The cell wall is the major fungal structure involved in the interaction with the host and most of the immunological effects observed with intact fungal cells have been reproduced with cell-wall components. As a result of the exposure to fungal antigens, most individuals develop both cellular and antibody responses intended to limit the invasiveness or to eradicate the fungus from the infected tissues. However, a number of fungi including Candida albicans, Cryptococcus neoformans, Blastomyces dermatitidis, Coccidioides immitis, Trichophyton spp. and Histoplasma capsulatum can also induce T- and B-suppressive activities. A wide diversity of immunodominant cell-wall antigens for both cell-mediated and humoral responses have been identified in the most important fungal pathogens, although considerable differences exist in the information available at the molecular level among the different mycoses. Cellular responses require macrophage and Th1 activation, whereas humoral responses comprise the activation of the complement system and the induction of antibodies. The ability of fungal cell-wall components to elicit cellular or humoral immune responses has been traditionally used in the serodiagnosis of mycoses, the identification of fungal organisms and the development of vaccines for the prevention of mycoses. In the future, the analysis of such molecules will provide critical information in understanding the nature of host–fungus interactions.

**Keywords**  
cell-wall antigens, cellular response, fungi, humoral response

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**Introduction**

Some members of the kingdom Fungi are adapted to grow on mucosal surfaces and internal tissues from vertebrate hosts. As a result of this exposure to fungal antigens, most individuals develop both cellular and antibody responses intended, depending on the body site, to limit the invasiveness or to eradicate the fungus from the infected tissues. Studies from animal models and infected patients suggest that the immune response mounted is complex but basically similar in the different mycoses. It has been established that protection against a variety of mycosis including systemic candidiasis, cryptococcosis, aspergillosis, blastomycosis, histoplasmosis, coccidioidomycosis and paracoccidioidomycosis correlates with the balance occurring between CD4$^+$ T-helper type 1 (Th1) and Th2 responses [1–5]. Generation of Th1 cytokine responses activates neutrophils and macrophages to kill the fungal cells, whereas Th2 responses contribute to disease exacerbation and pathology most likely by deactivating the fungicidal effector cells [6]. In general, the development of protective antifungal Th1 responses requires the concerted positive action of several cytokines such as interferon (IFN)-γ and interleukin IL12, and the relative absence of Th2 cytokines, such as IL4 and IL10, that inhibit development of Th1 responses [7]. The same type of systemic Th1 response is involved in protection in oropharyngeal and esophageal but not in vaginal candidiasis [8], where a vaginally restricted Th1 response has been recently described [9]. Lymphocyte responses in mice infected by Pneumocystis carinii are not clearly dichotomous between Th1 and Th2 responses, and both Th1 and Th2 subsets can participate in clearance of infection [10]. Although non-viable cells and antigenic extracts are able to induce cell-mediated
responses, viable organisms, which persist in the host for some time, induce a stronger, long-lived cell-mediated immunity [11,12]. The cellular immunity to fungal antigens has been the subject of several reviews [3,6,8,11,13–26].

Recent evidence shows that antibody immunity may also be involved in protection against certain mycoses, in particular cryptococcosis and candidiasis, and there is increasing awareness of the interdependence of both the cellular and humoral arms of the immune system in dealing with infectious agents [13,14]. One of the problems of establishing the relevance of antibody immunity in protection relies in the complex antigenic nature of fungal cells, as protective antibodies with specificity to a limited number of epitopes may not be produced at protective levels [13]. In fact, it has been reported that during infection or immunization, antibodies with a wide range of specificities are induced and polyclonal antisera usually comprise a mixture of protective, irrelevant and harmful antibodies [27]. In spite of the difficulties in reaching protection with polyclonal antibodies, anti-Candida IgA antibodies produced as a result of both systemic infection and intravaginal immunization with killed yeast cells enhanced resistance in a rat model of vaginal candidiasis [28].

Despite their ability to elicit immune responses in immunocompetent hosts, a number of fungi including Candida albicans, Cryptococcus neoformans, Blastomyces dermatitidis, Coccidioides immitis, Trichophyton spp. and Histoplasma capsulatum can also induce T- and B-suppressive activities [11,17–21,29,30].

