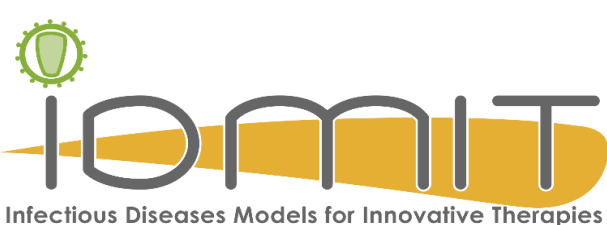


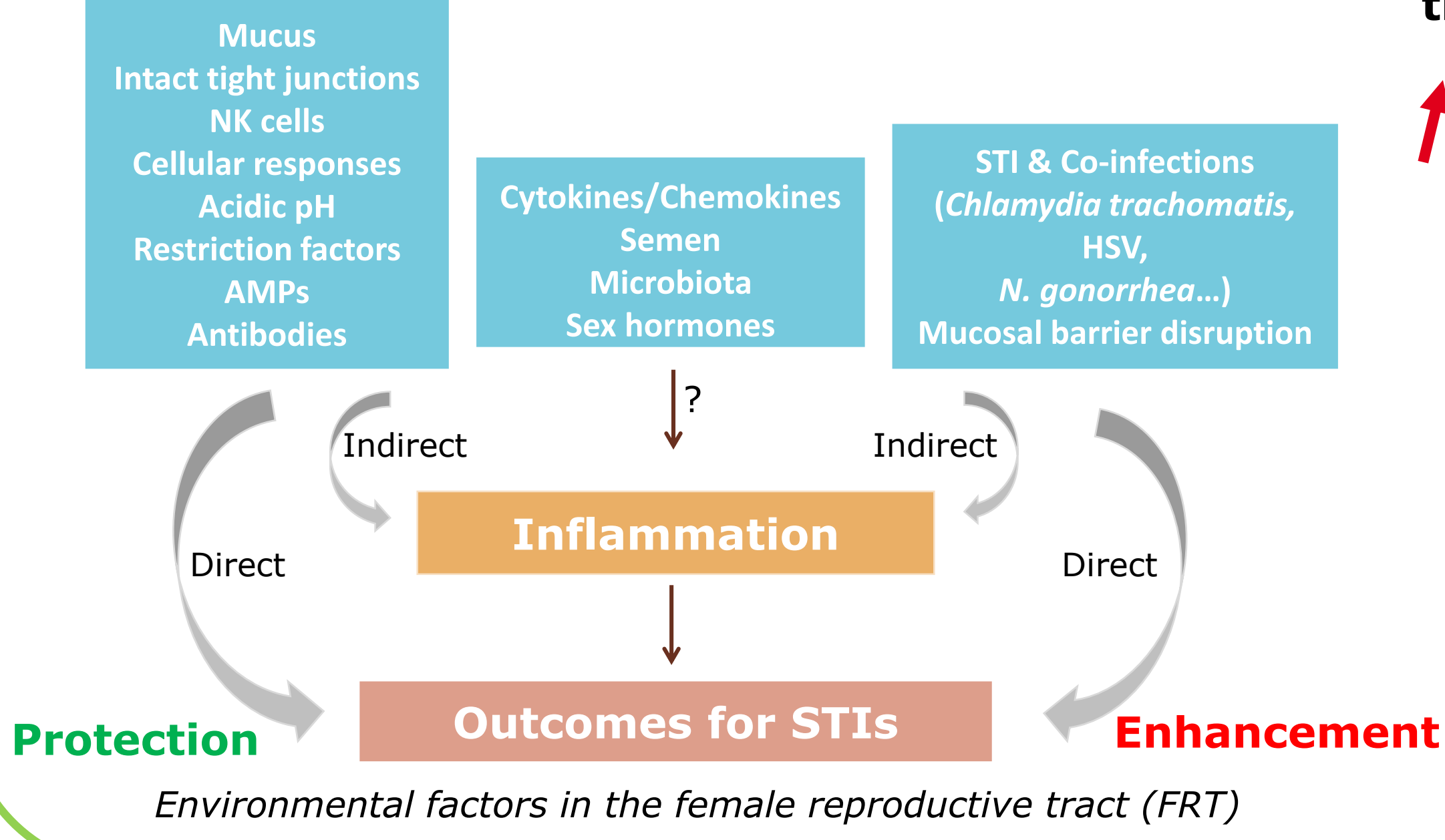
Interactions between the local environmental factors within the female reproductive tract in physiological conditions and during *Chlamydia trachomatis* infection

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BACKGROUND:



Heterosexual transmission from male to female is the major route of sexually transmitted infections (STI)

Local inflammation (cytokines & neutrophil recruitment):

- ❖ *Chlamydia trachomatis* (CT)
- ❖ Dysbiotic vaginal microbiota (*Lactobacillus spp.* ↑ Anaerobic bacteria)
- ❖ Seminal plasma (SP), cell-free fraction of the sperm

