



Sciences biologiques,
Écologie et Environnement
**CONFÉRENCES
JACQUES-MONOD**



Roscoff (France), 3-7 septembre 2011

**Coévolution entre virulence parasitaire et défenses
immunitaires**

*Coevolutionary arms race between parasite virulence
and host immune defence: challenges from state of the
art research*

Président : **Gabriele SORCI**

Biogéosciences, CNRS, Université de Bourgogne, Dijon, France

Vice-Président : **Manfred MILINSKI**

Department of Evolutionary Ecology, Max Planck Institute for Evolutionary Ecology, Plön, Allemagne

Rapport sur la Conférence

Conference Report

RESUME DU RAPPORT

Conférence Jacques Monod intitulée : Coévolution entre virulence parasitaire et défenses immunitaires Roscoff, 3-7 septembre 2011

La Conférence Jacques Monod « Coévolution entre virulence parasitaire et défenses immunitaires » a eu lieu à Roscoff du 3 au 7 septembre 2011. Elle a réuni 86 chercheurs, postdocs et étudiants de 13 pays différents. Vingt-trois conférenciers invités ont présenté leurs travaux ainsi que 13 chercheurs sélectionnés parmi les inscrits. A cela, il faut rajouter 50 présentations sous la forme d'affiches.

La conférence s'est articulée sur 7 sessions.

Session I : Coévolution entre hôtes et parasites

Les exposés de cette session ont porté essentiellement sur la génétique des interactions coévolutives entre hôtes et parasites.

Session II : Compromis évolutifs dans les interactions hôte-parasite

Cette session a couvert plusieurs aspects liés à l'évolution des traits d'histoire de vie chez les hôtes et les parasites.

Session III : Immunogénétique

Les gènes impliqués dans la réponse immunitaire sont parmi les cibles principales de la sélection exercée par les parasites. Les interactions entre gènes immunitaires et sélection exercée par les parasites ont été au cœur des trois exposés présentés dans cette session.

Session IV : Immunité et virulence

La session IV a porté sur l'impact que l'immunité des hôtes peut avoir sur l'expression et l'évolution de la virulence parasitaire.

Session V : Spécificité et effets intergénérationnels

L'issue de l'interaction entre hôtes et parasites dépend d'un très grand nombre de paramètres, parmi lesquels l'environnement joue un rôle primordial. Les exposés de cette session ont porté sur une forme particulière de transmission de la résistance/tolérance vis-à-vis des parasites : les effets maternels.

Session VI : Economie de la réponse immunitaire

Il est maintenant établi que la réponse immunitaire induit des coûts. Les deux exposés de cette session nous ont montré l'ampleur de ces coûts et leur nature.

Session V : Régulation immunitaire

Enfin, dans la dernière session, nous avons eu l'opportunité de nous intéresser aux mécanismes qui régulent la réponse immunitaire et aux forces sélectives qui jouent sur ces effecteurs.

De l'avis de tous les participants, la conférence a été un très grand succès. L'adhésion des participants au projet porté par les Conférences Jacques Monod s'est traduite par la volonté explicitement exprimée de renouveler cette expérience lors d'une nouvelle conférence en 2014. A cette fin, les participants ont voté à l'unanimité pour que Manfred Milinski (MPI, Plön, Allemagne) et Ana Rivero (CNRS, Montpellier) jouent le rôle de président et de vice-président, respectivement.

CONFERENCE REPORT

Final report from the Jacques-Monod Conference entitled: Coevolutionary arms race between parasite virulence and host immune defence: challenges from state of the art research Roscoff, September 24-28, 2011

GENERAL ASPECTS

In September 2007, a Jacques Monod Conference entitled "EVOLUTIONARY GENETICS OF HOST-PARASITE RELATIONSHIPS" was held in Roscoff, organized by Dieter Ebert (President) and Gabriele Sorci (Vice-President). This conference was a big success and the participants voted in favour of a follow up conference. Manfred Milinski was elected as the new Vice-President. The follow-up conference took place in Roscoff from 3-7 September 2011. This document summarizes the key issues of the 2011 JMC.

