



**RESEARCH CONFERENCES**

ESF-FWF Conference in Partnership with LFUI

# The Impact of the Environment on Innate Immunity: The Threat of Diseases

Universitätszentrum Obergurgl (Ötz Valley, near Innsbruck) • Austria  
4-9 May 2009

Chair:

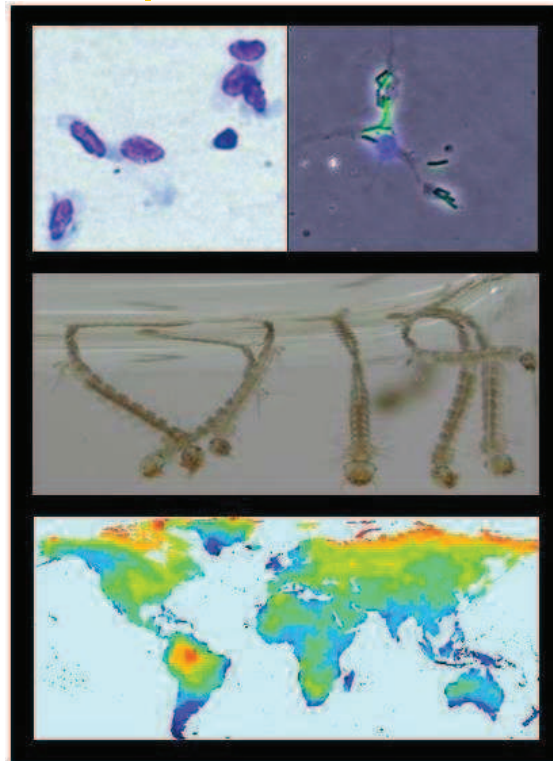
**Joachim Kurtz**, University of Münster, DE

Co-Chairs:

**Sophie Armitage**, University of Münster, DE

**Paul Schmid-Hempel**, ETH Zürich, CH

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## Conference Highlights

*Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)*

Almost 100 scientists met at the University Center in Obergurgl in the Austrian alps to discuss issues of the impact of the environment on infectious diseases, in particular the relevance of innate immunity. The conference was based on the general observation that host-parasite interactions, irrespective of whether they are caused by bacterial parasites or macroparasites, show a large degree of variation due to both genetic differences (in hosts and their parasites) and environmental factors. Even though such systems show a huge amount of variation, it became clear during the conference that there are several general principles that help when comparing different systems and drawing general conclusions. One of the main principles the conference was based upon is the mutual evolutionary adaptation of host and parasites, which may lead to coevolutionary arms races. Another general concept is that immune reactions are normally costly to hosts, such that there are trade-offs with other life-history traits. It became clear that innate immunity, as a first-line defence that is often active long before an adaptive immune response starts, provides a vital protective barrier against a large range of pathogens and parasites. While we start to gather more knowledge on how this system works in diverse animal taxa, it turns out that these innate defence systems are far more complex and elaborate than anticipated. Several talks showed that innate immune systems are influenced by a range of environmental factors. As a consequence, it is currently hard to predict what exactly the effect of global change on innate defence and therefore the spread of novel parasites will be. However, the in-depth study of natural host-parasite systems and disease dynamics in the field can provide useful information. Accordingly, some of the most fascinating examples from the conference included such studies, for example, of bacterial diseases of corals, and emerging diseases in frogs, bees and birds. It became clear that such studies could provide us with useful knowledge about general principles that may also help us to have a better understanding of human infectious diseases.

I hereby authorize ESF – and the conference partners to use the information contained in the above section on ‘Conference Highlights’ in their communication on the scheme.

# Scientific Report

## Executive Summary

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(2 pages max)

The major challenges for the 21st century include facing the consequences of climatic change, degradation and pollution of the environment, together with a trend towards larger and denser human populations. Stress imposed by deterioration in the environment is likely to compromise the immunological protection of all organisms, and these anticipated environmental alterations will bring with them new selection pressures on the immune system and corresponding evolutionary changes. Even though our knowledge of these issues has made considerable progress over the last decade, we still lack a good understanding about how pathogens on the one hand and the innate immune defence of the host on the other, will adapt to such unprecedented and rapid environmental changes, and consequently what impact this will have on the spread of diseases. The objective of this conference was to directly address these issues with a programme containing talks by the most innovative researchers at the forefront of their fields. Indeed the timeliness and importance of understanding more about parasite jumps into novel hosts and the spread of diseases was highlighted by the outbreak of swine flu just a few weeks before the start of the conference.

