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## INTRODUCTION

### Vulvovaginal Candidiasis (VVC)

- Infection is caused by opportunistic fungal pathogen, *Candida albicans* or *Candida glabrata*. *C. albicans* has high recurrence rate (50%) and most *C. glabrata* fail to respond treatment.
- Estimated 75% of women will have episodes, symptoms include burning, redness, painful intercourse
- Current treatments oral Fluconazole may require months of therapy if not lifelong, increasingly strains are resistant

### Bacterial Vaginosis (BV)

- The loss of healthy *Lactobacillus* bacteria and the overgrowth of bad bacteria (*Gardnerella*, *Atopobium*, *Prevotella*, and more) in the vagina.
- Affects about 30% of female population 14-49 yrs in the USA. Symptoms include itching, odor, discharge, painful intercourse
- The main problem is not resistance to treatments, but recurrence at up to 80% in a year. Why recurrence happens is not known.
- BV can lead to many other health complications, such as:
  - premature delivery
  - increased risk of contracting sexually transmitted infections including HIV
  - pelvic inflammatory disease

CURRENT TREATMENTS FOR VVC AND BV ARE NOT ADEQUATE. PROBIOTIC SUPPLEMENTS TO TREATMENT ARE WORTH INVESTIGATION

## Major Questions

- Do “healthy” vaginal bacteria antagonize *Candida* species?
  - Implication if yes: Absence of *Lactobacillus* may promote *Candida* and VVC; treatment of BV should be coupled with treatment for VVC.
  - Utility: Some species or strains of *Lactobacillus* may be useful as probiotics to prevent VVC or its recurrence
- Do strains of *Candida* antagonize *Lactobacillus* strains?
  - Implication: *Candida* colonization or infection may promote BV, and treatment of VVC should be coupled with treatment for BV
- Do antagonisms depend on the species or strain of *Lactobacillus*? Of *Candida*?
  - Implication: strain dependent antagonisms will require that a probiotic approach will match individual patient strains of *Candida* with a library of *Lactobacillus* strains

## METHODS

### Mixed vaginal bacteria inhibit *Candida* in vitro?

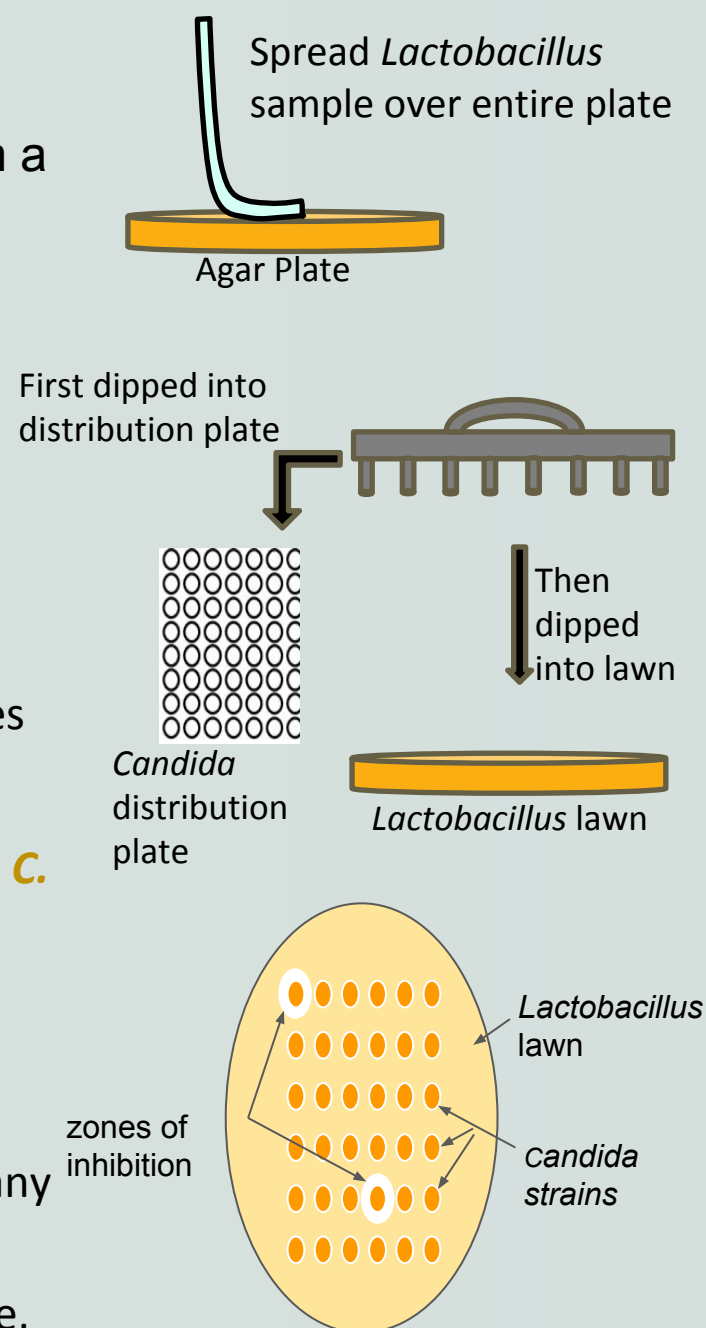
- Tested using bacteria from a vaginal swab, initially *Lactobacillus*-dominant, grown in the presence of *Candida* species