PART 1: PROGRAM OVERVIEW

The original proposal listed three topics:

- Topic 1. Immune regulation and parasite virulence
- Topic 2. Host immunogenetics and parasite mediated balancing selection
- Topic 3. Parasite mediated costs and benefits of the immune response

For the program of the conference we used a different structure with seven sessions:

- Session I Coevolutionary interactions between hosts and parasites
Coévolution entre hôtes et parasites
- Session II Evolutionary trade-off in host-parasite interactions
Compromis évolutifs dans les interactions hôte-parasite
- Session III Immunogenetics
Immunogénétique
- Session IV Immunity and virulence
Immunité et virulence
- Session V Specificity and intergenerational effects
Spécificité et effets intergénérationnels
- Session VI The economics of the immune response
Economie de la réponse immunitaire
- Session VII Immune regulation
Régulation immunitaire

For the poster sessions, we used an open format, i.e. we did not allocate posters to sessions. There were a total of 50 posters.

PART 2: PARTICIPANTS

Invited speakers

Each invited speaker gave a 30 minute presentation about her/his work.

Speaker / Institution / Country

Dieter Ebert / University of Basel / Switzerland
Michael Hochberg / CNRS / France
Sylvain Gandon / CNRS / France
Rob de Boer / Utrecht University / The Netherlands
Wayne Potts / University of Utah / USA
Geoff Parker / University of Liverpool / UK
Yannis Michalakis / CNRS / France
Ana Rivero / CNRS / France
Manfred Milinski / Max Planck Institute / Germany
Jim Kaufman / Cambridge University / UK
Scott Edwards / Harvard University / USA
Andrea Graham / Princeton University / USA
Dominik Wodarz / University of California, Irvine / USA
Margaret Mackinnon / KEMRI, Wellcome Trust / Kenya
Joachim Kurtz / University of Münster / Germany
Heinz Richner / University of Bern / Switzerland
Yannick Moret / CNRS / France
Paul Schmid-Hempel / ETH /Switzerland
Thierry Boulinier / CNRS / France
Kirk Klasing / University of California, Davis / USA
Shelley Adamo / Dalhousie University / Canada
Christine Coustau / CNRS / France
Gabriele Sorci / CNRS / France

Steve Paterson, University of Liverpool (UK) had to cancel its participation in the last minute, for personal reasons. This resulted in 23 talks by invited speakers.

Five out of 23 invited speakers were females. This substantially deviates from our original program because four female invited speakers who had confirmed their participation to the conference (Polly Matzinger, Sonia Altizer, Marlene Zuk, and Nathalie Charbonnel) cancelled during the few weeks that preceded the conference. It is regrettable that for Polly Matzinger the reason for non-attending the conference was the lack of agreement between the CNRS and the NIH on the reimbursement procedure.

Six of the 23 invited speakers (26%) had been at the previous JMC (Sept. 2007). Eight invited speakers were from France, 8 from Europe (outside France) and 7 were from outside Europe. Besides the invited speakers, the following people were selected based on their abstract to give 15 minute presentations:

André Dhondt (Cornell University, USA)
Mathieu Sicard (Université de Poitiers, France)
Simon Frost (Cambridge University, UK)
Olivier Restif (Cambridge University, UK)
Flore Ponton (University of Sydney, Australia)
Honour McCann (University of Toronto, Canada)
Rebecca Schulte (University of Osnabrueck, Germany)

Aude Gilabert (MNHN, France)
Bridget Penman (Oxford University, UK)
Stéphane Dupas (IRD, France)
Laura Pollitt (University of Edinburgh, UK)
Colin Parrish (Cornell University, USA)
Michel Chapuisat (Université de Lausanne, Switzerland)

Non-invited participants

A total of 63 non-invited people from 11 countries took part in the conference. Of those, 22 were from France, 31 were from Europe (outside France) and 10 were from outside Europe. Fifty posters were presented. The average quality of the posters was very high.

