The use of biomarkers for the detection of fungal infections is of interest to complement histopathological and culture methods. Since the production of antibodies in immunocompromised patients is scarce, detection of a specific antigen could be effective for early diagnosis. D-Galactofuranose (Gal\(\text{f}\)) is the antigenic epitope in glycoconjugates of several pathogenic fungi. Since Gal\(\text{f}\) is not biosynthesized by mammals, it is an attractive candidate for diagnosis of infection. A monoclonal antibody that recognizes Gal\(\text{f}\) is commercialized for detection of aspergillosis. The linkage of Gal\(\text{f}\) in the natural glycans and the chemical structures of the synthesized Gal\(\text{f}\)-containing oligosaccharides are described in this paper. The oligosaccharides could be used for the synthesis of artificial carbohydrate-based antigens, not enough exploited for diagnosis.

Lay abstract: D-Galactofuranose (Gal\(\text{f}\)) is the unit in polysaccharides and glycoconjugates of several pathogenic fungi that is recognized by the immune system. Since Gal\(\text{f}\) is not synthesized by mammals, it is an attractive candidate for diagnosis of infection. Since the production of antibodies in immunocompromised patients is scarce, detection of a specific antigen could be effective for early diagnosis. An antibody that recognizes Gal\(\text{f}\) is commercialized for the detection of aspergillosis. Chemically synthesized Gal\(\text{f}\)-containing oligosaccharides, reviewed in this paper, could therefore be used for the synthesis of artificial carbohydrate-based antigens and in diagnosis.
Effective serodiagnosis of systemic fungal infections is of increasing importance, particularly with regard to the identification of the infective organism. Early diagnosis, before infection is advanced, is still a challenge for efficient therapy. Clinical signs and culture detection methods for diagnosis of fungal infections are often slow, not specific and/or lack sensitivity.[1,2]. Although they remain the usual approaches for diagnosis of mycoses [3], lately, faster, nonculture-based methods have been developed, including immunoassays based on the presence of circulating galactofuranose (Galf) antigens[4,5,6,7,8,9]. Since immunocompromised patients are not capable of producing enough antibodies for their detection in conventional serological tests, monoclonal antibodies have been obtained for the detection of specific antigens [5].

Aspergillosis is the most studied fungus-related disease and thus it will be preferentially referred. Invasive aspergillosis affects the lungs mainly in immunocompromised patients [10]. A review on molecular methods for diagnosis of invasive aspergillosis has been recently published [11].

The monosaccharide D-galactose (D-Gal) is very common in nature as a component of oligosaccharides and glycoconjugates [12]. It is interesting to remark that mammals are only able to synthesize the sugar in the pyranose configuration whereas some bacteria, fungi and protozoa have the unique enzyme UDP-Galp mutase (UGM) that catalyzes the conversion of UDP-Galp to UDP-Galf, which is the donor of Galf in the biosynthesis of Galf-containing molecules [13,14]. The presence of Galf was also reported in some nematodes [15,16]. In fungi, recombinant UGM from Aspergillus fumigatus was described [17]. Studies on the crystal structure and substrate-binding mechanism, revealed differences with the prokaryotic UGM [18]. The synthesis of the substrate UDP-Galp is mediated by a UGE, which catalyzes the interconversion of UDP-Glc and UDP-Galp [19]. In A. fumigatus, three genes encoding putative UGE have been reported [20], however, only one of them was required for the synthesis of Galf-containing galactomannans and was essential for normal growth. Based on homology, a UGE was identified in A. niger [21]. A genetic and transcriptomic analysis of the cell wall of A. niger in response to the absence of Galf was described [22].

Since UDP-Galf is synthesized in the cytosol [23] and Galf is incorporated in the Golgi, a UDP-Galf transporter is required, and has been identified in A. fumigatus [24]. In this fungus, deletion of UGM caused attenuated virulence of the strain [18,25]. The Galf transferases that incorporate Galf into the glycans have been studied mainly in Mycobacterium tuberculosis[26,27]. In Aspergillus spp, a Galf transferase involved in the biosynthesis of antigenic O-glycans was identified [28]. The glycans that contain Galf are involved in immunological reactions [29,30,31], therefore they are envisioned as targets for diagnosis. This article aims to explore the perspective of methods based on synthetic sugar antigens for the production of monoclonal antibodies for serological detection of fungus-specific antigens.

β-galactofuranosyl structures in human infective fungi
Galf is mainly present in the β-configuration in fungi, many of them involved in mammal infections. It is also present in plant pathogenic fungi, but these will not be discussed in the present review.