The focus of the conference was on innate immune defence, as this is the first line of defence that an organism has and is therefore a prime focus for where new diseases can be controlled; innate immunity is also evolutionarily ancient and found across taxa, meaning that we may be able to find general principles that would apply to more than just the model organism. To help us to fully understand the current issues and the future perspectives for host-parasite interactions and disease spread in changing environments, it is necessary to be aware of different ways of addressing this problem, so we aimed for an interdisciplinary approach, bringing together researchers working on 'how questions' (proximate mechanisms) and 'why questions' (ultimate evolutionary), and in a wide range of model organisms.

Five themes on the broad topic of the threat of diseases were spread across four days. We started with an introduction to the principles of innate immune defence and how this knowledge has been applied therapeutically. Host-parasite interactions came next, with an introduction to general principles as well as specific examples from humans to crustaceans. The third theme discussed the effect on innate immunity of a range of environmental stressors, such as marine and freshwater pollutants, and how the environment can affect resistance to disease. The model systems and vectors of disease that were introduced in the fourth session focussed on the mosquito as a vector of malaria, and how the fruit fly has been successfully used as a model for innate immune defence. Finally, theme five covered research relating to how innate immunity may be affected by a changing world, for example the spread of emerging diseases in frogs and house finches. In addition the talks were complemented by evening poster sessions that facilitated more discussions.

In spite of the variety of approaches and systems, some general principles could be distilled from the conference. For example, the mutual evolutionary adaptation of hosts and their parasites and that this may lead to a coevolutionary arms race and the idea that we should have in mind the costs of a particular immune defence as this may impact other fitness traits of the organism and therefore affect its ability to deal with environmental changes. It was also clear that we are just at the beginning of understanding how the environment can impact the spread of diseases and that

there is really a need for more research to understand the basics before we can use this information in a predictive way.

There was a truly international feel to the conference with almost 100 participants from many different countries. We received a great deal of positive feedback on the conference, with especially more junior scientists saying that the atmosphere was very good for talking about their research and for meeting senior scientists, and there was much enthusiasm for a follow-up conference.

## Scientific Content of the Conference

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(1 page min.)

- Summary of the conference sessions focusing on the scientific highlights
- Assessment of the results and their potential impact on future research or applications

The scientific highlights of the conference were published in *Biology Letters* ('Host-parasite interactions: resist or tolerate but never stop running' doi: 10.1098/rsbl.2009.0444), by Jay Evans, an invited speaker at the conference. The PDF is attached.

### Session 1: Principles and applications of innate defence

This session served to set the stage by introducing the basic design principles of innate immune systems and general principles such as immunopathology. It became apparent that great scientific discoveries often start from seemingly simple observations, such as the question why certain animal tissues such as the eye rarely get infected (M. Zasloff). The session also included talks that considered the potentially important but as yet in this field of research under represented aspect of immunosenescence (M. Tinsley). More generally, over an animals' life time negative side-effects of defence reactions might play an important role for fitness (J. Rolff). The inclusion of such collateral damage of immune defence may change our view of immunity in a life-history context, where immediate fitness advantages might be offset by long-term negative effects. Such a situation may select for tolerance rather than resistance, an aspect that was also raised in other sessions and most intensively in the discussions.

### Session 2: Host-parasite interactions

The second session started with a useful categorisation of host-parasite interactions and its main principles, highlighting open questions such as the sources of variation in virulence and the influence of the genetic architecture of host defence on its evolution (P. Schmid-Hempel). The term 'interactome' was coined as a useful approach to describe the genes and proteins that determine the interaction of host and parasites. The following talks showed that host-parasite systems might largely differ in their peculiarities, making it difficult to generalise over different systems. For example, innate immune defences against filarial nematodes and consequently also pathogenic effects of infection are largely influenced by endosymbiotic *Wolbachia* (K. Pfarr).

### Session 3: Environmental stressors and innate immunity

This session prepared the ground for later discussions of the potential of host-parasite interactions and the innate immune system to react and evolve under selection pressures of environmental change. The range of environmental stressors treated during this session was broad, including the parasitic stressors themselves, with the obvious but often neglected effect of potentially strongly varying probability of attack (J. Jokela) to the use of parasitic pressure as a cue to phenotypically adjust the strength of the immune system, which may even extent non-genetically to the offspring generation (O. Roth). Other important environmental stressors are pollutants, with sometimes

counter-intuitive effects (B. Sures) and the nutritional environment (K. Wilson) up to self-medication by insects (M. Simone).

