Journal of Glycobiology
ISSN: 2168-958X

Mora-Montes, J Glycobiology 2011, 1:1
DOI: 10.4172/2168-958X.1000e103

Editorial Open Access

When Glycobiology and Immunology Work Together: The Immunoglycobiology of Fungal Immune Sensing

Héctor M. Mora-Montes

Departamento de Biología, División de Ciencias Naturales y Exactas, Campus Guanajuato, Universidad de Guanajuato, Noria Alta s/n, Col. Noria Alta, Guanajuato, Gto. CP 36050, México

Carbohydrates are a universal feature present on the surface of all living cells: they may be covalently linked to either lipids, proteins or other sugars forming polysaccharides. Even some enveloped viruses of eukaryotes contain glycoproteins embedded in the viral membrane. So, when it comes to the recognition of pathogens by the immune system, it is easy to realize that the outermost, exposed molecules of pathogens, i.e., those based on sugar moieties, are among the first components to be sensed and to drive an immune response towards the antigen source.

Among all the medically relevant fungal species, some of them have the ability to intrinsically damage the host regardless the status of the host immune system, but the opportunistic fungal pathogens rely on a temporal or permanent impairment of the immune system, in order to successfully colonize and invade the host tissues [1]. Thus, there is a close balance between immune sensing of fungal cells and disease establishment. The antigenic properties and the immune system-fungus interaction have been extensively studied during the last fifty years, and although we have a significant advance understanding this relation, we are still far away to have the whole picture of this event. Nowadays, it is quite clear that the fungal cell wall components are the first molecules to be in contact with the immune cells, and therefore are the pathogen-associated molecular patterns and main antigens involved in triggering an antifungal immune response. *Candida albicans* is one of the most studied opportunistic fungal pathogens in terms of its cell wall composition and relevance of its components for immune sensing; and there is a significant advance in establishing the relative importance of the cell wall components for the *C. albicans* immune recognition [2]. We know, for example, that β1,3-glucan and mannans, the latter are the glycan moieties attached to cell wall glycoproteins, are the main cell wall stimuli for pro- and anti-inflammatory cytokine production, phagocytosis, and establishment of a successful anti-*Candida* immune response [2-4]; the glycolipid phospholipomannan is also an important element for innate immune sensing of this fungus [2], and interestingly, chitin seems to be a cell wall polysaccharide that blocks the proper innate immune sensing of *C. albicans* [5]. This great advance in fungal sensing seems to be quite promising to dissect this interaction and might lead to unveil an Achilles' heel to fight fungal pathogens using immunomodulatory approaches. However, when these observations are extrapolated to other fungal pathogens the scenario is in some cases totally different: the amount and kind of structural cell wall polysaccharides may vary from fungal species (some of them may have higher levels of chitosan, different ratios of β-glucans, presence of α-glucans that are absent from the *C. albicans* cell wall). Glycoproteins and glycolipids are cell wall components with structural variability across fungal species: while *C. albicans* contains mannans attached to cell wall proteins, other fungi may have complex glycans conformed by a variety of different monosaccharides, as galactomannans in *Aspergillus fumigatus* [6] and rhamnomannan in *Sporothrix schenckii* [7]. Furthermore, these cell wall polysaccharides can play in favor of the fungal pathogen, helping establishing immune evasion strategies: α1,3-glucan and *N*-linked mannans form a shield covering the immune stimulating factors of *Histoplasma capsulatum* and *Saccharomyces cerevisiae* cell walls, respectively [8,9]; *A. fumigatus* galactomannans induce non protective Th_2 and Th_{17} lymphocyte stimulation [6], and *Cryptococcus neoformans* capsular galactoxylomannans are strong negative immunomodulators that stimulate apoptosis of immune cells [10]. Although these are big leaps towards the dissection of the fungal immune sensing, the field still has limited information on the detailed structure of oligosaccharides present on the cell wall of fungal pathogens different to *C. albicans*. Even *S. cerevisiae*, a close phylogenetic relative of *C. albicans,* has mannans that are significantly different in their structures, and these changes are enough to avoid recognition by DC-SIGN receptor [11]. We currently lack information about the glycan structures present in *C. neoformans*, other *Candida* species, *Blastomyces dermatitidis*, *H. capsulatum*, *Paracoccidioides spp*., *Coccidioides spp*., etc. Bioinformatics efforts have been done to predict the presence and structure of glycans in fungal cells [12]; and this is indeed a good starting point, but experimental analyses must be conducted to establish the abundance of glycans and their localization within the cell wall. Thus, this is an area of opportunity where glycobiology as a field can make a significant contribution to the immune sensing of fungal pathogens, solving the structure of complex glycans, assessing the abundance of specific sugar moieties by lectin-based microarrays, etc. These studies, along with molecular and genetic approaches will provide significant information to understand the complexity, organization and composition of the cell wall of different fungal pathogens, and might generate useful tools to continue dissecting the fungus-host immune system interaction.

