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Résumé en anglais	*Aspergillus fumigatus* is the major filamentous fungus colonizing the airways of cystic fibrosis patients (CF). It is usually responsible for a chronic colonization and sometimes for chronic respiratory infections. However, it may also cause severe infections in patients undergoing lung transplantation. The prognosis for these infections still remains uncertain and there is an urgent need for the identification of new antifungal targets. Among the fungal components which have been studied, melanin of the conidial wall was confirmed as an important virulence factor, protecting the fungus against the host immune defences. Using isolates deficient in melanin synthesis because of a mutation in the *ALB1* (white isolates) or in the *ARP2* gene (brown isolate), we showed that melanin is required for correct assembly of the different layers of the conidial wall and, therefore, for the expression of adhesins and other virulence factors at the conidial surface. Mutations in the *ALB1* gene have been shown to result in a marked reduction in virulence of the fungus in a mouse model of disseminated aspergillosis, but nothing is known about the role of the *ARP2* gene. We therefore focused our attention on the brown isolate IHEM 15998, mutated in the *ARP2* gene, which was recovered from respiratory secretions of a CF patient, but not detected in later samples while chronic colonization by a wild-type (WT) strain of *A. fumigatus* was observed. *In vitro* experiments were first conducted, which revealed that mutation in the *ARP2* gene resulted in a fitness cost when co-cultivated with the WT strain. Likewise, flow cytometry was used to investigate the oxidative burst response of phagocytes co-incubated with the conidia. Compared to the WT strain, stimulation of neutrophils as well as macrophages was higher with the brown isolate. FITC-labeled conidia were also incubated with human cytokine-induced cultured macrophages, afterward phagocytosis was quantified by flow cytometry, which revealed an increased conidial uptake for the brown isolate. Virulence was studied in immunosuppressed (inhalation of conidia) or immunocompetent mice (intravenous inoculation). Conversely to that observed in immunosuppressed mice, mortality in immunocompetent mice was significantly lower with the brown isolate compared to a WT strain. Together, these results confirmed that the partial deficiency in melanin biosynthesis observed in the *ARP2* mutant isolate could be responsible for its lack of competitivity.
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