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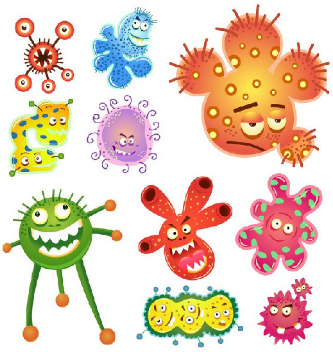
DOPIS EDITOROVI / LETTER TO THE EDITOR

HOST PATHOGEN INTERACTION FORUM HAS ACHIEVED INTERNATIONAL RECOGNITION



Introduction

The 13th Host Pathogen Interaction Forum was held in Slavonice, Czech Republic, between April 16 and April 19, 2018. The Forum is traditionally organized by the Faculty of Military Health Sciences, Hradec Králové, Czech Republic, in collaboration with the Czech Immunological Society in Prague, Czech Republic. The venues for our Forums are selected with respect to historically significant areas of the Czech Republic. The Forum's reputation has grown steadily over the years such that it has earned a place on the calendars of important scientists in the field of studies on pathogen interactions with their hosts. Due to the scientific orientations of the organizers, the forums bring together scientists working mostly with intracellular (bacterial as well as viral) pathogens.

Short history of the Host–pathogen Interaction Forums

The history of these meetings began at the hotel Aurum in the town of Zlaté hory in April 2001, when approximately 20 colleagues from different branches of immunology and infection biology gathered to debate basic issues of mutual interaction between hosts and microbes. The topics of the first meeting concerned primarily interactions of intracellular bacteria with eukaryotic host cells, including such relationships as parasitism, mutualism, syntrophy, and endosymbiosis. All participants of the first Forum agreed that they would meet regularly to discuss prominent topics of interaction between pathogens and their hosts. The second Forum, held in Jablonné nad Orlicí with the overriding theme "Intracellular bacterial pathogens: From structure to pathogenicity," already was attended by scientists from Sweden and Germany. The following forums were held in, for example, Valtice, Hradec Králové, Velké Karlovice, Třeboň, Mikulov, and Broumov.

The 13th Forum in Slavonice

This year's forum was focused on traditional topics of host–pathogen interactions and their consequences for both hosts and microorganisms. The program has been extended to the utilization of high throughput technologies applied to studies on molecular and cellular aspects of infection biology. A substantial innovation was the final general discussion unifying the presented data and generating new ideas for orienting research on critical questions concerning mutual interaction of the eukaryotic host with the prokaryotic guest. The keynote lecture, "Will it be possible to develop an efficacious vaccine against *Francisella tularensis*," was presented by Anders Sjöstedt (SE) with just such goals in mind. The program as a whole can be roughly summarized under the following headings:

Multifunctional proteins as virulence factors

The first session documented the complexity and difficulty of identifying virulence factors of bacteria that occupy the intracellular niches inside the different subtypes of host cells. Alan Charbit (FR) demonstrated the role of two enzymes of *Francisella tularensis* occupying a central position in glycolysis and gluconeogenesis pathways for *Francisella* pathogenesis. These two enzymes can be seen as exemplifying the importance of complete metabolic pathways for bacterial virulence. Monika Kopečková (CZ), Petra Špidlová (CZ), and Pavla Stojková (CZ) demonstrated on this same infection model the problem of identifying the functions of multifunctional proteins that have additional, non-enzymatic functions and are indispensable for the expression of bacterial virulence. A similar problem with identifying individual bacterial protein function that influences virulence was demonstrated by Sherry Mou (US) on the *Coxiella burnetii* infection model.

Spatiotemporal relationships of multiple factors to maintain homeostasis

The second session opened with a lecture by Charles L. Bevins (US) dedicated to the function of Paneth cells and their antimicrobial peptides and proteins, which contribute to maintaining homeostasis in the early stages of host–microbe interaction in the intestine. Intestinal tract colonization was the subject of the following block of three lectures presented by Ivan Rychlík, Tereza Kubasová, and Miloslava Kollarčíková (all CZ). Their use of a chicken model seems to be advantageous for experimental analyses of the close interrelationships between specific genera of the microbiota and the fitness of the host, which can lead to constructing a new generation of probiotics and, in reality, has an economic impact. Although the microbiota has a significant effect on the effective functioning of the immune system, Lenka Plzáková (CZ) documented that there are few, if any, significant differences in the relative frequency of individual cell (sub)types between *F. tularensis*-infected germ-free and SPF mice.