PART 3: SCIENTIFIC PROGRAM

Parasites and pathogens are an increasingly pervasive threat for their hosts, as shown by the recent epidemics and pandemics (i.e. HIV, SARS, bird flu, swine flu) that have involved humans. More than 40% of known species are parasitic and approximately 75% of the links in food webs involve a parasitic species. Thus, all organisms have to face pathogens during their lifespan. Early evolution of parasitic lifestyle has certainly favoured the simultaneous evolution of defence mechanisms aiming at preventing and/or limiting the fitness costs of infection. Although antiparasitic defences can be as diverse as avoidance of infected conspecifics or the use of chemical compounds for self-medication, it is obvious that immune defences play the central role in host resistance. Recognizing pathogenic organisms and clearing infection is the primary function of immunity and such a function is present in basically all organisms, including plants. The capacity to recognize intruders already exists in unicellular organisms that produce microbicidal molecules, and reaches a high degree of complexity in vertebrates with a wide array of tissues, cells and molecular effectors that operate to cope with pathogenic invaders. Because of its importance for the control of infectious diseases, the study of immune defences has taken a central role within life sciences. Studying the complex molecular mechanisms underlying the immune response is, obviously, of crucial importance for the improvement of human and animal health. Nevertheless, living organisms, both hosts and parasites, are not static entities. Immune defences and parasitic strategies to overcome them are constantly exposed to selection pressures and, as such, do evolve. Understanding and predicting the outcome of a host-parasite interaction, therefore, has to be based on evolutionary thinking.

The immune system is exposed to selection forces exerted by biotic and abiotic factors. Parasites and pathogens are, of course, the main biotic factor shaping the evolution of immune defences. It is generally thought that the diversity of immune effectors is the product of the coevolutionary arms race between hosts and parasites. Using a metaphor drawn from the ecological literature, we can depict the interaction between the immune system and an invading parasite as a predator-prey system. Immune cells and effectors act as predators on micro-organisms which, as prey, are selected to escape the predators. Indeed, pathogens have evolved an amazing diversity of strategies as to avoid/escape the immune response, including antigenic variation, molecular mimicry or immune suppression. Understanding how these reciprocal, coevolutionary, interactions affect the evolution of some of the most important features of host-parasite interactions, such as the expression of parasite virulence is currently the focus of intense research.

The JMC in September 2011 in Roscoff saw many examples of the way how host and parasite evolve or coevolve. The conference covered the entire field of host and parasite evolutionary ecology and coevolution.

Session I: Coevolutionary interactions between hosts and parasites

The first session covered the field of the genetic coevolutionary interactions between hosts and parasites. Dieter Ebert gave a thoughtful talk on the complex interactions between *Daphnia* clones and bacteria isolates that infect them and stressed the importance of specificity and that resistance is presumably coded by few loci. Michael Hochberg presented a theoretical work exploring the victim-enemy coevolution in a model that explicitly includes resource availability and population dynamics. Sylvain Gandon took over with an overview on how spatial structure, maternal effects and the use of drugs can affect the evolution of host defences. Rob de Boer presented a fascinating work on the coevolution between host immune genes and pathogens. In particular, he focused on the different levels of heterogeneity that characterize genes involved in the antigen-presentation process (proteasome, TAP, MHC), and how the interaction with pathogens can help us to understand why selection has promoted the evolution of highly polymorphic MHC genes and monomorphic proteasome and TAP. Finally, Wayne Potts showed convincing evidence in support to the Red Queen hypothesis using experimental evolution of viruses infecting MHC congenic mice.

Session II: Evolutionary trade-off in host-parasite interactions

This session was devoted to the evolution of life history traits in interacting hosts and parasites. Geoff Parker focused on the adaptations of helminths to their intermediate hosts. Yannis Michalakis stressed the importance of mixed infections for a number of host and parasite traits, including the evolution of virulence, host proteome, host NO production. This work has been done using the yellow fever mosquito (*Aedes aegypti*) and the microsporidia *Vavraia culicis* and *Edhazardia aegypti*. Finally, Ana Rivero highlighted how the evolution of insecticide resistance can affect the interaction between *Culex pipens* mosquitos and *Plasmodium relictum*, the agent of the avian malaria.

