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Cloning and molecular biology of fungal allergens

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Endemic and opportunistic fungal infections have become an important medical problem, concomitantly with the increasing number of patients undergoing immunosuppressive forms of medical treatment and with increases in congenital and acquired immunodeficiency (Murphy et al. 1993). Morbidity and mortality rates associated with fungal species that are normally harmless to immunocompetent hosts, such as *Candida*, *Aspergillus*, *Fusarium* and *Trichosporum*, are high (Levitz, 1992) and diagnosis and treatment of these infections remain difficult. These fungal species are, together with *Cladosporium* and *Alternaria*, leading allergenic moulds (Karlsson-Borga et al., 1989). The ability to diagnose fungal infections and allergies, as well as to study immune responses to fungi has been so far hampered by the lack of well defined antigens (Levitz, 1992). The same reason also hinders the precise diagnosis of allergic bronchopulmonary aspergillosis (Cramer, 1996). Significant advances in our understanding of immune defence mechanisms to fungal infections and fungal sensitisation can be expected from the application of molecular biology leading to improved definition of fungal antigens/allergens. Molecular cloning and production of recombinant antigens/allergens provide modern methods to produce standardised reagents with a great potential to improve both, diagnosis of fungal complications (Cramer et al. 1996a) and basic research (Scheiner & Kraft, 1995). Classical cloning methods (Achatz et al. 1995) as well as the development of a new cDNA cloning system based on phage surface display technology (Cramer 1997) allow fast isolation and characterisation of cDNAs encoding fungal allergens. Most of the cloned allergens correspond to phylogenetically highly conserved proteins and include enolase, aldehyde dehydrogenase, alcohol dehydrogenase, P2 acidic ribosomal protein (Achatz et al. 1995) and manganese superoxide dismutase (MnSOD, Cramer et al. 1996b), proteins which occur in all eukaryotic organisms. The homologous proteins isolated from different fungal sources share a high degree of sequence identity and similarity when compared with each other and also to the corresponding human proteins (Achatz et al. 1995; Cramer et al. 1996b). In the case of MnSOD it has been shown that both, the fungal and the human enzyme are recognised by IgE antibodies from subjects allergic to the *A. fumigatus* protein and elicited specific immediate type allergic skin reactions in these individuals (Cramer et al. 1996b). Whether these autoimmune reactions are caused by

molecular mimicry between conserved T and B cell epitopes present on the fungal and on the structurally related human enzyme or by sensitisation to human MnSOD due to an inflammatory process, remains to be elucidated. Besides these allergenic proteins which can be clearly classified in terms of biochemical function, a number fungal cDNAs encoding IgE-binding proteins with unknown function have been reported (Cramer, 1996; De Vouge et al. 1996; Banerjee et al. 1996). None of the fungal allergens that have been sequenced so far correspond with respect to sequence and/or enzymatic function to previously sequenced non-fungal allergens, although many of these allergens do occur as homologous allergens in more than one fungal species. These results suggest that fungal sensitisation could be a phenomenon related to cross-reactive fungus-specific molecular structures among phylogenetically closely related organisms.

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