Fungal immunology: from simple to very complex concepts

Jean-Paul Latgé

Received: 17 December 2014 / Accepted: 17 December 2014 / Published online: 6 February 2015
© Springer-Verlag Berlin Heidelberg 2015

Sensing of a foreign fungus (which could be either a mesophilic saprophyte or a thermophilic opportunist pathogen) (Vacher et al. in this issue) always starts from the contact between a pathogen-associated molecular pattern (PAMP) and a pattern recognition receptor (PRR) (Fig. 1, level 1). These ligand-receptor interactions are the simplest ones in the immunological cascade. However, if the biochemical understanding of these interactions is clear in a few cases such as the seminal β 1,3-glucan Dectin1 story, most of the fungal PAMPs and their respective PRRs remain unknown or controversial (Plato et al. and Becker et al. in this issue). Moreover, it is unknown why some molecules become a PAMP to be recognized by humans, whereas others are not (Cramer et al. in this issue). In the early time, proteins were considered to be the major drivers of the immune response, whereas to date, polysaccharides and even lipids have emerged as important molecules in fungal immunology (Fradin et al. in this issue).

If the interaction of 1 PAMP-1PRR is the simplest, the reality is different since recognition of non-self by the immune cells is a complex event where many PAMPs with different structures and composition are recognized by hundreds of receptors on the same phagocytic cells (Fig. 1, level 2). As an example, around hundred C-type lectins able to scrutinize carbohydrate-based PAMPs have been annotated in the human genome.

A third level of complexity (Fig. 1, level 3) also results from the different fungal species and morphotypes that the

host encounters and has to recognize to mount a specific antifungal response against each individual invading microorganisms (Bain et al., Heinekamp et al. and Eddens et al. this issue). Accordingly, some of the PAMPs will be common to all fungi, whereas others will be encountered only in a single species or even more be strain-specific (although this topic remains almost untackled in medical mycology). This increased cellular complexity is also seen on the host side, since multiple PAMPs can be differentially sensed by different immune cells which can then induce different and sometimes opposite immunological responses in complicated networks.

The last layer of complexity comes from the non-fungal as well as the non-immune cells that can influence the host-pathogen interactions (Fig. 1, level 4). This has been recently shown by numerous studies documenting the impact of the microbiota in modulating directly or indirectly the immune response, since the microbiota can modify the physiology and composition of the fungal pathogen (Romani et al. this issue). In addition, if most of the immunological studies are exclusively based on the recognition of the fungus by the host, it should not be forgotten that the fungus itself has a deleterious impact due to toxins or enzymes on the host tissues including immune cells and these damages are able to modify the host response. This certainly influences negatively the capacity of the host to respond to the fungal pathogen. Moreover, genetic or pharmacological immunosuppressions have a global impact on the host immunity which is not enough taken into account to understand the host response towards the opportunistic pathogens commonly found in our industrialized countries (Wojtowicz et al. in this issue).

Even though the complexity of the immune response towards fungal cells has not been fully deciphered, it is clear today that immunotherapy is an alternative of the future of

This article is a contribution to the special issue on Immunopathology of Fungal Diseases - Guest Editor: Jean-Paul Latgé

J.-P. Latgé (✉)
Aspergillus unit, Institut Pasteur, Paris, France
e-mail: jean-paul.latge@pasteur.fr

Fig. 1 Sensing of a foreign fungus by its human host. Level 1: one PAMP/one PRR. Level 2: one fungal cell with several PAMPs vs. one human cell with several PRRs. Level 3: several fungal species and morphotypes recognised by several human cells. Level 4: maximal complexity level where non-fungal cells (bacteria and viruses) influence fungal biology and non-immune cells modulate the global immune response

antifungal treatments to fight fungal infections (Elluru et al. and Levitz et al. in this issue). This is especially true to date when the level of antifungal-resistant strains and the cost of the antifungal therapy are continuously rising. Future vaccines are currently focused on the development of specific and unspecific humoral and cellular immune responses directed against purified or complex extracts. In

the latter case, the impact of each molecule in the extract remains poorly defined.

This series in *Seminars in Immunopathology* arises from the ALLFUN-FP7 project led by L. Romani (FP7/2007-2013HEALTH-2010-260338) which had been a tremendous push for the collaboration between European immunologists and medical mycologists.