Fungi that infect mammals and contain glycans with Galf are listed in Table 1. Galf is usually present as terminal sugar, linked to each other by β(1→6) or β(1→5) linkages or branching a mannan core at the O-2 or O-3 position of mannose.

In 1985, Bennet et al. showed that galactofuranosyl groups are immunodominant in A. fumigatus galactomannan (GM) [45], and accordingly, Galf-deficient mutants of A. fumigatus display an attenuated virulence [25].

The cell walls of A. fumigatus have at least four different types of molecules containing Galf, which are important for cell wall integrity (Table 1) [29,32,33,34,46,47]. Galf units were identified in O- and N-linked chains of glycoproteins and also in glycosylophosphorylceramides [48]. The glycosylophosphorylceramides with Galf(β1→6) linked to a mannose core were highly immunogenic.

Neosartorya spp., teleomorph of A. fumigatus, are a cause of invasive disease in immunocompromised patients [49]. Acute respiratory distress syndrome has been attributed to N. udagawae [50]. The structure [→6]-Galf[β1→5]-Gal/[β1→5]-D-Gal/[β1→] has been determined in polysaccharides of some species of Neosartorya [36].

Fusarium is a pathogen of plants, but some species are pathogenic for humans, particularly Fusarium verticillioides and F. proliferatum [51]. Fusarium species cause a broad range of opportunistic infections in humans. In healthy individuals, the most common clinical manifestations are onychomycosis, skin infections and keratitis, whereas in immunocompromised patients disseminated infections with multiple necrotic lesions may occur [52].

It is important to discriminate Aspergillus from Fusarium infections since both differ in their response to common antifungals. Using a combination of two antibodies, both species could be differentiated by immunohistology (see below) [31].

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Considered a major health problem in animals, they adapted to infect humans and are now considered a major health problem in humans. Due to immunosuppressive effects, impairment of lymphocyte proliferation was shown. One of the major cell wall components secreted to the medium is a GM. Structure determinations showed that \( \text{Galf}^\rightarrow \) terminal units are \( \beta(1\rightarrow3) \) linked to a mannan core. Polygalactofuranosyl chains, similar to those produced by \( \text{T. mentagrophytes} \) and \( \text{T. rubrum} \), cause chronic dermatophyte infections, often associated with infection of the nails (onychomycosis) \[58\]. Although they first infected animals, they adapted to infect humans and are now considered a major health problem \[54\]. Cell wall antigens secreted by the fungus may diffuse into the dermis and establish the infection, due to immunosuppressive effects. Impairment of lymphocyte proliferation was shown \[59\]. One of the major cell wall components secreted to the medium is a GM. Structure determinations showed that \( \text{Galf}^\rightarrow \) terminal units are \( \beta(1\rightarrow3) \) linked to a mannan core. Polygalactofuranosyl chains, similar to those produced by \( \text{A. fumigatus} \), have not been found in \( \text{T. mentagrophytes} \) and \( \text{T. rubrum} \). Accordingly, a monoclonal antibody against the GM of \( \text{A. fumigatus} \) showed very low cross-reactivity with exoantigens from cultures obtained from clinical specimens \[56\]. Glycosylphosphatidylinositols labeled with \(^{[3]H}\)-galactose and \(^{[3]H}\)-mannose were biosynthesized by membrane preparations of \( \text{T. rubrum} \). The lability to acid of the galactose suggested its furanosic configuration \[57\].

A linear chain of \( \beta1\rightarrow6 \) linked \( \text{Galf}^\rightarrow \) attached to a small mannan was also found in polysaccharides of \( \text{Malassezia spp.} \). \( \text{Malassezia spp.} \) are human pathogens responsible for skin diseases and they are also associated with catheter-related fungaemia \[58\].