Similarities between female cynomolgus macaque & Human

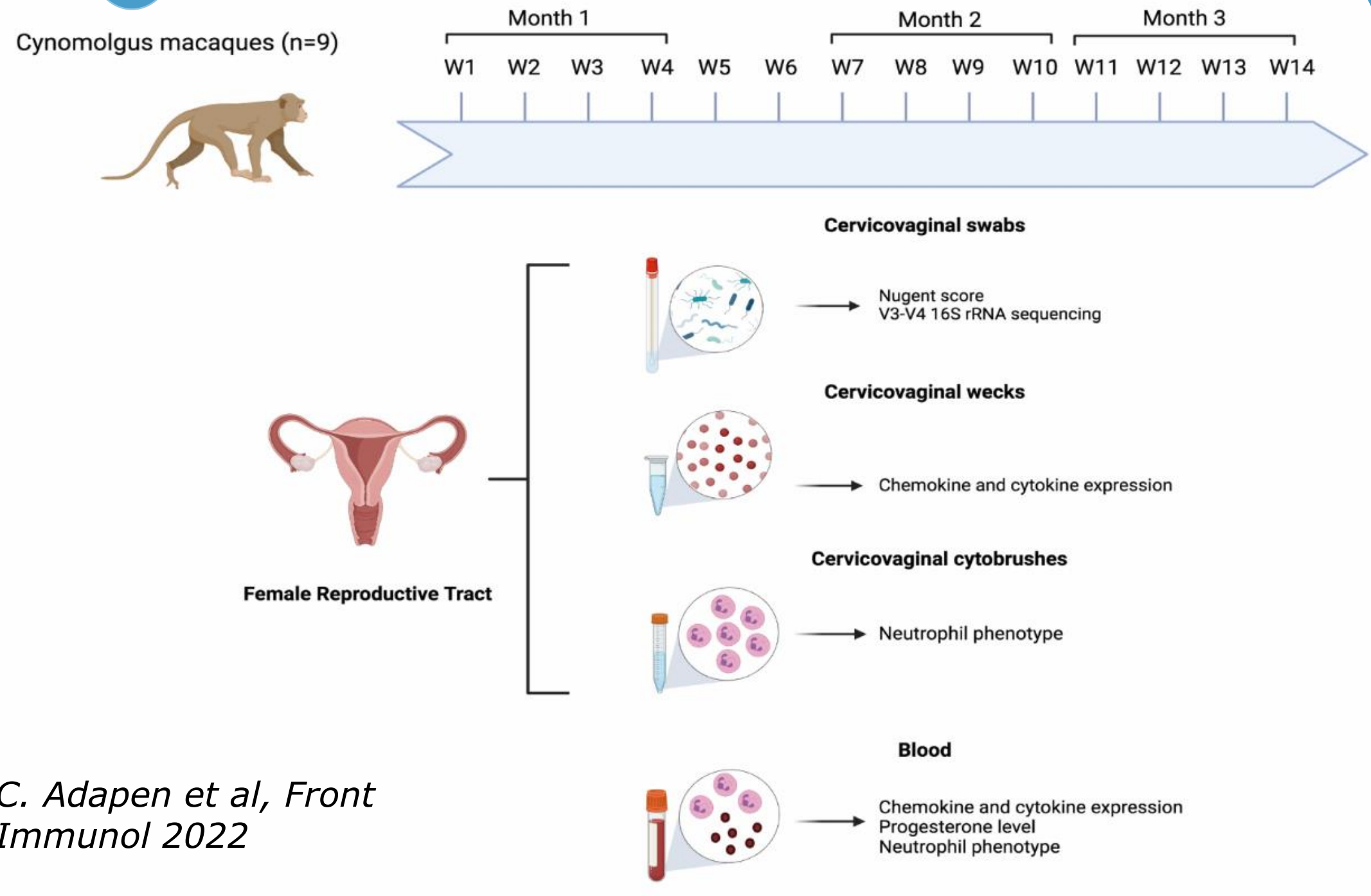
- ❖ Menstrual cycle ✓
- ❖ Immune cell repartition in the FRT ✓
- ❖ Anatomy of the FRT ✓

OBJECTIVES:

1. Study the interplay between vaginal microbiota and local inflammation (cytokine profil and neutrophil phenotype/recruitment) according to the menstrual cycle
2. Evaluate the effect of *Lactobacillus crispatus* enrichment in the vaginal microbiota on CT infection
3. Determine the impact of SP on CT acquisition and inflammation

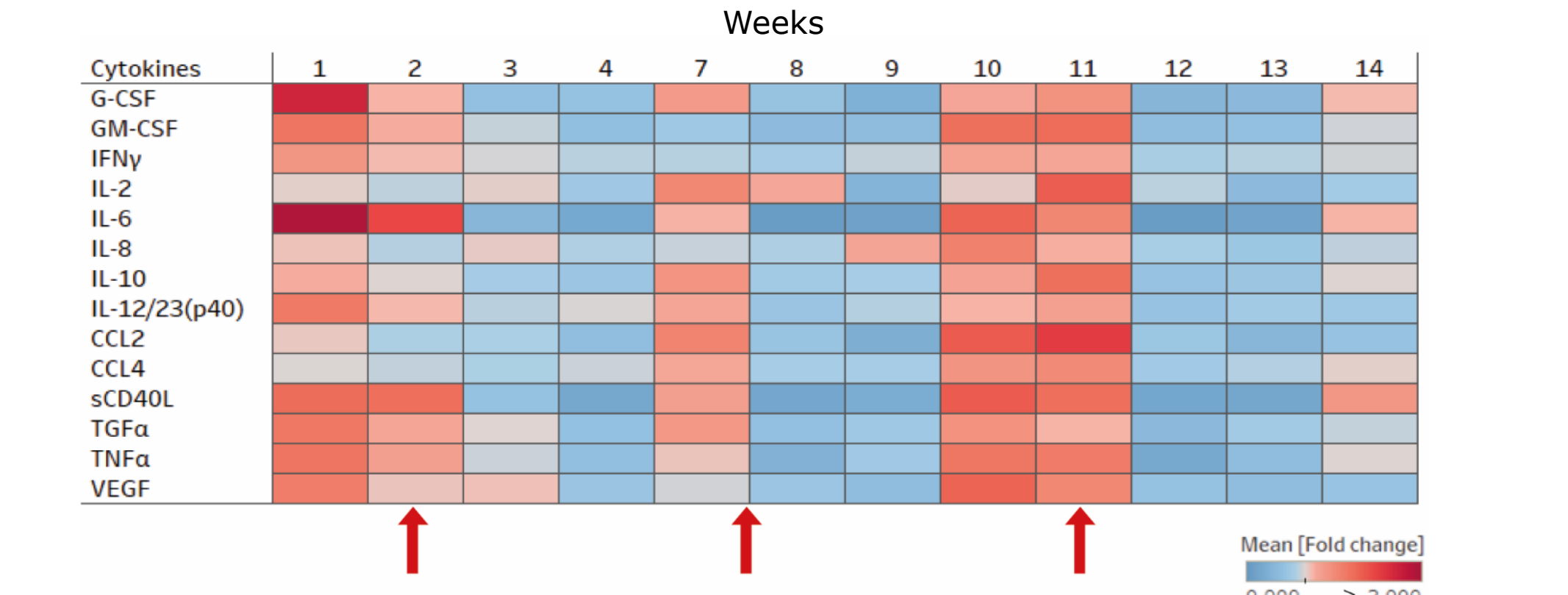
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METHODOLOGY:

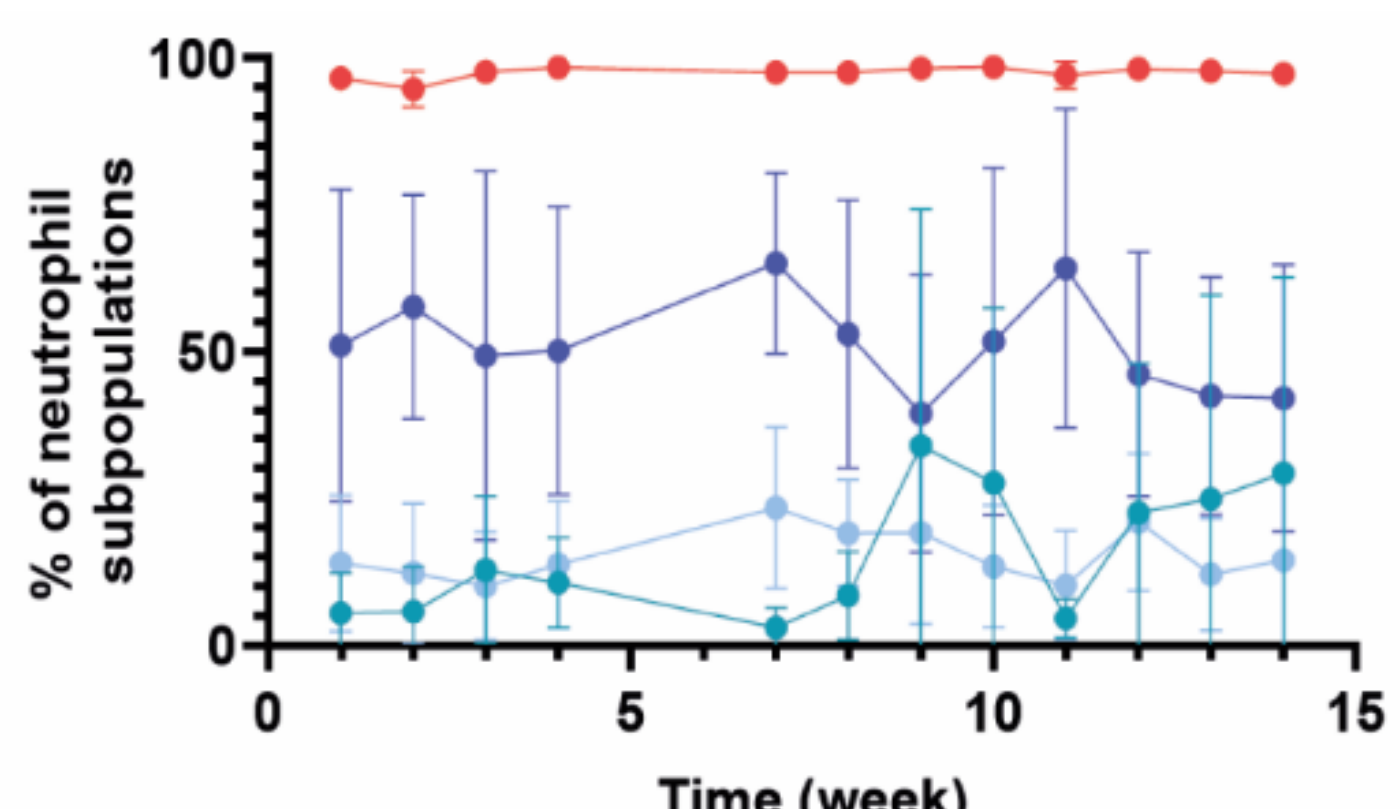


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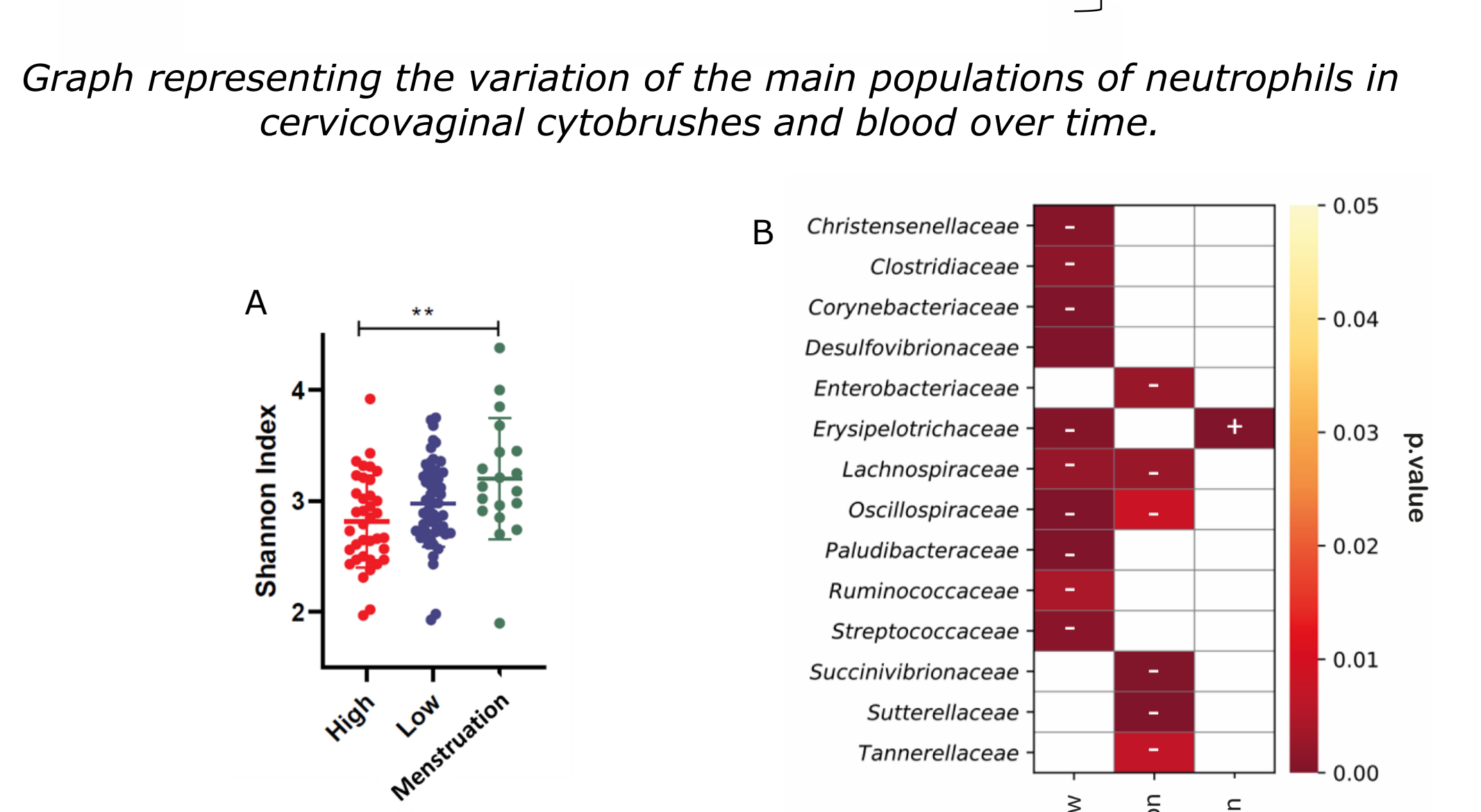
RESULTS:



Heatmap representing the modulation of cytokine concentration (increase and decrease) in cervicovaginal fluids of all females over time. Arrows represent menstruation. Numbers 1 to 14 refer to weeks.