Table 1  Major fungal cell-wall antigens that modulate cellular responses

<table>
<thead>
<tr>
<th>Fungus</th>
<th>Antigen</th>
<th>Immunomodulation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. albicans</td>
<td>Mannan</td>
<td>SUP</td>
<td>[16,31]</td>
</tr>
<tr>
<td></td>
<td>SMP200</td>
<td>STI</td>
<td>[32]</td>
</tr>
<tr>
<td></td>
<td>MP65</td>
<td>STI</td>
<td>[33]</td>
</tr>
<tr>
<td></td>
<td>β-1–2 Oligomannosides</td>
<td>STI</td>
<td>[34]</td>
</tr>
<tr>
<td></td>
<td>β-1–6 Glucan</td>
<td>STI</td>
<td>[35–37]</td>
</tr>
<tr>
<td></td>
<td>Chitin</td>
<td>STI</td>
<td>[38]</td>
</tr>
<tr>
<td></td>
<td>Hisp70</td>
<td>STI</td>
<td>[39]</td>
</tr>
<tr>
<td>T. rubrum</td>
<td>Mannan</td>
<td>SUP</td>
<td>[28]</td>
</tr>
<tr>
<td>C. immitis</td>
<td>GP58</td>
<td>STI</td>
<td>[40]</td>
</tr>
<tr>
<td></td>
<td>C-ASWS</td>
<td>STI</td>
<td>[41]</td>
</tr>
<tr>
<td></td>
<td>33-kDa</td>
<td>STI</td>
<td>[42]</td>
</tr>
<tr>
<td></td>
<td>Antigen 2</td>
<td>STI</td>
<td>[43]</td>
</tr>
<tr>
<td></td>
<td>4-Hydroxyphenylpiruvate dioxygenase</td>
<td>STI</td>
<td>[44]</td>
</tr>
<tr>
<td></td>
<td>Hisp60</td>
<td>STI</td>
<td>[45]</td>
</tr>
<tr>
<td>B. dermatitidis</td>
<td>WI-1</td>
<td>STI</td>
<td>[46]</td>
</tr>
<tr>
<td>C. neoformans</td>
<td>Glucuronoxylomannan</td>
<td>SUP</td>
<td>[47]</td>
</tr>
<tr>
<td></td>
<td>Cell wall proteins</td>
<td>STI</td>
<td>[48]</td>
</tr>
<tr>
<td></td>
<td>Capsular mannoproteins</td>
<td>STI</td>
<td>[49]</td>
</tr>
<tr>
<td>H. capsulatum</td>
<td>HIS-80</td>
<td>STI</td>
<td>[50]</td>
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<tr>
<td></td>
<td>HIS-62</td>
<td>STI</td>
<td>[51]</td>
</tr>
<tr>
<td>P. brasiliensis</td>
<td>Gp43</td>
<td>STI</td>
<td>[52]</td>
</tr>
<tr>
<td>P. carinii</td>
<td>Major surface glycoprotein</td>
<td>STI</td>
<td>[53,54]</td>
</tr>
</tbody>
</table>

SUP, suppression; STI, stimulation.
lactoferrin secretion, Th1 cytokines and activated effectors of human natural immunity, such as natural killer cells, macrophages and PMNs, to produce a full range of cytokines. Using affinity chromatography, they identified and characterized a mannoprotein of 65 kDa, designated MP65, that was considered the major T-cell immunogen in the MP-F2 fraction [33]. The gene encoding the protein component of MP65 has been cloned and both the recombinant and the native 65-kDa proteins were able to induce lymphoproliferation of peripheral blood mononuclear cells of healthy subjects and human T-cell clones specific for MP-F2 [57]. The highest T-cell reactivity has been mapped to the N-terminus region [33] and a motif sequence has been identified that represents the minimal epitope recognized by human T-cell clones [58]. A 200-kDa stress mannoprotein from *C. albicans* cell wall has been reported to induce increased tumour necrosis factor (TNF) secretion in ANA-1 murine macrophages [32]. β(1,2)-oligomannoside components from the cell wall of *C. albicans* have been reported to induce TNF-α production by human monocytes to an extent that was dependent on the length of the mannosyl chain [59, see also review by Cutler J.E., this issue]. Other polysaccharides present in the *C. albicans* cell wall such as glucans and chitin are much less immunogenic than mannans or mannoproteins but have also immunostimulatory potential, especially on macrophages [34,35,38].