The general basic assumption of immunity against microbes, as well as against tumors of cause, is that the response is based on the mechanisms of recognition and, equally important, on self–nonself discrimination. It is undoubtedly the case that the interactions of microbes with host cells are determined by the cell subtype with which the microbe interacts and the functional profile of expressed receptors at the microbe–host cell interface. Aleš Macela (CZ) demonstrated using the *Francisella tularensis* infection model the innate immune recognition as a multistep process that respects the spatiotemporal character of early stages of host–pathogen interactions. Subsequently, Jawid Ahmad (from the Czech Academy of Sciences) presented using the model of adenylate cyclase toxin of *Bordetella pertussis* the ability of bacterial components to modulate the evolutionarily established signaling pathways and subvert monocyte and macrophage functions. Finally, Marek Link (CZ), in his presentation of the MHC-II peptidome of *Francisella tularensis*-infected dendritic cells, recalled the long debated question of whether bypassing of the innate immunity and directly activating the acquired immunity during vaccination can have a positive effect on the quality and duration of induced adaptive immune response.

Complexity of mutual host–pathogen interactions

In general, microbial interactions with the host require the participation of lectins/adhesins and glycans. Such interactions can be disclosed using glycogenomic methods, and interpretation of the results can enrich the theoretical knowledge regarding the host–pathogen interactions. That knowledge also can be utilized for practical purposes, specifically for decontamination of sensitive surfaces, as was demonstrated by Lokesh Joshi (IE). The complex consequences of the interactions were documented in the presentation of Ruwen Yang (DE). He presented an integrated analysis of the significant changes in expression of host genes induced by combined infection of normal oral keratinocytes with HPV and Chlamydia trachomatis. Such an approach has provided evidence for the contribution of Chlamydia infection as a potential co-factor in HPV-induced carcinogenesis. A similar approach (e.g., transcriptomic analysis) was used for demonstrating the substantial modulation of gene expression of both the pathogen (*Bordetella pertussis*) and the monocyte-derived macrophages as the host (Branislav Večerek, CZ).

The last three lectures highlighted on the one hand the ability of *Bordetella pertussis* adenylate cyclase toxin to compromise physical barriers and innate immune functions (Shakir Hasan (from Czech Academy of Science). On the other hand, they disclosed hitherto unknown possibilities of communication within host–pathogen interactions using vesicles and nanotubules (the model of *Francisella tularensis* presented by Jana Klimentová, CZ) or by exosomes (presented by Jiří Volf, CZ).

The -omics technologies as an indispensable tool in infection biology

The lectures presented during the last session confirmed the indispensable role of laboratory throughput technologies for disclosing the molecular machinery that determine the definitive outcome of complex host–pathogen interactions. Frank Rösl (DE) presented results from utilization of a natural infection model (*Mastomys coucha*) to demonstrate that continual viral presence of papillomaviruses during carcinogenesis is dispensable in an experimental model, similarly as observed in patients with non-melanoma skin cancer. The great impact of -omics technologies for understanding host–pathogen interactions was demonstrated on several infection models. As a large-scale study of proteins, proteomics was used for demonstrating molecular differences between virulent and avirulent *Coxiella burnetii* phases (Miloslava Ďuráčová, CZ), for examining the antigenicity of *Rickettsia akari* proteins (František Csicsay, SK), and for seeking host targets of *Francisella* pathogenicity island effectors (Magdaléna Prokšová, CZ). Comparative genomics was used for identification of *Campylobacter jejuni* clinical and environmental samples genotypes (Darina Čejková, CZ). The phosphoproteomic approach revealed that activation of the signaling pathways in the very early stages of *Francisella*–bone marrow derived dendritic cells interaction occurs in waves that are differentially initiated by virulent strain FSC200 and its attenuated Δ*dsbA* mutant (Jiří Stulík, CZ). Subsequently, and using similar technology, Jakub Novák (CZ) presented the inhibition of mTOR signaling pathway as well as inhibition of SIK family kinases in the experimental model of adenylate cyclase toxin intoxicated primary murine bone marrow-derived dendritic cells. Finally, Jana Kamanová (CZ) demonstrated the active type III secretion system of *Bordetella pertussis* and the molecular basis for functional divergence of BTeA effector secreted by this secretion system.

Closing general discussion and future perspectives

The final general discussion was moderated by Lokesh Joshi (IE), Alain Charbit (FR), and Charles L. Bevins (US). A number of questions from the audience were related to utilization of the recent throughput laboratory technologies and the methods for evaluating and interpreting the enormous amounts of data thus obtained. Mention also was made as to the limits of *in vitro* technologies in the studies of host–microbe interaction models, and the complexity of such studies was repeatedly emphasized. As a promising area for future analyses of mutual interactions between the host and their microbial guests was mentioned the need to study not only the host–pathogen interactions but also the host cellular organelle–microbe interactions. Such considerations originated from the historical discussions during the past host pathogen interaction forums and recently were rekindled by the lecture of Jiří Stulík (CZ), in which he presented the invasion of *Francisella tularensis* into the mitochondrion of a host cell.

The Forum's scientific program was accompanied by a social program that met with a favorable response among the Forum participants. We all can look forward to seeing one another at the 14th Host Pathogen Interaction Forum in 2020.

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