INTRODUCTION: Epithelial cells play an important role in the defense of the organism, by forming a physical barrier, and by secreting antimicrobial peptides and inflammatory mediators, such as cytokines and chemokines, activating, in this manner, the innate immune response. Recently, our group described that the dimorphic fungus *Paracoccidioides brasiliensis* is able to induce secretion of interleukin (IL)-6 and IL-8 by human lung epithelial cell line A549, and that this cytokine secretion is dependent on activation of p38 MAPK and ERK1/2. OBJECTIVES: In this study, we investigated the involvement of protein kinases C (PKCs) in IL-6 and IL-8 secretion by A549 cells during infection with *P. brasiliensis* yeasts. MATERIALS AND METHODS: A549 cells were incubated overnight with *P. brasiliensis*. Next, IL-6, IL-8 and IL-10 levels in culture supernatants were determined by sandwich ELISA kits. Go6983 (broad spectrum PKC inhibitor), Rottlerin (PKC δ inhibitor), Peptide inhibitor of PKC δ, and silencing of PKC δ with small interfering RNA (siRNA) were used to evaluate the importance of these kinases on cytokine secretion. DISCUSSION AND RESULTS: We found higher levels of IL-6 and IL-8 in culture supernatants of A549 cells incubated with *P. brasiliensis* compared to A549 cells cultured in the absence of fungi. IL-10 was undetectable in these culture supernatants. Inhibition of PKCs with Go6983 and Rottlerin significantly reduced IL-6 and IL-8 secretion by A549 cells during interaction with *P. brasiliensis*. PKC δ peptide inhibitor, and PKC δ-directed siRNA also reduced IL-6 and IL-8 levels. CONCLUSIONS: Together these results indicate that *P. brasiliensis* induces activation of PKC δ in A549 cells, culminating in IL-6 and IL-8 secretion by these epithelial cells. Key words: Cytokines, *Paracoccidioides*, Protein kinase C. Supported by FAPESP, CNPq and CAPES.