Interestingly, hyphal forms of *C. albicans*, but not the yeast form, seem to modulate specific functions in macrophages [36]. β(1,6)-glucan has been shown to be a potent chemokine inducer, and differences in the stimulation of macrophages by yeast and hyphal forms of *C. albicans* have been attributed to a differential expression of β(1,6)-glucan on the cell-wall surface of both morphological forms [37]. In addition to the stimulatory properties displayed by different constituents of the *C. albicans* cell wall, mannan can also induce immunosuppressive activities mediated by both specific and non-specific T-suppressor responses [16,32]. Mannans are able to suppress neutrophil activity, and when administrated to mice immunized with *C. albicans*, mannan has been reported to suppress delayed-type hypersensitivity [60–62]. The immunosuppressive effect seems to be mediated by oligosaccharides having six or less mannose residues [63]. The suppressive effect induced by mannan can be abrogated by the derivate of endotoxin monophosphoryl lipid A [64]. A similar immunosuppressive phenomenon has been demonstrated with mannan from *Trichophyton rubrum* [28]. Several mechanisms have been proposed to explain the mannan-mediated immunosuppression, including defective lymphocytes and monocyte-macrophages, prosta-

glandin E₂ production, suppressor T-lymphocytes, interaction with cytokines, induction of IL-4 and IL-12p40, and interference with co-stimulation activities and leukocyte homing [65,66]. *C. albicans* heat shock protein 70 (hsp70) has been shown to be a strong inducer of cell-mediated immunity and the production of IFN-γ was similar to that induced by heat-inactivated *C. albicans* cells. This activity is mainly associated to the C-terminal region of the molecule [39].

A number of components from the cell wall of *C. immitis* spherules has been reported to elicit potent proliferative response of immune T cells. These constituents include a membranous outer wall component (spherule outer wall, SOW) [67], an alkaline-soluble, water-soluble antigen, designated C-ASWS [41], and a 33-kDa cell-wall antigen from mature spherules [42]. Antigen 2, a major immunoreactive component of *C. immitis* mycelium and spherule cell walls, has also been shown to elicit T-cell responses in mice immunized with *C. immitis* to a level comparable to that obtained with C-ASWS [43]. The reactivity induced by SOW is due to a glycoprotein of 58 kDa, as it stimulated T cells from skin test-positive individuals to produce Th1 cytokines [40]. The enzyme 4-hydroxyphenylpyruvate dioxygenase present in a soluble comidal cell-wall fraction (SCWF), and the *C. immitis* hsp60 homologue also stimulate T cells ([44,45] and review by Cole and Hung, this issue).

Klein and colleagues [68] identified a 120-kDa cell-wall protein, designated WI-1, which is an adhesin expressed at the cell-wall surface of *B. dermatitidis* that elicited a strong cellular and humoral responses in humans and dogs with blastomycosis. The WI-1 epitopes recognized by T-cells during human infection and the major histocompatibility complex antigens that bind and display these epitopes to human CD4⁺ T-cells have been identified. Interestingly, although the antibody response is mainly directed against a 25-amino acid repeat in the central region of the molecule, T-cell determinants are mapped to the amino terminus [46].

Information about major T-cell immunogens from cell walls of *C. neoformans*, *H. capsulatum*, *P. brasiliensis* and *P. carinii* is scarce. The glucuronoxylomannan, the major component of the capsular polysaccharide of *C. neoformans*, has been extensively studied in the induction of antibody responses and it has been shown to suppress T-cell responses [47], but it does not stimulate T-cells to produce a cell-mediated immune response [69]. However, a mannoprotein from the capsule and proteins present in a cell-wall and membrane extract of *C. neoformans* have been reported to induce strong lymphocyte proliferation [48,49]. The mannoproteins enhanced HIV replication in HIV-
infected human peripheral blood mononuclear cells [70]. Two proteins isolated from a cell-wall and cell membrane extract of *H. capsulatum* yeast cells, designated HIS-62 and HIS-80, the *H. capsulatum* homologues of hsp60 and hsp70, respectively [50,71], have been identified as major T-cell elicitors in patients with histoplasmosis [50,51]. A 43-kDa glycoprotein expressed at the cell-wall surface of *P. brasiliensis* has been shown to elicit both a strong humoral response and delayed-type hypersensitivity reaction in humans [52]. The gp43 T-cell epitope has recently been mapped to a 15-mer peptide, designated P10, which contains an essential epitope, HTLAIR, in the inner core [5]. A *P. carinii* surface mannoprotein of 120 kDa has been shown to elicit strong T-cell responses in immunized and naturally infected animals [53,54].