### Table 1. Structural units containing \( \beta\)-galactofuranose in mammal-pathogenic fungi.

| Organism          | Structure                                      | Study            | Ref.       |
|-------------------|-----------------------------------------------|------------------|------------|
| Aspergillus       | \( \text{Galf}(\beta1\rightarrow5)\text{Galf} \) | Latgé \[29,32,33,34,35\] |            |
|                   | \( \text{Galf}(\beta1\rightarrow3)\text{Man} \) | Tefsen et al.    |            |
|                   | \( \text{Galf}(\beta1\rightarrow6)\text{Man} \) | Fontaine et al.  |            |
|                   | \( \text{Galf}(\beta1\rightarrow2)\text{Man} \) | Jin              |            |
|                   | \( \text{Galf}(\beta1\rightarrow5)\text{Galf}(\beta1\rightarrow6)\text{Man}(\alpha1\rightarrow6)\text{Man} \) | Leitá et al.     |            |
| Neosartorya       | \( [\rightarrow6]\text{Galf}(\beta1\rightarrow5)\text{Galf}(\beta1\rightarrow5)\text{Galf}(\beta1) \) | Leal et al.      | \[36\]    |
| Neotestudina rosatii | \( \text{Glc}(\alpha1\rightarrow2)\text{Galf}(\beta1\rightarrow6)\text{Galf}^\beta \) | Leal et al.      | \[37\]    |
|                   | \( \text{Glc}(\alpha1\rightarrow2)\text{Galf}(\beta1\rightarrow2)\text{Man} \) | Ahrazem et al.   | \[31,38\] |
| Fusarium          | \( \text{Galf}(\beta1\rightarrow6)\text{Galf} \) | Wiedemann et al. |            |
| Trichophyton      | \( \text{Galf}(\beta1\rightarrow3)\text{Man} \) | Ikuta et al.     | \[39\]    |
| Malassezia        | \( \text{Galf}(\beta1\rightarrow6)\text{Galf} \) | Shibata et al.   | \[40\]    |
| Sporothrix schenckii | \( \text{Galf}(\beta1\rightarrow6)\text{Galf} \) | Mendonça-Previato et al. | \[41\] |
| Cladosporium herbarum | \( \text{Galf}(\beta1\rightarrow6)\text{Galf}(\beta1\rightarrow6)\text{Galf}(\beta1\rightarrow2)\text{Man}(\alpha1\rightarrow6)\text{Man} \) | Swärd-Nordmo et al. | \[42\] |
| Paracoccidioides  | \( \text{Galf}(\beta1\rightarrow6)\text{Man}(\alpha1\rightarrow2)\text{Man} \) | Almeida et al.   | \[30,38,118\] |
| Neotestudina rosatii | \( \text{Glc}(\alpha1\rightarrow2)\text{Galf}(\beta1\rightarrow6)\text{Galf}^\beta \) | Leal et al.      | \[37\]    |
| Fonseeca pedrosoi | \( \text{Glc}(\alpha1\rightarrow2)\text{Galf}(\beta1\rightarrow6)\text{Man}(\alpha1\rightarrow2)\text{Man} \) | Shibata et al.   | \[44\]    |

\[1\] When configuration is not indicated, it corresponds to the pyranosyl configuration. All the sugars belong to the D-series.
Sporothrix schenckii is the agent of sporotrichosis in humans and animals, producing skin and subcutaneous lesions. It is present in all continents, especially in tropical and subtropical areas [59,60]. In an early work, GalF-containing polysaccharides were isolated from the supernatants of S. schenckii cultures [41]. It was found that a mannan core is substituted by β-Galf chains which are responsible for cross-reactions with other fungal antigens. Apparently, no further studies on this GM were described. In turn, peptidorhamnomannans with both N- and O-linked carbohydrate chains as the immunodominant structures were obtained from extracts of the cell walls [61]. Later studies characterized a peptidorhammanan (Gp70) isolated from the yeast phase of S. schenckii as an adhesin involved in the host–pathogen interaction, but GalF was not reported as a constituent of this glycoprotein [62].

Cladosporium spp. are mainly plant pathogens but some may trigger allergic reactions in sensitive individuals. Prolonged exposure to a high concentration of spores may produce chronic asthma. A glycoprotein named Ag-54, which contains 80% carbohydrate, was an allergen purified from C. herbarum. Structural studies showed chains of β1→6 linked GalF bound to O-2 of 1→6 linked mannoses (Table 1) [42].

Paracoccidioides brasiliensis is endemic to regions of Latin America, causing a mycosis which spreads from the lungs to many organs and if not treated could be fatal [63]. Paracoccidioidomycosis (PCM) is commonly diagnosed by identifying budding yeast cells in biological fluids or histologically [64]. Glycolipids extracted from yeast and mycelium forms of P. brasiliensis reacted with sera from histoplasmosis patients [71]. The authors tentatively assigned the α-configuration for the GalF from the yeast form, in contrast with the configuration found for the GalF in the same phase in P. brasiliensis. The configuration of galactofuranosides is unequivocally assigned by NMR spectroscopy [12], which was not used by Barr et al. in 1984 [71]. The glycosphingolipids from the mycelial phase were not described.