### *C. albicans* inhibit isolates of *L. crispatus*?

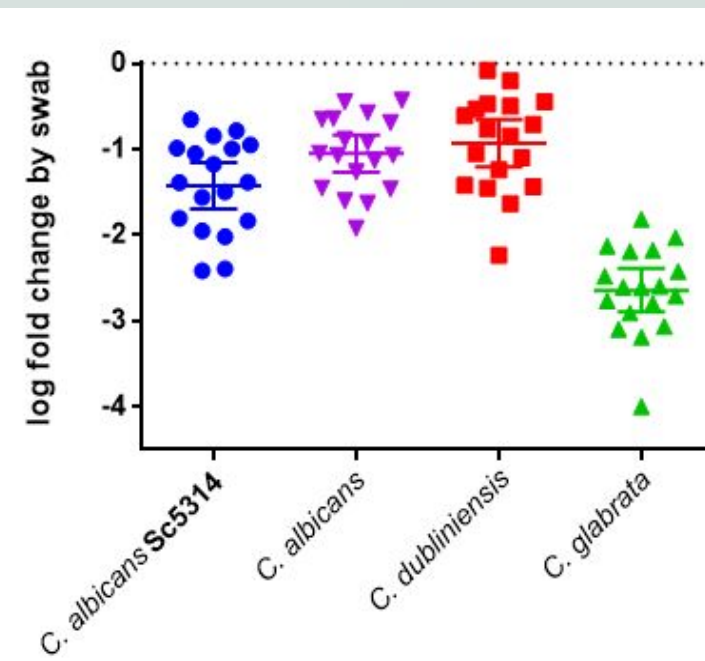
- Tested using lawns of vaginal *Lactobacillus* spotted with *Candida* isolates, scored zones of inhibition

### Do vaginal *Lactobacillus* inhibit *C. albicans* or *C. glabrata*?

- Tested using coinoculation of high titer vaginal *L. crispatus* and 100 cell of each *Candida* strain, then counting how many *Candida* colonies grew, compared to the control plate, *Candida* without *L. crispatus*



## RESULTS



**Figure 1.** Mixed vaginal bacteria from individual patients vary in ability to inhibit *Candida* species in vitro. *C. glabrata* is more sensitive to inhibition than *C. albicans*.

## REFERENCES

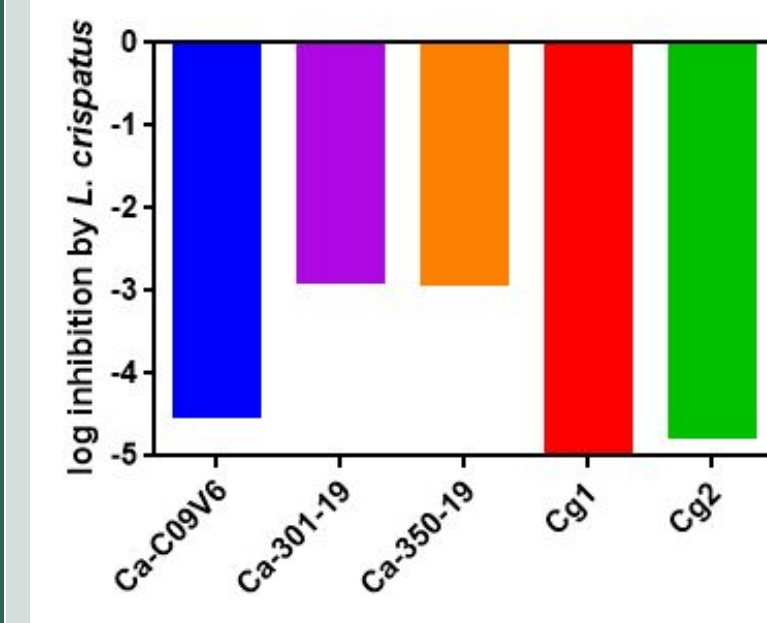
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**Table 1.** Probiotic *Lactobacillus* strains are not inhibited by most *C. albicans*

<i>C. albicans</i>	<i>Lactobacillus</i>	# <i>Lactobacillus</i> strains inhibited
Inhibitory	4 of 34 (11%)	4-5 of 6 strains

- Only 11 % of *C. albicans* isolates inhibited *Lactobacillus* isolates
- Most of the 6 tested *Lactobacillus* strains were inhibited by these “super” strains of *C. albicans*
- One screening criteria for probiotic *Lactobacillus* is that they are resistant to inhibition by “super” strains of *C. albicans*



**Figure 2.** At high initial titers, all tested strains of *L. crispatus* (6 strains) inhibited *C. albicans* (3 strains) and *C. glabrata* (2 strains)

## CONCLUSIONS

Results from the mixed vaginal bacteria against *Candida* strains in **Figure 1** suggests that many bacterial populations inhibited *C. albicans* by less than 10-fold, but others inhibited by 100-fold depending on the strain of *C. albicans*. Most bacterial populations inhibited *C. glabrata* by >100-fold. Probiotics should be simpler for *C. glabrata*, which may reduce its current high rate of failed responses to antifungals.

Questions we can now ask using the results from **Table 1** and **Figure 2** are: what is different about “super” strains of *C. albicans* that makes them inhibit *Lactobacillus*? Can a marker of these strains be developed to possibly alternative treatment of patients colonized with them?

Probiotic *Lactobacillus* strains meeting these three criteria would then be tested in vivo:

1. Strain is not inhibited by any *C. albicans* strain, especially “super” strains that inhibit most *Lactobacillus* isolates.
2. Strain at low initial titer inhibits the *Candida* strain recovered from the individual patient to be treated.
3. Strain at low initial titer is able to grow to predominance in a mixed culture started with a vaginal swab of the individual patient to be treated.