**Humoral responses to cell-wall components**

As in the case of the cellular immunity, fungal cell-wall components are potent elicitors of humoral responses in immunocompetent individuals. These responses comprise the activation of the complement system and the induction of antibodies. The complement activation by pathogenic fungi has been recently reviewed [72]. Research in the antibody response induced by fungal infections has been fuelled by its potential application to serodiagnosis of invasive mycosis. Consequently, considerable information exists about the antigenicity of cell-wall constituents of human fungal pathogens [27,52,73–83].

Mannans and mannoproteins are the major antigens in the fungal cell wall that stimulate B-cell responses and, as a consequence of that, patients with mycoses usually have anti-mannan antibodies in serum. Although there is some degree of cross-reactivity among them, a variety of mannans and mannoproteins have been described in the cell walls of fungi (Table 2). The antigenic structure of the *C. albicans* mannan has been studied extensively, as it was one of the first antigens used in the serodiagnosis of invasive candidiasis [73,75,76]. Identification of mannan epitopes involved in the reactivity with antibodies has been studied in some detail [84–88]. When analysing the differences in the antibody response against α- and β(1,2)-linked mannose residues, Jouault *et al.* [109] observed that sera from patients colonized by *Candida* had antibodies against both types of residues whereas patients with invasive candidiasis had strong antibody responses against α(1,2)-linked mannose residues but not against β(1,2)-linked oligomannosidic epitopes. Differences in epitopes within the mannan molecule are responsible for the two serotypes described in this fungus and the serotype A specificity has been mapped to the oligosaccharides Manpβ(1,2)Manpα(1,2)Manpα(1,2)Manpα(1,2)Man and Manpβ(1,2)Manpβ(1,2)Manpα(1,2)Manpα(1,2)Man [110]. In the cell wall of *C. albicans*, mannan is associated to proteins to form mannoproteins [111]. Several cell-wall mannoproteins, including a number of germ tube specific antigens with molecular weights of 155, 200 and >200 kDa [85], 62 and 70 kDa [86], 180 and 260 kDa [87], 235–250 kDa [88], 35 and 27 kDa [89], 43, 47 and 80 kDa [90], 20–67 kDa [91], 110–170 kDa [92], 43 kDa [93], 30 kDa [94], and 104 and 117 kDa [95], as well as a 58-kDa fibrinogen-binding component, mp58 [96], have been reported to elicit strong antibody responses in patients with invasive candidiasis or immunized animals. Detection of antibodies against germ tube specific antigens is considered of relevance in the serodiagnosis of invasive candidiasis [75]. By using sera from both mice and rabbits hyperimmunized with mp58, the highly reactive epitope HTHADGEVH has been recently identified in the C-terminal domain of mp58 [96]. A number of heat shock mannoproteins of 180–200, 130–150, 90–110 and 67–70 kDa from the cell wall of *C. albicans* have been identified as major targets for salivary secretory IgA [112].

Among the variety of antigens from *A. fumigatus* that induce antibody responses, galactomannan is the cell-wall antigen characterized with more detail. The consensus structure includes a mannan core containing α(1,2)- and α(1,6)-linked residues in a ratio of 3:1, and the antigenic side chains, branched on two α(1,2)-linked mannose residues, are composed of β(1,5)-galacto-

