and biological tools to generate and test hypotheses. The article by Torsten Meiners on EU-OPENSREEN illustrates an exciting opportunity for researchers to access chemical and screening tools across the European Union. This enables the creation of a chemical biology infrastructure facilitating research in plant biology, ecology, marine, and microbial biology.

Gerard van Weken from EMBL writes about another tool needed to realise the potential of chemical biology in agriculture: molecular modelling. He discusses proteochemometric modelling (PCM) as an aid in the quantification and prediction of resistance, comparing the opportunity to the successful application of PCM in medicinal chemistry.

Along with a toolkit, we also need knowledge of the molecular mechanisms of resistance. Andrew Crossthwaite and his colleagues from Syngenta illustrate the challenges associated with combatting Neonicotinoid resistance where we do not have a key piece of knowledge; how the target

¹ Food and Agriculture Organization of the United Nations; see <http://www.fao.org/docrep/u8480e/u8480e0a.htm>

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protein, the multi-meric nicotinic acetylcholine receptor, nAChR, assembles in vivo. To date, no one has successfully expressed a multi-meric insect nAChR in a heterologous cell system. Despite this, we know a lot about both metabolic and target-site resistance to Neonicotinoids. The paper discusses both mechanisms and focuses on the complexity of the system and the implications for chemical design.

Harry Streck from Bayer CropScience also discussed the mechanisms of resistance but this time focusing on herbicides and how other disciplines have influenced herbicide resistance research. Weed resistance is such a big issue that some farmers in the USA have gone back to mechanical weeding, despite the negative implications in terms of cost and soil erosion which this entails. This paper raises the spectre that herbicide resistance threatens modern agriculture and could be as problematic as late potato blight and the spread of Colorado potato beetle in the past. Without modern herbicides, crop yields will not be sufficient to address the challenges we face in feeding a growing population.

The final two papers in this special edition focus on fungicide resistance. In the past, infection by fungal pathogens has caused major crop failures resulting in widespread famine. These pathogens are still present in our fields but are held in check by the application of fungicides. Matthias Hahn discusses the rising threat of fungicide resistance using *Botrytis* as a case study, which illustrates the diversity of metabolic mechanisms underpinning resistance. During the symposium, Steve Kelly focused on the resistance mechanisms of the azole fungicides that act on the P₄₅₀ enzyme CYP51. This important mode-of-resistance work is detailed in the paper by Parker *et al.*

The symposium was unique in bringing together over 70 delegates from both industry and academia to focus on the issues associated with agrochemical resistance, and the role chemical biology can play in finding solutions. This special edition of the Journal is intended to stimulate informed scientific debate by highlighting the challenges we face in combating resistance and its impact upon the grand challenge of feeding an increasing world population.