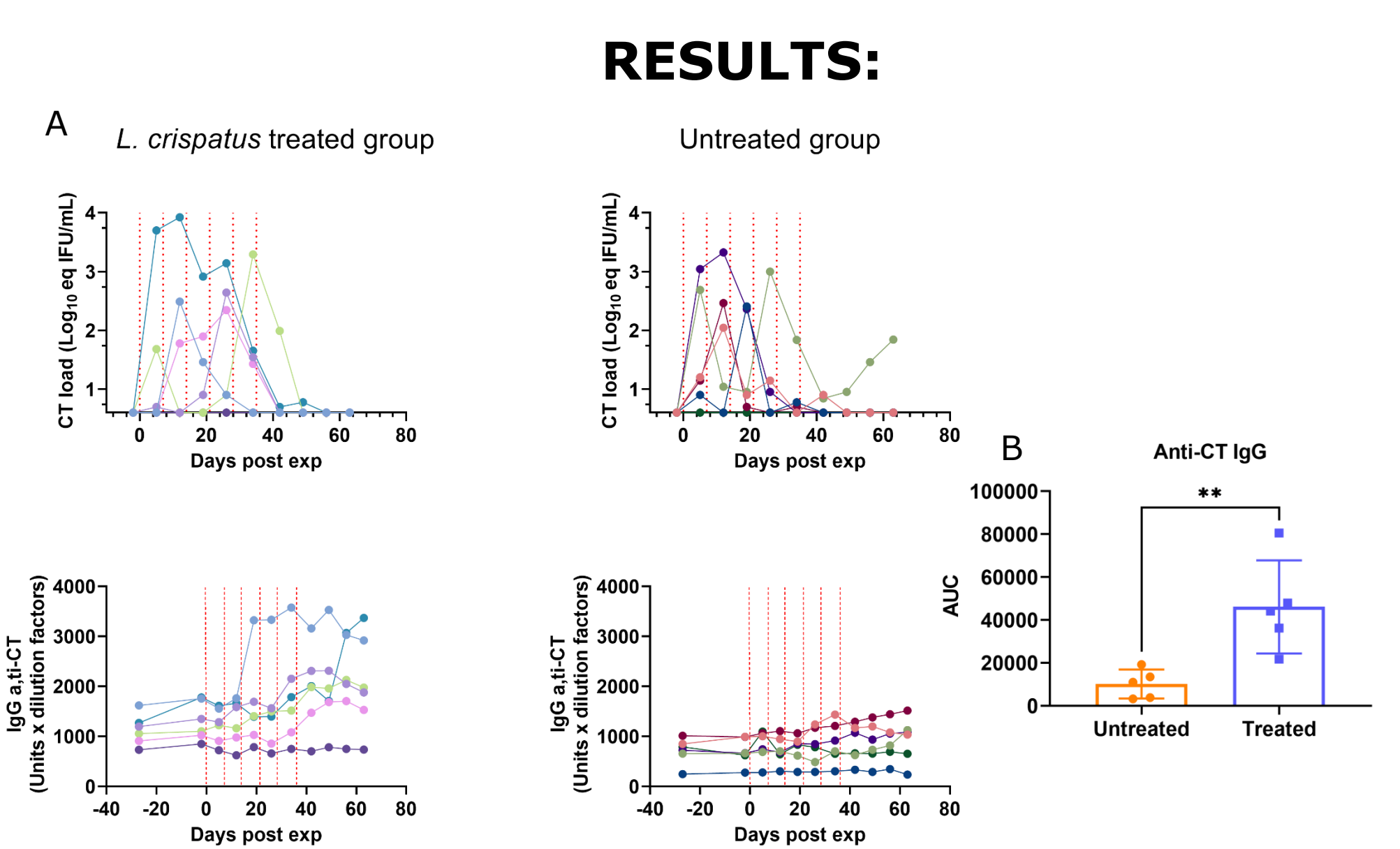
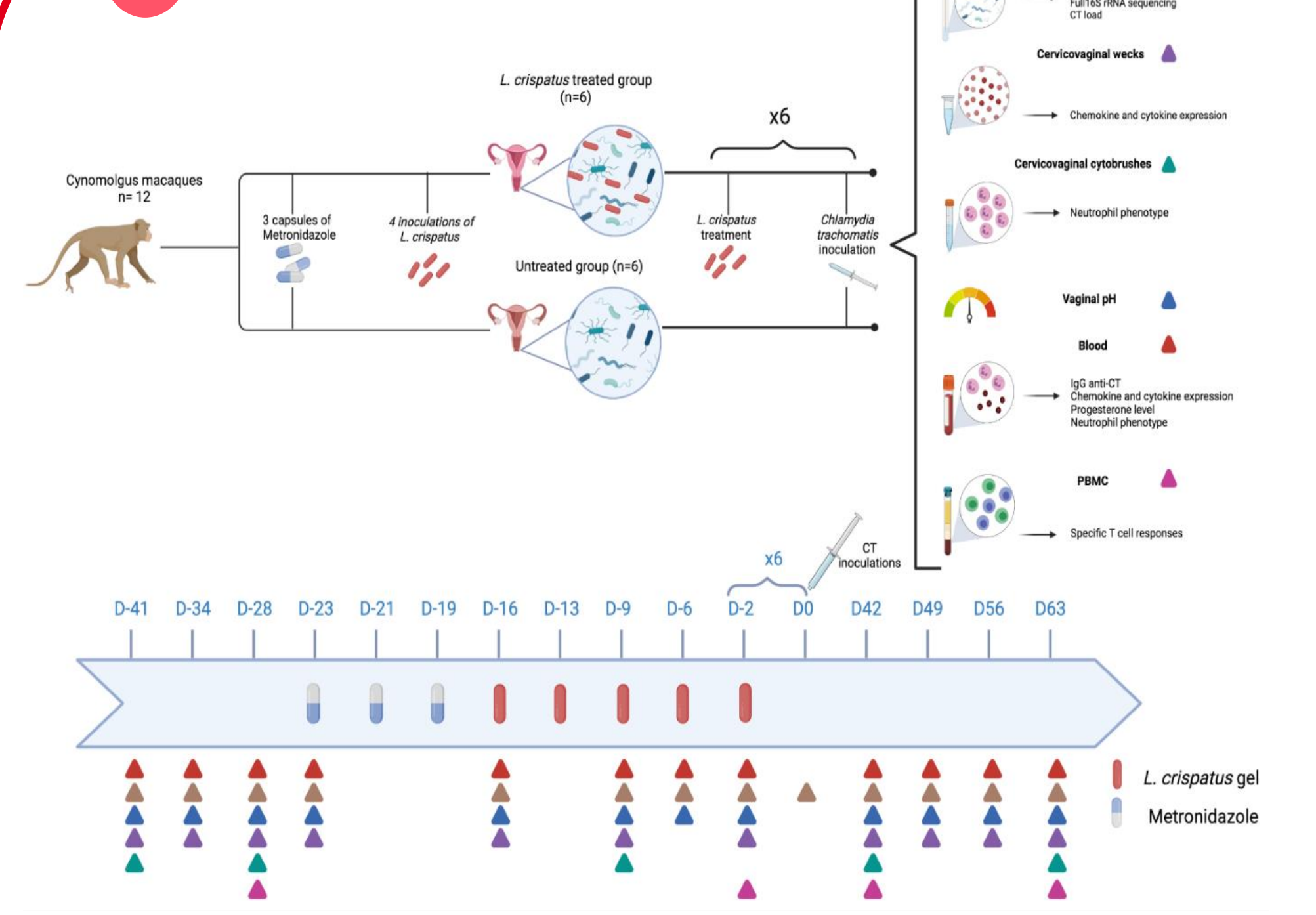
Graph representing the variation of the main populations of neutrophils in cervicovaginal cytobrushes and blood over time.



