ImmunoTools *special* Award 2014

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Immunomodulation in experimental fungal diseases: role of antigen-presenting cells in protection and tolerance against dermatophytes and Cryptococcus

Of all the pathogens of man, fungi are the least well studied and understood. Invasive fungal diseases are difficult to diagnose and treat and frequently have mortality rates exceeding 30% to 50%, despite the introduction of novel classes of antifungals in clinical practice. Alterations in immune status or breaching of physical barriers can render individuals susceptible to life threatening fungal diseases, and the incidence of these types of infections has increased substantially in the last few decades. The central role played by a deficient host defense in the pathogenesis of fungal infections, has led to the concept that adjunctive immunotherapeutic approaches should be developed to improve the outcome of the disease. To achieve this goal, we need to understand the underlying mechanisms of protective antifungal immunity.

In our laboratory we investigate the innate and adaptative immune response developed during two experimental models of fungal diseases: dermatophytosis and cryptoccosis.

Dermatophytes are highly specialized pathogenic fungi and the most common cause of cutaneous mycoses in humans and animals, with high rates of incidence and prevalence in most countries. These keratinophilic fungi are likely to infect every person at least once in their lifetime, but immunocompromised patients can experience severe, disseminated diseases. However, the mechanisms of the immune response against dermatophytes are still largely unknown.

The skin, and in particular the epidermis, is a physical barrier that protects the body from external threats and is critically involved in immune reactivity. Professional antigen-presenting cells, such as epidermal Langerhans cells and dermal dendritic cells, are gaining prominence as principal players orchestrating the decision between immunity and tolerance. However, the knowlegde about the role of these cells in skin infection remains currently limited.

In our laboratory, we are interested in understand the role of Langerhans cells in the cutaneous immunity to dermatophytes. By performing methods of isolation and

cultivation of epidermal cells, by developing models of skin infection in mice, and by using selective depletion of Langerhans cells using transgenic mice, we propose to determine the mechanisms involved in cutaneous antifungal immunity and to discover new microbial antigens capable of stimulating or inhibiting the function of epidermal antigen-presenting cells.

On the other hand, Cryptococcus is the most lethal fungal pathogen of man and cryptococcosis results from inhalation of fungal cells with subsequent lung infection and pneumonia. In the absence of an effective immune response, the fungus can disseminate to the brain to cause meningoencephalitis. We have recently demonstrated that eosinophils play a role of antigen-presenting cells inducing pulmonary and sistemic anti-cryptococcal T helper 1 immune response. Furthermore, we have also elucidated mechanisms of immunoevasion by *Cryptococcus neoformans* capsular polysaccharide, mediated by IL-10 and macrophage apoptosis. Now, we focus on to go further insight in protective and tolerogenic mechanims of anticryptococcal immunity in the lungs, which would critically determine the overcome of disease: fungal clearence, latency or extrapulmonary disemination.

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The ImmunoTools reagent will be used in analysis of antigen-presenting cells purified from tissues, studies of lymphocyte populations, and differentiation methods of dendritic cells from mice bone marrow.

ImmunoTools *special* AWARD for **Laura Chiapello** includes 25 reagents

FITC - conjugated anti-mouse CD3e, CD4, CD8a, CD11b, CD19, Gr-1, NK-cells, a/b TCR, g/d TCR, isotype control IgG2b,

PE - conjugated anti-mouse CD44, CD45R, CD45RC, CD62L, isotype control IgG2b,

APC - conjugated anti-mouse CD3e, CD4, CD8a, CD11b, CD19, CD25, isotype control IgG2b,

recombinant mouse cytokines: rm IL-1beta, rm GM-CSF, rmTNF

DETAILS more AWARDS