Letture consigliate da Flavia De Bernardis (giugno 2018)

Negli ultimi anni si è manifestato un progressivo incremento della vulvovaginite da *Candida*, tale da rendere questa patologia una delle più frequenti cause di consultazione ambulatoriale per il medico, fino ad arrivare alla percentuale del 42% di tutte le infezioni vaginali. Infatti studi epidemiologici hanno evidenziato che circa l' 80% delle donne in età fertile hanno avuto almeno un episodio di vulvovaginite da *Candida*, mentre circa il 5% della popolazione femminile soffre di episodi ricorrenti di candidosi vaginale refrattarie alla terapia antimicotica.
Sono stati studiati, in modelli animali di candidosi vaginale, i componenti dell'interazione ospite-fungo a livello della mucosa.
L'evidenza di una risposta immunitaria nel compartimento vaginale è stata molto incoraggiante per identificare gli obiettivi corretti per nuove strategie di vaccinazione o immunoterapia delle candidosi vaginali.

Letture consigliate

The Elusive Anti-*Candida* Vaccine: Lessons From the Past and Opportunities for the Future. Tso GHW, Reales-Calderon JA, Pavelka N. Front Immunol. 2018 Apr 27;9:897.

> Candidemia is a bloodstream fungal infection caused by *Candida* species and is most commonly observed in hospitalized patients. Even with proper antifungal drug treatment, mortality rates remain high at 40-50%. Therefore, prophylactic or preemptive antifungal medications are currently recommended in order to prevent infections in high-risk patients. Moreover, the majority of women experience at least one episode of vulvovaginal candidiasis (VVC) throughout their lifetime and many of them suffer from recurrent VVC (RVVC) with frequent relapses for the rest of their lives. While there currently exists no definitive cure, the only available treatment for RVVC is again represented by antifungal drug therapy. However, due to the limited number of existing antifungal drugs, their associated side effects and the increasing occurrence of drug resistance, other approaches are greatly needed. An obvious prevention measure for candidemia or RVVC relapse would be to immunize at-risk patients with a vaccine effective against *Candida* infections. In spite of the advanced and proven techniques successfully applied to the development of antibacterial or antiviral vaccines, however, no antifungal vaccine is still available on the market. In this review, we first summarize various efforts to date in the development of anti-*Candida* vaccines, highlighting advantages and disadvantages of each strategy. We next unfold and discuss general hurdles encountered along these efforts, such as the existence of large genomic variation and phenotypic plasticity across *Candida* strains and species, and the difficulty in mounting protective immune responses in immunocompromised or immunosuppressed patients. Lastly, we review the concept of "trained immunity" and discuss how induction of this rapid and nonspecific immune response may potentially open new and alternative preventive strategies against opportunistic infections by *Candida* species and potentially other pathogens.

Antibody-based vaccine strategies against intracellular pathogens. Casadevall A. Curr Opin Immunol. 2018 Apr 25;53:74-80.

> Historically, antibody-mediated immunity was considered effective against toxins, extracellular pathogens and viruses, while control of intracellular pathogens was the domain of cellular immunity. However, numerous observations in recent decades have conclusively shown that antibody can protect against intracellular pathogens. This paradigmatic shift has tremendous implications for immunology and vaccine design. For immunology the observation that antibody can protect against intracellular pathogens has led to the discovery of new mechanisms of antibody action. For vaccine design the knowledge that humoral immunity can be effective in protection means that

the knowledge acquired in more than a century of antibody studies can be applied to make new vaccines against this class of pathogens.

Candida vaginitis: virulence, host response and vaccine prospects. De Bernardis F, Graziani S, Tirelli F, Antonopoulou S. Med Mycol. 2018 Apr 1;56(suppl_1):26-31

Vulvovaginal candidiasis is a common mucosal infection affecting a large proportion of women with some of them affected by recurrent often intractable forms of the disease. Thus, there is an increasing interest in understanding the pathogenesis of this disease. The aim of our work was to characterize, in animal models of vaginal candidiasis, the components of the host-fungus interaction at the mucosal level.The evidence of an immune response in the vaginal compartment was very encouraging to identify the proper targets for new strategies for vaccination or immunotherapy of vaginal candidiasis. Aspartyl-proteinase (Sap2), which is an important immunodominant antigens and virulence factors of C.albicans acting in mucosal infections, was assembled with virosomes and a vaccine PEV7 was obtained. The results obtained in the mouse model and in the clinical trial conducted by Pevion on women have evidenced that the vaccine PEV7, intravaginally administered, has an encouraging therapeutic potential for the treatment of recurrent vulvovaginal candidiasis. This opens the way to a modality for anti-Candida protection at mucosal level.