In A. niger, α-Galf(1→2) linked to mannose was characterized [72]. Although this species is less pathogenic for humans than A. fumigatus, it could produce allergic reactions in high concentrations.

**Table 2. Structural units containing α-galactofuranose in mammal-pathogenic fungi.**

| Organism                  | Structure          | Study          | Ref.   |
|---------------------------|--------------------|----------------|--------|
| Paracoccidioides brasiliensis | Galf (α1→6) Man (α1→2) Man | Ahrazem et al. | [38,70] |
|                           |                    | San-Blas et al. |        |
| Histoplasma capsulatum    | Galf (α1→6) Man (α1→2 or 6) | Barr et al. | [71]   |
| Aspergillus niger         | Galf (α1→2) Man    | Takayanagi et al. | [72]   |

*All the sugars belong to the D-series.*
Table 3. Structures with galactofuranose units found in fungal glycans which have been chemically synthesized.

| Structure | Study | Ref. |
|-----------|-------|------|
| A n = 0   | R = H, Bn | van Heeswijk et al. [26,76,77,78,79,80] |
| n = 0–5   | R = CH₃ | Lederkremer et al. [81,82] |
| n = 2     | R = C₆H₁₀ | Completo and Lowary |
|           | R = H, Pr | Pathak et al. |
|           | R = H, allyl | Gurjar et al. |
|           | R = (CH₂)₂CHNH₂COOH | Sugawara et al. |
|           | R = arm–biotin | Veeneman et al. |
|           |         | Cattiaux et al. |
| B n = 0   | R = CH₃ | Marino et al. [26,79,83,84,85] |
| n = 4     | R = C₆H₁₀ | Completo and Lowary |
|           | R = allyl | Euzen et al. |
|           | R = allyl | Pathak et al. |
|           |         | Splain and Kiessling, Zhang et al. |
| C R = decenyl |               | Gandolfi-Donadio et al. [26,87] |
| R = octyl |               | Completo and Lowary |
| D R = decenyl |               | Gandolfi-Donadio et al. [26,87,88] |
| R = octyl |               | Completo and Lowary |
| R = CH₃ |               | Deng et al. |
| E R = H |               | Marino et al. [89,90,91] |
| R = decenyl |               | Baldoni and Marino |
| R = (CH₂)₄CO₂CH₃ |               | Tsui et al. |
The antigenic properties of β-galactofuranosides are well known [29,30,31] but the immunological role of α-Galf was apparently not described. The differences in the Galf configuration in the galactomannans of the infective P. braziliensis and A. fumigatus could explain the low cross-reactivity in serological tests using a specific antibody [73].

### Structural analysis of Galf-containing polysaccharides or glycoconjugates

In earlier works, the identification of Galf units in glycoconjugates was performed using chemical methods. Taking advantage of the greater lability of furanosic linkages with respect to the pyranosic bonds, terminal Galf units may be selectively released from the molecule by mild acid hydrolysis, separated by chromatographic techniques or by dialysis, depending on the MW of the remaining degraded molecule, and then analyzed by chromatographic methods or even GC–MS. Also, the exocyclic chain of terminal Galf could be selectively oxidized by periodate under mild conditions, and upon reduction with NaBH₄ converted to arabinofuranose, which may be identified after acid hydrolysis by GC–MS. Application of these methods is exemplified in the report on the determination of the structure of glycolipids of P. brasilien-sis [65]. Information on the substitution position of the galactofuranosyl linkages is provided by methylation analysis [74].

NMR has also been useful for the identification of Galf units in oligosaccharides. ¹H NMR spectra usually show deshielded anomeric signals for Galf units, compared with those of pyranosic units. Particularly useful is the ¹³C NMR spectroscopy because the furanosyl ring has a specific signal pattern, easily distinguishable from the pyranosyl analog. For β-Galf units, signals corresponding to the anomeric carbon, and C-2 and C-4 resonate significantly deshielded in comparison with pyranosic signals. In addition, α-Galf has also a particular pattern. Advances in NMR spectroscopy have facilitated the characterization of oligosaccharides. Thus, bidimensional techniques allow not only the identification of the monosaccharides and their anomeric configuration but also to establish the position of substitution and sequences [35,39,75].