**Table 2** Major fungal cell-wall antigens that stimulate antibody responses

<table>
<thead>
<tr>
<th>Fungus</th>
<th>Antigen</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>A. fumigatus</em></td>
<td>Galactomannan</td>
<td>[78]</td>
</tr>
<tr>
<td></td>
<td>33-kDa serine protease</td>
<td>[78,84]</td>
</tr>
<tr>
<td></td>
<td>18-kDa RNase</td>
<td>[78,84]</td>
</tr>
<tr>
<td></td>
<td>90-kDa Catalase</td>
<td>[78,84]</td>
</tr>
<tr>
<td><em>B. dermatitidis</em></td>
<td>WI-1</td>
<td>[83]</td>
</tr>
<tr>
<td><em>C. albicans</em></td>
<td>Mannan</td>
<td>[73,76]</td>
</tr>
<tr>
<td></td>
<td>Germ tube specific antigens</td>
<td>[85–95]</td>
</tr>
<tr>
<td></td>
<td>MP58</td>
<td>[96]</td>
</tr>
<tr>
<td></td>
<td>Hsp90</td>
<td>[97]</td>
</tr>
<tr>
<td></td>
<td>Enolase</td>
<td>[98]</td>
</tr>
<tr>
<td><em>C. immittis</em></td>
<td>β-Glucosidase</td>
<td>[82]</td>
</tr>
<tr>
<td></td>
<td>Antigen 2</td>
<td>[81]</td>
</tr>
<tr>
<td></td>
<td>33-kDa</td>
<td>[42]</td>
</tr>
<tr>
<td></td>
<td>Gp58</td>
<td>[40]</td>
</tr>
<tr>
<td>*C. neoformans</td>
<td>Glucuronoxylomannan</td>
<td>[99]</td>
</tr>
<tr>
<td></td>
<td>Ceramide monohexoside</td>
<td>[100]</td>
</tr>
<tr>
<td><em>P. brasiliensis</em></td>
<td>Gp43</td>
<td>[101]</td>
</tr>
<tr>
<td><em>P. marneffei</em></td>
<td>Mp1p</td>
<td>[102]</td>
</tr>
<tr>
<td><em>P. carinii</em></td>
<td>Major surface glycoprotein</td>
<td>[103]</td>
</tr>
</tbody>
</table>
furanosyl residues with an average degree of polymerization of four [78]. Other putative cell-wall antigens of *A. fumigatus* are shown in Table 2. Galactomannan is a minor component of the *H. capsulatum* yeast cell wall but is a major antigen. Antigenic variability in this component is the basis for the differentiation of five serotypes in this fungus [79]. Similarly, epitopes in the glucuronoxylomannan, the main capsular component of *C. neoformans*, are responsible for the four serotypes described (serotypes A, B, C and D) [80]. A highly antigenic cell-wall mannanprotein has been identified in *Penicillium marneffei* [102].

A number of glycosylated components have been described in the cell walls of fungi. The cell-wall glycoprotein of *C. immitis* mycelium and spherules designated antigen 2 expresses both linear and conformational epitopes for antibodies from patients with coccidiodomycosis, which have been mapped to a domain comprised of amino acids 19–96 [81]. A 120-kDa wall-associated glycoprotein showing β-glucosidase activity has been shown to react with precipitin antibodies present in sera from patients with coccidioidomycosis [82]. Sera from most patients with paracoccidioidomycosis have high titers of antibodies preferentially directed to conformational peptide epitopes of gp43 [101], which tend to decrease with successful treatment [113]. The glucan component of the cell wall of *C. neoformans* has been reported to induce the IgG antibody response that is detected in normal human serum [114].

A variety of proteins with the ability to stimulate antibody responses have been described in the fungal cell wall. Among them, members of the heat shock protein family are considered immunodominant B-cell antigens. A 47-kDa breakdown product of the hsp90 present in the cell wall of *C. albicans* has been shown to induce antibody responses in patients who recovered from invasive candidiasis [115] and therefore, detection of antibodies to the 47 kDa antigen may be of prognostic value [116]. Several cell-wall antigens with enzymatic activity have also been reported to induce antibody responses in patients with invasive candidiasis. Among them, a monomeric subunit of 44–52 kDa from the glycolytic enzyme enolase, and the glyceraldehyde 3-phosphate dehydrogenase, phosphoglycerate kinase and alcohol dehydrogenase, have been used in the serodiagnosis of different types of candidiasis [75,76].

Most humans and dogs with blastomycosis produce strong antibody responses against the WI-1 protein antigen expressed at the cell-wall surface of *B. dermatitidis* [83,117]. Immunization with WI-1 induces mainly an IgG1 and IgG2b antibody responses [118]. The WI-1 epitopes recognized by antibodies during human infection have been identified. The antibody response is mainly directed against a 25-amino acid repeat that shows homology with a *Yersinia pestis* invasin whereas T-cell determinants are mapped to the amino terminus [46,117].

### Applications of the immunological reactivity of cell-wall components

The ability of fungal cell wall components to elicit cellular or humoral immune responses has traditionally been used in three main areas: (i) the serodiagnosis of mycoses, (ii) the identification of fungal organisms and (iii) the development of vaccines for the prevention of mycoses.

