Working Group Interim report

1	Title of Working Group	WG9 Mucosal candidiasis
2	Name(s) of Coordinator(s)	Flavia de Bernardis –Stavroula Antonopoulou
3	Objectives Initial objectives – as specified in the original application	The aim of this project is to extend previous clinical and microbiological investigations and, through international collaborations, to understand host-parasite interactions in candidiasis and try to generate novel efficient therapeutic and/or immunological tools. Particularly, we will try to understand the fungal and host components involved in the pathogenesis of mucosal candidiasis and to assess the protective role of recombinant proteins (Sap2 and mannoprotein) as potential candidate vaccines against mucosal candidiasis. The following specific objectives will be pursued: 1) To assess the protective role of recombinant proteins (Sap2 and mannoproteins) as potential candidate vaccine against mucosal candidiasis 2) Evaluation of protective role of vaginal dendritic cells in mucosal candidiasis . 3) Isolation and identification of *Candida* spp. from vaginal fluids taken from women with recurrent vaginitis and carriers. 4) Detection of cytokine expression in women with recurrent vaginitis and carriers. 5) Expression of *C. albicans* proteinase genes in the oral and vaginal fluids by RT-PCR and Real time PCR. **6)** Evaluation of pathogenicity of *Candida* isolates in animal models .
4	Achievements of the Working Group in last year	*Candida albicans* is a human commensal of the gastrointestinal tract and vagina, thus, host mechanisms of resistance and tolerance cooperate to limit fungal burden and inflammation at the different body sites. We evaluated resistance and tolerance to the fungus in experimental and

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		human vulvovaginal candidiasis (VVC) as well as in recurrent VVC (RVVC). Resistance and tolerance mechanisms were both activated in murine VVC, involving IL-22 and IL-10-producing regulatory T cells, respectively, with a major contribution by the enzyme indoleamine 2,3-dioxygenase 1 (IDO1). Thus, IL-22 and IDO1 are crucial in balancing resistance with tolerance to *Candida*, their deficiencies are risk factors for RVVC. Then, we investigated the relationship between recurrent vulvovaginal candidiasis (RVVC) and immune mediators in vaginal fluids of women. Preliminary results indicate that women with RVVC had elevated concentration of IL-4, IL-5 and IL-13 in vaginal fluids. Women with RVVC may have acquired a local immune defect which can influence the induction of cytokine production and may induce suppression of Th-1 immune response. The immune suppression may be the cause of their symptoms and *Candida* proliferation. *C.parapsilosis*, frequenly isolated from human vaginal infections, is a complex of different species, the pathogenic potential of *C. parapsilosis*, *C. metapsilosis* and *C. orthopsilosis* was also compared in an *in vivo* model of murine vaginal candidiasis. The results indicate that *C. orthopsilosis* and *C. metapsilosis* are able to induce vaginitis in a similar way to *C. parapsilosis* and evidenced the reduced pathogenicity of *C. metapsilosis* in terms of adhesive ability and pathogenic potential.
5	Publications and Conference talks	Bertini A., **De Bernardis F**., Hensgens LA., Sandini S., Senesi S., Tavanti A. Comparison of *Candida parapsilosis*, *Candida orthopsilosis* and *Candida metapsilosis* adhesive properties and pathogenicity. **International Journal of Medical Microbiology 2013** 303: 98-103. De Luca A, Carvalho A, Cunha C, Iannitti RG, Pitzurra L, Giovannini G, Mencacci A, Bartolommei L, Moretti S, Massi-Benedetti C, Fuchs D, **De Bernardis F**, Puccetti P, Romani L. 2013. IL-22 and IDO1 affect immunity and tolerance to murin and human vaginal candidiasis. **PLoS Pathogen, 2013** 9, e1003486. **De Bernardis F**., Arancia S., Tringali G., Greco M. C., Ragazzoni E., Calugi C, Trabocchi A., Sandini, S., Graziani S., Cauda R., Cassone A., , Antonio Guarna A., Navarra P. Evaluation of efficacy, pharmacokinetics and tolerability of peptidomimetic aspartic proteinase inhibitors as cream

		formulation in experimental vaginal candidiasis. **Journal of Pharmacy and Pharmacology. 2014**(in press). **De Bernardis F.** Arancia S., Sandini S., Graziani S. Studies of immune responses in *Candida* vaginitis. Embo workshop on AIDS-related Mycoses Cape Town, South Africa 3-5 luglio 2013.
	Is your Working Group going to continue for the next two years?	Yes, we would like to continue for the next two years.