Meeting report

Host–parasite interactions: resist or tolerate but never stop running

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A conference exploring ‘The impact of the environment on innate immunity: the threat of diseases’ was held on 4–9 May 2009 in Obergurgl, Austria, thanks to the support from the European Science Foundation, Innsbruck University and the Austrian Science Foundation. The goals of the conference were to explore how the outcomes of host–parasite interactions depend on variation across individuals, their parasites and the environment in which they both find themselves. Central themes were the inherent costs of mounting an immune response, the ability of some organisms to preempt infection by ‘priming’ their immune systems, the fact that parasites learn to evade immune responses over time and the use of theory to predict when diseases will get out of hand. Many of the systems presented had clear impacts on human health, agriculture or the maintenance of complex ecosystems. There was common ground throughout in developing methodologies and embracing what one of the organizers termed the ‘interactome’ between hosts and those which would exploit them.

Keywords: innate immunity; immune memory; host–parasite interactions; antimicrobial peptides; epidemiology; Red Queen

1. INTRODUCTION

Approximately 100 students, researchers and teachers met at the University of Innsbruck’s alpine conference centre to share thoughts and advances related to how plants and animals fend off disease and how external factors weigh in on the outcomes of disease battles. Co-organizers Joachim Kurtz (University of Muenster), Sophie Armitage (University of Muenster) and Paul Schmid-Hempel (ETH-Zurich) built a diverse programme around theoretical and empirical advances in this field. The conference built on a 2007 meeting (Carpenter *et al.* 2008) at the same scenic alpine venue by expanding discussions of immune mechanisms to cover on-the-ground (or in-the-pond) interactions that help shape the lives of organisms. Below are several thematic highlights along with emergent directions for resolving the mechanics and outcomes of host–parasite encounters.

2. AN ARMY MARCHES ON ITS STOMACH: COSTS OF IMMUNITY

Defences raised to reduce the impacts of parasites are not without costs. These costs might be purely

energetic, brought on by the production of expensive immune-related proteins and cells, or they might arise from autotoxicity implicit in immune function. Caterpillars appear to counter the costs of induced defences by shifting their diet preferences to a more protein-rich food (Ken Wilson, University of Leicester), while honey bees use plant resins as a low-maintenance barrier for microbes (Michael Simone, University of Minnesota) and leafcutter ants enlist the help of a beneficial bacterial associate (Sophie Armitage, University of Muenster). Jens Rolff (University of Sheffield) described a case of autotoxicity, whereby a defensive response by beetles can lead to organ damage later on. Similarly, the worst impacts of filarial disease in humans come not from the worms themselves but from an overactive immune response to them and their *Wolbachia* bacterial associates (Ken Pfarr, University Clinic-Bonn). Over evolutionary time, the tradeoff between strong immune function and fitness in a parasite-free world was signalled by shortened lifespans for immune-competent flies (Matthew Tinsley, Stirling University).

3. RED QUEENS AND THE INTERACTOME

Hosts are constantly working to outpace their parasites, a process forever linked by Van Valen (1973) to the poor Red Queen in Lewis Carroll’s ‘Through the Looking Glass’ who is constantly running just to stay in one place. Red Queen dynamics reflective of an escalated arms race were shown for nematode worms and a bacterial pathogen (Rebecca Schulte, University of Osnabrück). Similarly, selection favouring rare host genotypes that evade or deter the prevailing parasite lineages can drive a continuous circle of variation in important immune traits. This was shown brilliantly for the crustacean *Daphnia*. Thanks to stratified ‘seed banks’, *Daphnia* clones were experimentally exposed to their past, present and future parasites, showing that the parasite currently at hand is often the worst kind (Ellen Decaestecker, University of Leuven).

Co-organizer Paul Schmid-Hempel (ETH-Zurich) recommended a framework for understanding short- and long-term relationships between hosts and parasites that explicitly accounts for the fitness parameters of each as well as their tools for deterring or exploiting the other. This ‘interactome’ depends upon the life histories of both partners, their specific genotypes and aspects of their biotic and abiotic environment that influence the host–parasite dance. The resulting reaction norms might be used to predict when diseases will be manifest in nature and to predict the selective forces that shape how interactions will be shaped by evolution. Critical hosts might reduce parasite damage through resistance (attempts to actively clear the body of invaders) or tolerance (attempts to limit the damage, e.g. sequester or otherwise enfeeble parasites or repair the self-inflicted damage of an immune response). David Schneider (Stanford University) described complex responses by fruitflies challenged with different bacterial pathogens. Depending on the bacterial threat, genetically identical flies sometimes eliminated the agent, sometimes coped through tolerance and other times did neither well. From the parasite viewpoint, discussions touched on whether virulence was driven by a need to disable host defences, to grow more quickly or to (rarely) change