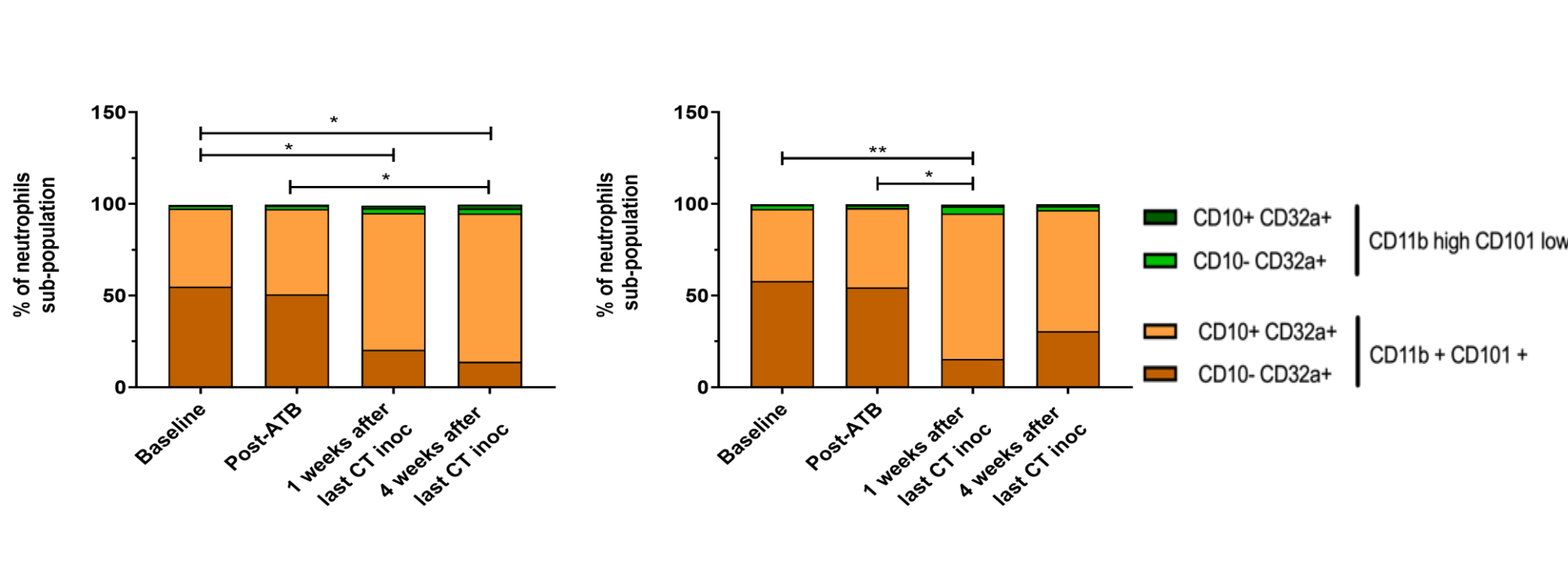
(A) Alpha diversity of the vaginal microbiota when the level of progesterone is high, low or during menstruation. (B) Heatmap representing the p-value of differentially abundant bacterial taxa at the family level (+: increase, -: decrease). The sign is associated with the group in bold.

2

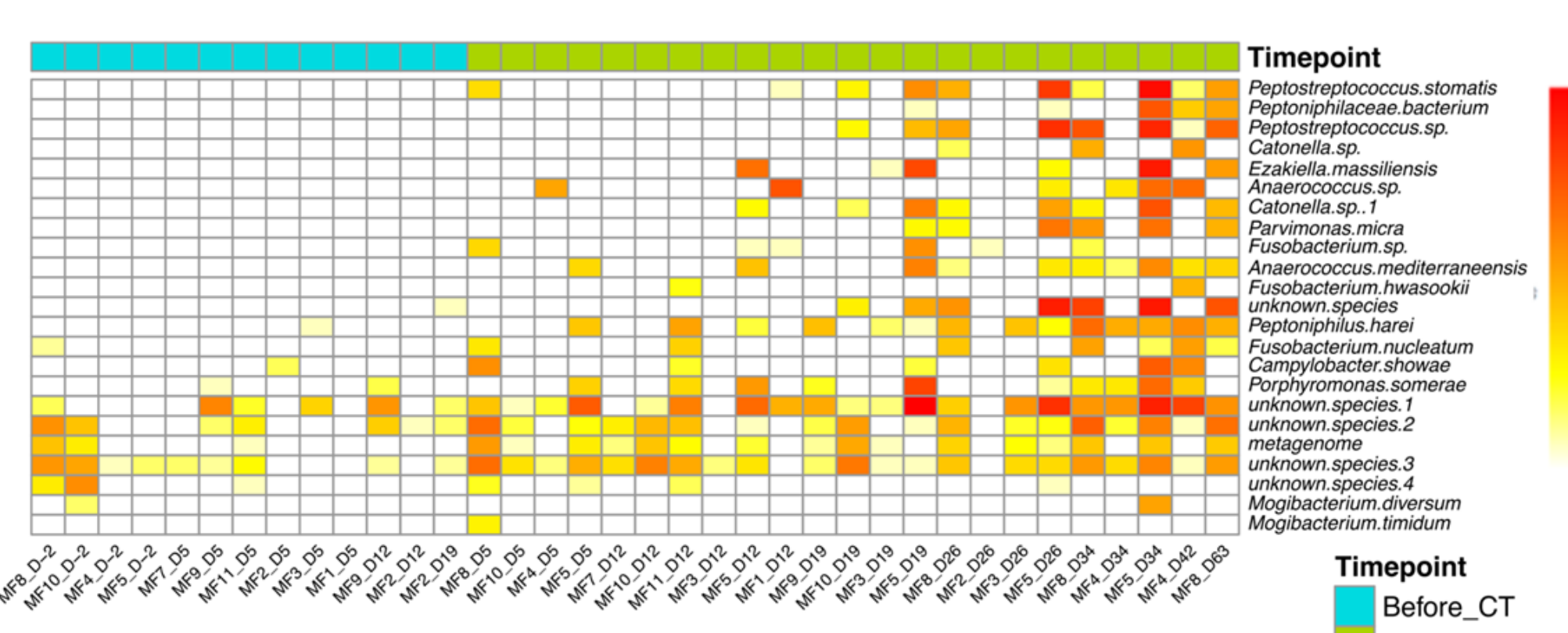
METHODOLOGY:



(A) Bacterial load in cervicovaginal fluids (top) and serum specific anti-CT IgG (bottom) in both groups of animals. (B) AUC of anti-CT IgG in *L. crispatus* treated and untreated animals.