Scientific knowledge generation must be accompanied by forums where science can be communicated to general and specific audiences, and scientific journals have traditionally been the way to do it. Glycobiology has specialized journals dedicated to communicate research made in this area, but the open access options are quite limited so far. At first glance open access may be an expensive way to communicate science, and in a way it is; however, gives authors the means to reach a broader audience and to spread quicker their finding. In addition, nowadays some funding agencies such The Wellcome Trust and NIH are supporting the ideology to make science freely available to the community and absorb the expensive publication fees.

References

1. Casadevall A, Pirofski L-a (2003) The damage-response framework of microbial pathogenesis. Nat Rev Microbiol 1: 17-24.

2. Netea MG, Brown GD, Kullberg BJ, Gow NA (2008) An integrated model of the recognition of *Candida albicans* by the innate immune system. Nat Rev Microbiol 6: 67-78.

Corresponding author: Departamento de Biología, División de Ciencias Naturales y Exactas, Campus Guanajuato, Universidad de Guanajuato, Noria Alta s/n, Col. Noria Alta, Guanajuato, Gto. CP 36050, México, Tel: (+52) 473-7320006; Fax: (+52) 473-7320006; E-mail: hmora@ugto.mx

Received November 14, 2011; **Accepted** December 18, 2011; **Published** December 19, 2011

Citation: Mora-Montes HM (2011) When Glycobiology and Immunology Work Together: The Immunoglycobiology of Fungal Immune Sensing. J Glycobiology 1:e103. doi:10.4172/2168-958X.1000e103

3. Heinsbroek SEM, Taylor PR, Martinez FO, Martinez-Pomares L, Brown GD, et al. (2008) Stage-specific sampling by pattern recognition receptors during *Candida albicans* phagocytosis. PLoS Pathog 4: e1000218.

4. McKenzie CGJ, Koser U, Lewis LE, Bain JM, Mora-Montes HM, et al. (2010) Contribution of *Candida albicans* cell wall components to recognition by and escape from murine macrophages. Infect Immun 78: 1650-1658.

5. Mora-Montes HM, Netea MG, Ferwerda G, Lenardon MD, Brown GD, et al. (2011) Recognition and blocking of innate immunity cells by *Candida albicans* chitin. Infect Immun 79: 1961-1970.

6. Bozza S, Clavaud C, Giovannini G, Fontaine T, Beauvais A, et al. (2009) Immune sensing of *Aspergillus fumigatus* proteins, glycolipids, and polysaccharides and the Impact on Th immunity and vaccination. J Immunol 183: 2407-2414.

7. López-Romero E, Reyes-Montes MR, Pérez-Torres A, Ruiz-Baca E, Villagómez-Castro JC, et al. (2011) *Sporothrix schenckii* complex and sporotrichosis, an emerging health problem. Future Microbiol 6: 85-102.

8. Rappleye CA, Eissenberg LG, Goldman WE (2007) *Histoplasma capsulatum* β-(1,3)-glucan blocks innate immune recognition by the α-glucan receptor. Proc Natl Acad Sci USA 104: 1366-1370.

9. Wheeler RT, Fink GR (2006) A drug-sensitive genetic network masks fungi from the immune system. PLoS Pathog 2: e35.

10. Vecchiarelli A, Pericolini E, Gabrielli E, Chow S-K, Bistoni F, et al. (2011) *Cryptococcus neoformans* galactoxylomannan is a potent negative immunomodulator, inspiring new approaches in anti-inflammatory immunotherapy. Immunotherapy 3: 997-1005.

11. Cambi A, Netea MG, Mora-Montes HM, Gow NA, Hato SV, et al. (2008) Dendritic cell interaction with *Candida albicans* critically depends on *N*-linked mannan. J Biol Chem 283: 20590-20599.

12. Deshpande N, Wilkins MR, Packer N, Nevalainen H (2008) Protein glycosylation pathways in filamentous fungi. Glycobiology 18: 626-637.