Session III: Immunogenetics

Immune genes are among the major targets of parasite-mediated selection. The three talks of this session covered the coevolutionary interactions between immune genes and pathogens. Manfred Milinski reported evidence for an adaptive shift in MHC allele frequency in experimental populations of sticklebacks infected with two nematode species. This is the first experimental demonstration of parasite-mediated selection on MHC genes at the population level. Jim Kaufman stressed how gene co-evolution has shaped the pattern of pathogen resistance using the chicken MHC/TAP system as a model. Finally, Scott Edwards has used a genomic approach to identify the genes involved in the resistance to the bacterial pathogen *Mycoplasma gallisepticum*, which has been responsible for an epidemic among natural populations of house finches in the USA.

Session IV: Immunity and virulence

What is parasite virulence? Is it a parasite trait, a host trait? These questions are at the core of the study of host-parasite interactions. It seems clear now that virulence is a composite trait emerging from the interaction between host and parasite traits. In particular, it has been suggested that the immune response does substantially contribute to determine the cost paid by an infected host. Andrea Graham and Margaret Mackinnon gave an updated overview of the interaction between host immunity and parasite virulence using the rodent malaria (*Plasmodium chabaudi*) and the human malaria (*Plasmodium falciparum*) as model systems.

Host immunity does also affect the competitive interactions among pathogens co-infecting the same host. Dominik Wodarz drew the audience attention to this particular point using a series of theoretical models focusing on the competition dynamics of viruses.

Session V: Specificity and intergenerational effects

The outcome of a host-parasite interaction obviously depends on a number of traits. The genetic make-up of both partners of the interaction is primordial as it is the environment where the interaction takes place. As such, the maternal environment can shape the resistance/susceptibility profile of the progeny, independently of any genetic inheritance. This session focused on such intergenerational effects in both invertebrate (Joachim Kurtz, Yannick Moret) and vertebrate hosts (Heinz Richner, Thierry Boulinier). Specificity of defences is also a key feature of antagonistic coevolution as stressed in the talks of Paul Schmid-Hempel and Joachim Kurtz.

Session VI: The economics of the immune response

As mentioned above, the immune response can generate immunopathological costs that add up to the host exploitation to determine parasite virulence. In addition to this, the immune response also interferes with other physiological functions of the host. In two fascinating talks, Shelley Adamo and Kirk Klasing illustrated this type of interferences focusing on the stress response of insects (Shelley Adamo) and the nutritional/metabolic requirements of birds (Kirk Klasing).

Session VI: Immune regulation

The last session dealt with the mechanisms of immune regulation and the selection pressures acting on them. Christine Coustau presented evidence for the evolution of cytokine-like regulatory molecules in molluscs and Gabriele Sorci highlighted the form of selection (correlational selection) acting on pro- and anti-inflammatory cytokines. He also showed how parasites can take advantage of down-regulated hosts and can adapt to them based on the experimental evolution of avian malaria.

FINAL COMMENTS

The goal of this conference was to support excellent and innovative research in the field of the coevolutionary interactions between hosts and parasites, with a special focus on host defences and parasite exploitation strategies. One of the goals of this conference was to bridge the gap between theory and empirical work. We also wished to bring together students with a strong immunology-oriented background and evolutionary ecologists. We believe that both goals were achieved. Undoubtedly, the other major strength of the conference was to see that attendees had very fruitful discussions and interactions. The conference also allowed younger people to obtain an overview over this rapidly growing field. As evidenced by the cutting edge and largely unpublished research described at the conference, a conceptual framework is beginning to emerge which allows us to better understand the way in which hosts and parasites evolve and coevolve. While modern techniques using genomics or protein engineering clearly made their way into the field, experimental evolution studies have been shown to be able to produce new and exciting data. Evolutionary biology is more than ever a growing field, which allows us to bring many biological disciplines under one umbrella. The unifying concept of evolution provides a framework to bring these disciplines together and to reach overarching conclusions as well as otherwise unthought predictions.

PERSPECTIVES

The participants felt there is a need for organizing another meeting on the issue in 2014. They elected Ana Rivero (Montpellier) to act as the next vice-president, Manfred Milinski (MPI, Plön, Germany) taking over the charge of president for the next conference. Together they are asked to apply for another Jacques Monod Conference on host - parasite interactions and evolution.