SECRETORY ASPARTYL PEPTIDASE FROM MYCELIA OF *Fonsecaea pedrosoi*: EFFECT OF HIV ASPARTYL PROTEOLYTIC INHIBITORS

Vanila F. Palmeira[1], Lucimar F. Kneipp[2], Celuta S. Alviano[1], André L.S. Santos[1,*]

[1]*Departamento de Microbiologia Geral, UFRJ;* [2]*Departamento de Micologia, FIOCRUZ; Brazil.*

Fonsecaea pedrosoi is the principal causative agent of chromoblastomycosis. Very little is known about the hydrolytic enzymes produced by this fungus. Conversely, peptidases are incriminated as virulence factors in several pathogenic fungi. Here, we have identified secretory aspartyl peptidase activity during 15 days of fungal growth under chemically defined conditions using BSA as the soluble substrate and pH 2.0. This proteolytic activity was totally inhibited by pepstatin, a classical aspartyl peptidase inhibitor. Conversely, *o*-phenanthroline, E-64 and PMSF failed to inhibit the peptidase. We also evaluated the effect of four HIV aspartyl peptidase inhibitors on the secretory peptidase of *F. pedrosoi* mycelia. Indinavir, ritonavir and nelfinavir powerfully inhibited the activity by approximately 97, 96 and 87%, respectively, whereas saquinavir did not interfere with the BSA hydrolysis. The mycelial secretory aspartyl peptidase cleaved several proteinaceous substrates including human albumin, fibrinogen, fibronectin, laminin and type I collagen. As previously reported by our group, conidia also produce secretory aspartyl peptidase. In this context, we investigated the effect of pepstatin on *F. pedrosoi* development. Pepstatin inhibited the growth of conidium and its transformation into mycelium. Collectively, our results suggest a possible participation of aspartyl peptidases in the essential process of *F. pedrosoi*, such as growth, differentiation, nutrition and cleavage of relevant host components.

Supported by: CNPq, PRONEX, FUJB, FAPERJ.