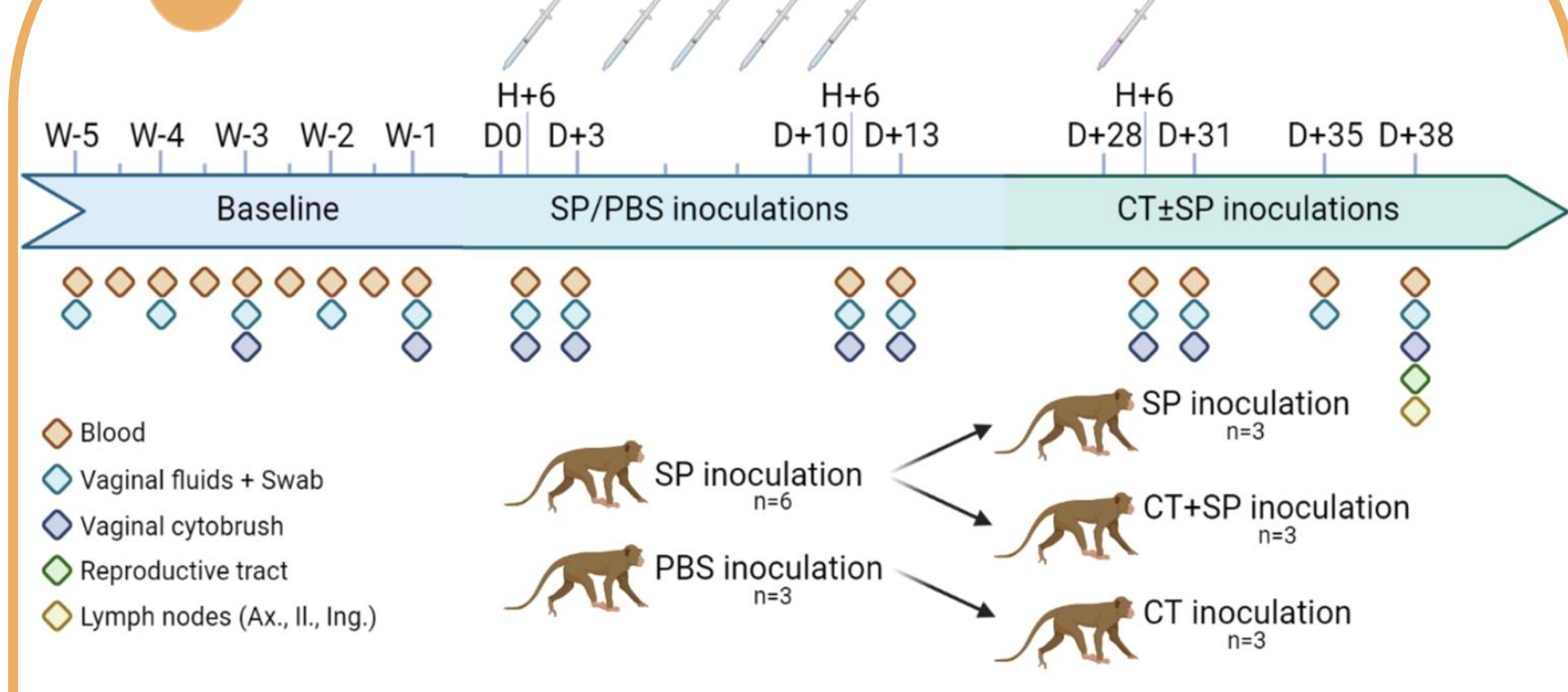
Phenotype of peripheral blood neutrophils in both groups of animals



