

LUCA SPAGGIARI<sup>1</sup>, ARIANNA SALA<sup>1</sup>, ANDREA ARDIZZONI<sup>1</sup>, CLAUDIO CERMELLI<sup>1,2</sup>,  
SAMUELE PEPPOLONI<sup>1,2</sup>, ELISABETTA BLASI<sup>1,2</sup>, EVA PERICOLINI<sup>1,2</sup>

**Compounds released from *Lactobacillus (L.) acidophilus*, *L. plantarum*, *L. rhamnosus* and *L. reuteri* inhibit *Candida parapsilosis* pathogenic potential after infection of vaginal epithelial cells *in vitro*.**

<sup>1</sup>*Department of Surgical, Medical, Dental and Morphological Sciences with interest in Transplant, Oncological and Regenerative Medicine, University of Modena and Reggio Emilia, Modena, Italy*

<sup>2</sup>*Graduate School of Microbiology and Virology, University of Modena and Reggio Emilia, Modena, Italy*

**INTRODUCTION.** *Lactobacillus spp.* are the most represented microorganisms in the vaginal microbiota of healthy women, where they provide a shelter against infections from several pathogens, such as the yeasts belonging to the genus *Candida*. The latter are responsible for the vulvovaginal candidiasis (VVC), a condition affecting up to 75% of women during their child-bearing age at least once in their lifetime. Moreover, 5-8% of such women develop the recurrent form of the disease (RVVC), consisting of at least 5 VVC episodes per year. Notwithstanding *C. albicans* is the main responsible of VVC cases, in the last decades, the incidence of VVC cases by non-*albicans Candida* (NAC) species has become prevalent, especially in some geographical areas. *C. parapsilosis*, in particular, has been reported to be second species most commonly isolated from women affected by VVC. However, little is known on this species, and on its role in the pathogenesis of VVC.

**MATERIALS AND METHODS.** Cell-free supernatants (CFS) were obtained following an overnight culture of 4 different *Lactobacilli* species (*L. acidophilus*, *L. plantarum*, *L. rhamnosus*, *L. reuteri*). *Lactobacilli*-released compounds, contained in CFS, were assessed for their effect on several virulence factors of *C. parapsilosis* (strain CLIB214), such as growth rate, capacity to form pseudohyphae, capacity to adhere to a vaginal epithelium *in vitro* (A-431 cells monolayer) and to induce cell damage. The latter was evaluated by measuring lactate dehydrogenase (LDH) release from A431 cells.

**RESULTS.** *C. parapsilosis* growth inhibition by *L. acidophilus*, *L. plantarum* and *L. reuteri* CFS was 47%, 55% and 52% respectively, whereas *L. rhamnosus* CFS effect was weaker (33% inhibition growth). All the *Lactobacilli* significantly inhibited *C. parapsilosis* adhesion to vaginal epithelial cells: upon incubation with CFS, only 5-7% of fungal cells adhered to epithelial cells, after 90 minutes incubation; differently, the adhesion of the control reached 19%. Interestingly, no effect on pseudohyphae formation by any of the CSF was ever observed. Finally, the *C. parapsilosis*-induced damage on A-431 cells was significantly reduced by the addition of the CSF.

**DISCUSSION AND CONCLUSIONS.** Our results show that the investigated species of *Lactobacilli* release compounds capable to impair several *C. parapsilosis* virulence factors, such as growth rate and adhesion to vaginal epithelial cells; interestingly, while not affecting fungal capacity to form pseudohyphae, such compounds significantly reduce *Candida*-mediated epithelial damage.. These data suggest that, in the context of vaginal microbiota, these *Lactobacilli* species may play an important role in counteracting the onset of mucosal *Candida* infections.