### Chemically synthesized oligosaccharides of antigenic glycan

The use of chemically synthesized oligosaccharides of defined structure avoids the disadvantages of glycan obtained from natural sources, such as, the difficulty of isolating and purifying sufficient quantities, and problems associated with their heterogeneity. Also, more specificity may be achieved by using a neoantigen. Following this line, a biotinylated tetrasaccharide with Galf(1→3)Galβf linkages was synthesized (Table 3A; n = 2). This synthetic antigen was recognized by the monoclonal antibody EB-A2 against Aspergillus [76].

In Table 3, the structures of Galf-containing oligosaccharides, which have been chemically synthesized and are part of fungal glycan, are shown. Most efforts have been directed to the synthesis of oligosaccharides containing Galf(1→3)Galβf, the antigenic unit in Aspergillus [26,77,78,79,80,81,82].

Several chemical syntheses for the Galf(1→6)Galβf disaccharide have been reported (Table 3B) [26,83,84,85]. This is the minimal epitope in Fusarium glycan [31]. A hexasaccharide with the same linkages was synthesized [86]. The two trisaccharides containing both types of linkages (Table 3C & D) were prepared because of their importance as repeating units in the arabinogalactan of M. tuberculosis [93], but is also present in a polysaccharide extracted from Neosartorya [36]. Galf is frequently linked to mannose forming galactomannans. The synthesis of the disaccharide Galf(1→3)Man (Table 3E) [89,90,91] and the more complex heterotetrasaccharide (Figure 1F) [92], which was indicated as the minimal epitope in the mycelial cell wall of A. fumigatus [35], were described.

The synthesis of Galf-containing molecules requires the efficient preparation of derivatives of
D-Gal in the furanosic configuration, free from the pyranosic forms, as precursors of Gal\(\beta\)-units in the target molecules. Furthermore, efficient glycosylation methodologies and the consequent availability of galactofuranosyl donors as well as conveniently substituted derivatives as glycosyl acceptors are required (Figure 1) [27,94,95,96].

Most sugars lead by conventional methods to pyranosic derivatives, which are thermodynamically more stable. However, in conditions under which other monosaccharides lead mainly to pyranosic products, large proportions of galactofuranosic derivatives can be obtained from galactose. This is the case of the traditional Fisher glycosylation, which yields a mixture of furanosic and pyranosic glycosides that must be separated by chromatography [27]. An example may be found in the preparation of the pentenyl galactofuranosides which were used as precursors in glycosylation reactions [97].

The peracylated derivatives are commonly used as precursors, particularly penta-O-benzoyl-Gal\(\beta\)-furanosyl (BzGal\(\beta\)) that may be obtained as crystalline products, in one step, from galactose [98]. Glycosylation of BzGal\(\beta\) promoted by a Lewis acid affords the \(\beta\)-galactofuranosides, as a result of anchimeric assistance. In Figure 2, an example for the synthesis of the natural disaccharides Gal\(\beta\)[(1→5)Gal\(\gamma\)] [83] and Gal\(\beta\)[(1→6)Gal\(\gamma\)] [78] is shown.

One of the most popular glycosylation procedures is the trichloroacetimidate method [99], which is compatible with acid-sensitive acceptors and was used first for the synthesis of Gal\(\beta\)[(1→3)]GlcNAc [100]. As this is an area of active research, several more methods have been designed and extensively reviewed [26,95,96]. The synthetic oligosaccharides could be precursors for artificial antigens to be used for diagnosis [101] or for the construction of synthetic vaccines [102,103].

**Immunologic detection of Gal\(\beta\)-containing molecules**

A monoclonal antibody, which recognized Gal\(\beta\)[(1→5)]Gal\(\beta\)-epitopes was produced by immunizing rats with an extract of *A. fumigatus* mycelia. The antibody called EB-A2 also detected the GM of other *Aspergillus* species, using an ELISA assay [104,105]. It was commercialized as Platelia™ *Aspergillus* ELISA (Bio-Rad Laboratories and Sanofi Diagnostics, CA, USA). The specificity and sensitivity of the assay were reviewed [106]. Multivalent gold nanoparticles carrying Gal\(\beta\) were recognized by this antibody [107]. The presence of GM in circulation depends on the manifestation of the disease. For instance, negative results are commonly obtained for the detection of GM in sera of allergic bronchopulmonary aspergillosis. Reviews on diagnosis of aspergillosis have been published [108,109,110]. Apparently, this is the only commercialized test based on detection of Gal\(\beta\). It was shown that EB-A2 detects GM in supernatants of several *Fusarium* species [111,112]. However, Wiedemann *et al.* described a novel monoclonal antibody, AB 135–8, which recognizes Gal\(\beta\)in *Fusarium* but as part of a different antigen [31]. In fact, the structural unit Gal\(\beta\)[(1→6)]Gal\(\gamma\), was characterized in a polysaccharide extracted from *Fusarium* [75] but it was not reported in *Aspergillus* (Table 1). The same antigenic disaccharide was found in *Malassezia* galactomannans, which did not react with the EB-A2 antibody against *A. fumigatus*, but apparently was not tested with AB 135–8 against *Fusarium*. Antibodies against *M. fursiu* did not react with galactomannans of *A. fumigatus*, *T. rubrum* or *F. pedrosoi*, confirming the presence of a different linkage for the Gal\(\beta\)-units, but apparently these were not tested with AB 135–8 against *Fusarium* [40].