Among the existing possibilities to diagnose a mycosis, detection of antibodies in the infected patient continues to be useful in the diagnosis of a number of mycoses including allergic bronchopulmonary aspergillosis and aspergillosis [78], candidiasis [75], paracoccidioidomycosis [119], histoplasmosis [119], blastomyces [83] coccidioidomycosis [120] and sporotrichosis [77]. Research performed in the last few decades has resulted in the use of purified and/or recombinant antigens that have been the basis for the development of more sensitive and specific tests. Some of these antigens are located in the fungal cell wall and antibodies against them are being used for the diagnosis of patients with candidiasis [75], paracoccidioidomycosis [119], blastomyces [83] and coccidioidomycosis [81,82].

The specific nature of the antigen–antibody reaction can be exploited for identification purposes and a variety of antibodies are currently used for the rapid identification of fungal organisms. The antigenic differences observed in the cell wall of members of the genus *Candida* allowed Tsuchiya and colleagues [121] to develop a slide agglutination scheme to differentiate several *Candida* species, and antibodies against capsular and cell-wall components have been traditionally used for the serotyping of *C. albicans* [73], *C. neoformans* [80] and *H. capsulatum* isolates [79]. Latex particles or microtitre wells coated with antibodies are widely used for the detection of fungal antigens [75,80] and for the rapid identification of *C. albicans* and *C. krusei* [122,123]. Polyclonal antibodies, and more recently, monoclonal antibodies, are useful for the identification of fungal isolates in the exoantigen test [124] or in histological specimens [125,126]. The antibody response produced by patients with mycoses can be used for the identification of the etiological agent when blood culture or other diagnostic techniques are negative. As an example, antigenic differences described between *C. dubliniensis* and *C. albicans* were useful to differentiate...
candidemia caused by *C. dubliniensis* from that caused by *C. albicans*, both in a patient with invasive candidiasis by *C. dubliniensis* and in a rabbit model of systemic infection by *C. dubliniensis* [127–129]. The patient and the infected animals presented a characteristic and specific antibody response against a cell-wall component of 160–170 kDa not observed in the extracts from *C. albicans* [128,129].

Another area in which the immunological potential of the cell-wall components can be exploited is the development of fungal vaccines, which may be an interesting approach to control certain mycosis. Although there is no fungal vaccine currently licensed, a phase I trial with an antitoxogonococcal glucuronyl-b-mannan–tetanus toxoid conjugate vaccine has been carried out to determine its safety and efficacy in humans [130]. A number of reviews have summarized the growing interest in this field [26,118,130], and several cell-wall antigens have been identified as potential candidate vaccines (Table 3).

In conclusion, studies of the immunoreactivity of cell-wall components of clinically relevant fungi are providing important insights into the way in which fungal cells are recognized and dealt with by the immune system and in how the fungus overcomes immunological defenses to establish infection. Furthermore, serodiagnosis and vaccination can be refined in the modern era through the recognition of organism specific antigens and manipulation of the gene encoding such molecules to investigate their role in particular mycoses.

### Acknowledgements

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### References


### Table 3  Cell-wall antigens that confer protection against mycoses

<table>
<thead>
<tr>
<th>Fungus</th>
<th>Antigen</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. dermatitidis</em></td>
<td>WI-1</td>
<td>[118]</td>
</tr>
<tr>
<td><em>C. albicans</em></td>
<td>Mannan</td>
<td>[27,131,132]</td>
</tr>
<tr>
<td></td>
<td>β(1,2)-mannotriose</td>
<td>[133]</td>
</tr>
<tr>
<td></td>
<td>MP-F2</td>
<td>[30]</td>
</tr>
<tr>
<td></td>
<td>Aspartyl proteinases</td>
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<tr>
<td></td>
<td>Hsp90</td>
<td>[134]</td>
</tr>
<tr>
<td></td>
<td>Chitin</td>
<td>[135]</td>
</tr>
<tr>
<td></td>
<td>Killer toxin receptor</td>
<td>[14,136]</td>
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</tr>
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<td></td>
<td>Antigen 2</td>
<td>[137]</td>
</tr>
<tr>
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<td>4-Hydroxyphenylpiruvate</td>
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<tr>
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<td>dioxynase</td>
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<td><em>P. brasiliensis</em></td>
<td>Gp43</td>
<td>[5]</td>
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<tr>
<td><em>P. carinii</em></td>
<td>Major surface glycoprotein</td>
<td>[141]</td>
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137 Jiang C, Magee DM, Quitugua TN, Cox RA. Genetic vaccination against *Coccidioides immitis*: comparison of vaccine efficacy of recombinant antigen 2 and antigen 2 cDNA. * Infect Immun* 1999; 67: 630–635.