#### Session 4: Introduction to model systems and vectors of disease

The session focused on the *Anopheles/malaria* system and on *Drosophila* as a model for innate immunity. It became apparent that, despite the increasing knowledge of insect immunity, the reasons why an insect may be healthy *versus* sick often still remains obscure. The aspects of tolerance as an alternative to resistance, as well as the relevance of physiological changes in response to infection were stressed (D. Schneider). Importantly, whole-organism responses to infection might depend on host and parasite genotypes as well as environmental conditions, and might include many more aspects than immunity alone, cautioning against having simple expectations from the comparatively simple processes in the innate immune system.

#### Session 5: Innate immunity and disease in a changing world

After the foundations had been laid with the previous talks, this last session, which focused on one of the main conference topics, was among the highlights of the conference. In a controversial yet very inspiring approach, the effect of symbiotic organisms on immunity and health of its host was exemplified with a special focus on corals, where coral bleaching is a major problem (E. Rosenberg, C. Palmer). The aspect of environmentally-induced change of the meta-genome (i.e. the genome of a host combined with its symbionts) is certainly one that should be followed up in the future. Another highlight was a large-scale study in finches, a rare example where an emergent pathogen was tracked in real-time during its spread in the population (A. Dobson). A talk by R. Lucius in the context of the hygiene hypothesis once again highlighted the distance between scientific observation (of the immunomodulatory effect of parasite proteins in this case) and its medical application.

## Forward Look

(1 page min.)

- Assessment of the results
- Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe
- Identification of emerging topics

Participants of the conference were all very positive about the results of the talks and discussions, with a special appreciation of the high level and value of interdisciplinarity encountered during the conference. Several emerging issues were identified as important for future research and follow-up conferences for a 5-10 years time frame. These included:

- The degree to which the border between innate and adaptive immunity is being blurred based on the research presented during the conference (plus other recently published research in the field) cannot be underestimated. It becomes clear that innate immunity is highly dynamic and changing phenotypically as well as evolving rapidly. It was anticipated that future research will further substantiate this emerging trend, to a degree that even the names 'innate' and 'adaptive' immunity might need to be redefined.
- The distinction between infection and disease (resulting directly from infection or side-effects of it) will likely become an important one. We will need to ask 'what makes a fly sick?' rather than only whether or not it gets infected. In this context, issues such as tolerance versus resistance, costs of immunity and immunopathology will be important for future studies.



- Future studies will need to more closely link phenomena with mechanisms, i.e. ultimate and proximate questions ('why' and 'how'). Even though the current conference brought together people working on both questions, it is still often unclear for described phenomena what the underlying mechanisms are. On the other hand, there was some debate on whether or not it is always necessary to know a huge amount of mechanistic details in order to understand main principles.
- A talk on the coral 'holobiont' and related talks have brought up the issue of the level of selection – is it an organism or the organism plus its symbionts? Especially for innate immunity, symbionts clearly affect the outcome of host-parasite interactions. However, a controversially debated topic was whether or not it improves current concepts to include a view where the genome of a host is seen as an entity with the genomes of its symbionts.
- An emerging topic is the study of invasive host and parasite species and immunological ramifications thereof. The question of what enables parasites to jump host species and the effect of novel pathogens on their hosts (e.g. are they resisting or tolerating?) will need consideration in the future. In this context, the question of specificity in the adaptations of hosts and parasites will need special attention.

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▪ Is there a need for a foresight-type initiative?

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Questions of global change and innate immunity are both at the forefront of current research. The topic of this conference, which combined these questions, may be included in a broader foresight-type initiative on the health issues of global change. Alternatively, evolutionary and environmental/ecological aspects of infectious diseases could be considered for such an initiative.

## Atmosphere and Infrastructure

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▪ *The reaction of the participants to the location and the organization, including networking, and any other relevant comments*

We received positive feedback on the beautiful location of the conference. Despite the travelling time being quite long and it not being the easiest place to get to, especially for people coming from outside Europe, participants could certainly see the value of holding the meeting in Obergurgl. Participants also felt that the organisation was of a high standard. We consistently heard that especially more junior scientists found the atmosphere conducive to talking about their research and to meeting senior scientists. In that respect, the number of participants was also highly amenable to networking and establishing interactions that will certainly last beyond the time frame of the conference.

We also received feedback on ways in which the conference could be improved in the future. For example,

- 1) To have small discussion groups at the end of each day to discuss matters arising from the talks.
- 2) To have more free time and reduce the senior scientist talks to 30 minutes rather than 45 minutes
- 3) To have more and smaller poster sessions and more space around the posters