host development or behaviour in order to escape a destroyed carcass. Virulence in the field often reflects the interactions of hosts with two or more parasites, and it is clear in mosquitoes (Yannis Michalakis, CNRS-Montpellier and George Christophides, Imperial College) and bees (Jay Evans, US Department of Agriculture) that interactions among parasites can play a role in the realization of parasite virulence.

Some of the more gripping examples of virulence involve parasite efforts to change host behaviour. As one example, parasitized *Gammarus* amphipods swim towards both light and their fish predators, behaviours that can be best understood from the standpoint of an internal parasite seeking entry into its final host. Resistant *Gammarus* individuals appear to be of two minds whether to swim towards light, fish or neither (Thierry Rigaud, University of Bourgogne).

4. REPEAT OFFENDERS AND IMMUNE MEMORY IN NATURAL SYSTEMS

Claims that organisms without bones show immune ‘memory’, the ability to respond adaptively to a parasite seen previously, have been greeted with some scepticism, despite compelling evidence from experimental studies (Little & Kraaijeveld 2004; Schmid-Hempel 2005). This criticism has focused primarily on the lack of an apparent mechanism for this phenomenon (Rowley & Powell 2007), as invertebrate immune memory must depend on wholly different mechanisms for adaptive immunity than those shown by jawed vertebrates. Recent efforts have identified new cases of immune memory along with plausible mechanisms to achieve this (Joachim Kurtz, University of Muenster). An interesting variation on this theme occurs when parents ‘prime’ their offspring with adaptive cues related to likely disease agents (Moret 2006). Such trans-generational signals, and the degree to which offspring might respond adaptively, are hot topics in invertebrate immunology and the phenomenon has been shown in Crustacea and bees. Olivia Roth (ETH-Zurich and University of Muenster) described a remarkable new case of immune transference by both male and female parents in beetles. Given the above tradeoffs, efforts by parents to stimulate the immune function of their offspring require reliable cues, lest they instead only fate their offspring to shorter lives.

5. FLU CASTING: PREDICTING THE SPREAD AND IMPACTS OF DISEASE

Several speakers spoke of the difficulties inherent in predicting and explaining real-world incidence of disease. Startling population declines in bees, birds, corals and amphibians have been correlated with parasite pressures. In corals, the outcome of host–parasite interactions appears to be sensitive to changing water temperatures (Caroline Palmer, Newcastle University), perhaps in combination with as-yet unresolved interactions among microbial players (Eugene Rosenberg, Tel Aviv University). Amphibian losses worldwide have been associated with a slow-growing chytrid fungus (Longcore *et al.* 1999). While amphibians have a robust epithelial defence system (Michael Zasloff, Georgetown University) here, again, abiotic

factors seem critical in how well this system works (Robert Puschendorf, James Cook University; Douglas Woodhams, University of Zurich). Even with the help of 25 000 observant citizen scientists, predicting the continued spread of a mycoplasma that causes an important eye disease in house finches and other birds has proved challenging (Andrew Dobson, Princeton University). Understanding this disease requires a fuller understanding of strain effects on virulence, of the rates of pathogen ‘spillover’ from birds raised in agricultural settings and of the historical and current limits of gene flow and social contact in bird hosts.

Finally, the workshop took place near a peak of worries over human transmission of H1N1 and other influenza strains, spurring keen interest in the reliability of epidemiological predictions. Attempts are underway to predict the incidence of key human diseases from flu to meningitis and malaria and to develop immunization strategies where appropriate. These attempts will require an understanding of how parasites assess and evade immune responses and of the shifting landscape of immunity in their potential human hosts (Sunetra Gupta, Oxford University).

6. PAST, PRESENT AND FUTURE

Like all scientific endeavours, understanding the above interactions will benefit from technological advances, ranging from high-throughput sequencing to frog thermometers. Still, the enduring message from this workshop was the strength of evolutionary theory and rigorous hypothesis development, testing and improvement for making sense of the winners and losers of host–parasite battles. This was a fitting realization in the 200th year since Darwin’s birth.

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