The Platelia test was negative for yeast and mold forms of *S. scheneckii* [113]. Controversial results were

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**Figure 1. General strategy for the synthesis of Gal\(\beta\)-containing molecules.**
Figure 2. Synthesis of disaccharides present in fungal galactomannans. DSB: Disiamylborane; THF: Tetrahydrofuran.
reported for Cryptococcus neoformans. While a positive test was reported for a patient with C. meningitis [114], a later report revealed no cross-reaction with culture extracts, purified polysaccharides, clinical specimens and specimens from animals following experimental infection [115]. These results are explained by the composition of the cell wall of C. neoformans. Although galactoxylomannan is a constituent of the cell wall, and D-Gal is its major component, this sugar is mainly in the pyranosic configuration, with only 2% tentatively assigned to Gal, considering a small peak in the 13C NMR spectrum [116], which is as explained above, is not enough to guarantee the configuration. More recently, it was demonstrated that Gal is not required for growth or virulence of C. neoformans [117].

In P. brasiliensis, Gal is the immunodominant unit in a glycosylinositolphosphoryl ceramide [43], however, the main diagnostic antigen is the glycoprotein gp43. Studies of N-deglycosylation gave rise to a protein of 38 kDa, which strongly reacted with sera from patients with PCM [118]. Also, recombinant gp43 isoforms as N-mannosylated proteins were expressed in the yeast Pichia pastoris and showed good specificity for detection of PCM in sera [119]. These results indicate the presence of other epitopes in gp43, although the cause of cross-reactivity with sera from patients with other mycoses would be the terminal Gal [118][120]. Immunodiagnosis of gp43 in PCM using a latex test was recently described [73].

In the previous examples, Gal is present in the galactomannans in the β-anomeric configuration. A few examples of α-Gal may be seen in Table 2. The antigenic properties of α-Gal were apparently not described. As expected, isolates from H. capsulatum in yeast and mold phases were not recognized by the monoclonal antibody against the Aspergillus GM [113]. However, it was reported that some patients with disseminated histoplasmosis gave positive results with this antibody [121].

Conclusion & future perspective
Galβ is an antigenic structural unit in many infectious fungi, which is not biosynthesized by humans. The preparation of synthetic neoglycoconjugates containing β-Gal for the diagnosis of some extended mycoses as aspergillosis is a field worth to explore. The synthetic antigens would help define the structure of the corresponding epitopes and in a more ambitious project they could be the starting line for the synthesis of carbohydrate-based vaccines [102]. In reviewing the natural structures, it is challenging to understand why in some dimorphic fungi the commonly found β-Gal changes the anomeric configuration to α-Galβ in the transition between phases. The α-Galβ transferases necessary for the construction of the linkages in some galactomannans have not yet been described.

Authors’ contributions
C Marino and RM de Lederkremer contributed with the design, acquisition and interpretation of data, writing and revision. A Rinflerch provided her expertise in medical aspects.

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Executive summary
Biomarkers
• Diagnosis of fungal infections and identification of the causative agent is important for the selection of an accurate therapy. The use of biomarkers may provide faster results and complement culture and histological methods.
Carbohydrate-based markers
• Galactofuranose (Galβ) is an attractive candidate as a biomarker for diagnosis of infections, since it is the antigenic epitope in glycans of several pathogenic fungi and is not biosynthesized by mammals. An ELISA assay based on the EB-A2 antibody that detects the Galβ in the GM of Aspergillus is commercialized. The different linkages of the Galβ to other sugars in the fungal carbohydrates may provide specificity, a line of research that needs further studies.
Chemically synthesized oligosaccharides of antigenic glycans
• The impressive advance achieved in the chemical synthesis of the natural oligosaccharides encourages their use as specific antigens.
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