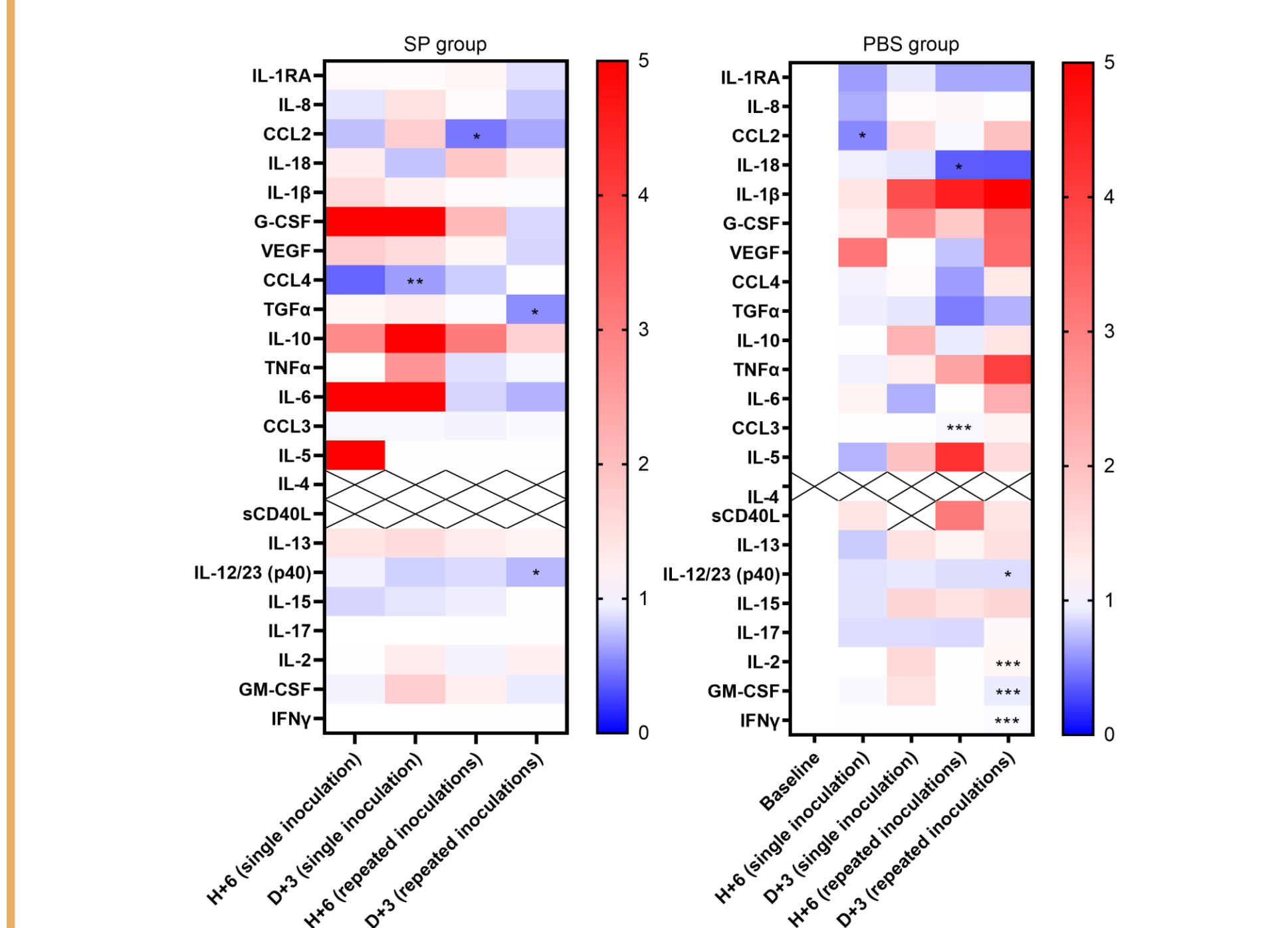
Heatmap representing the fold change after log₁₀ transformation of species increased or decreased in both conditions at CT infection compared to before CT infection (during CT inoculation w/o infection). The scale starts from 0 to above 4, red represents an increased abundance of the species.

3

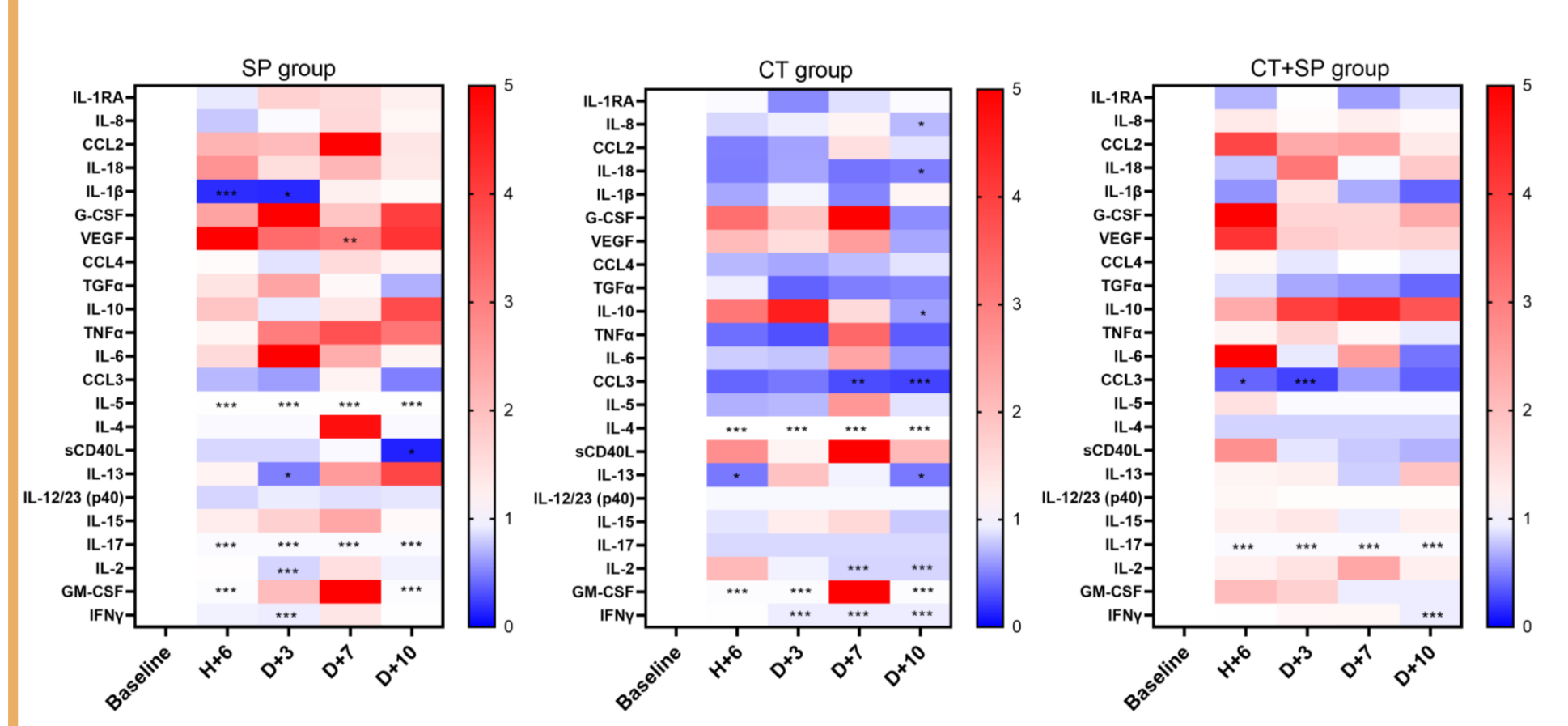
METHODOLOGY:



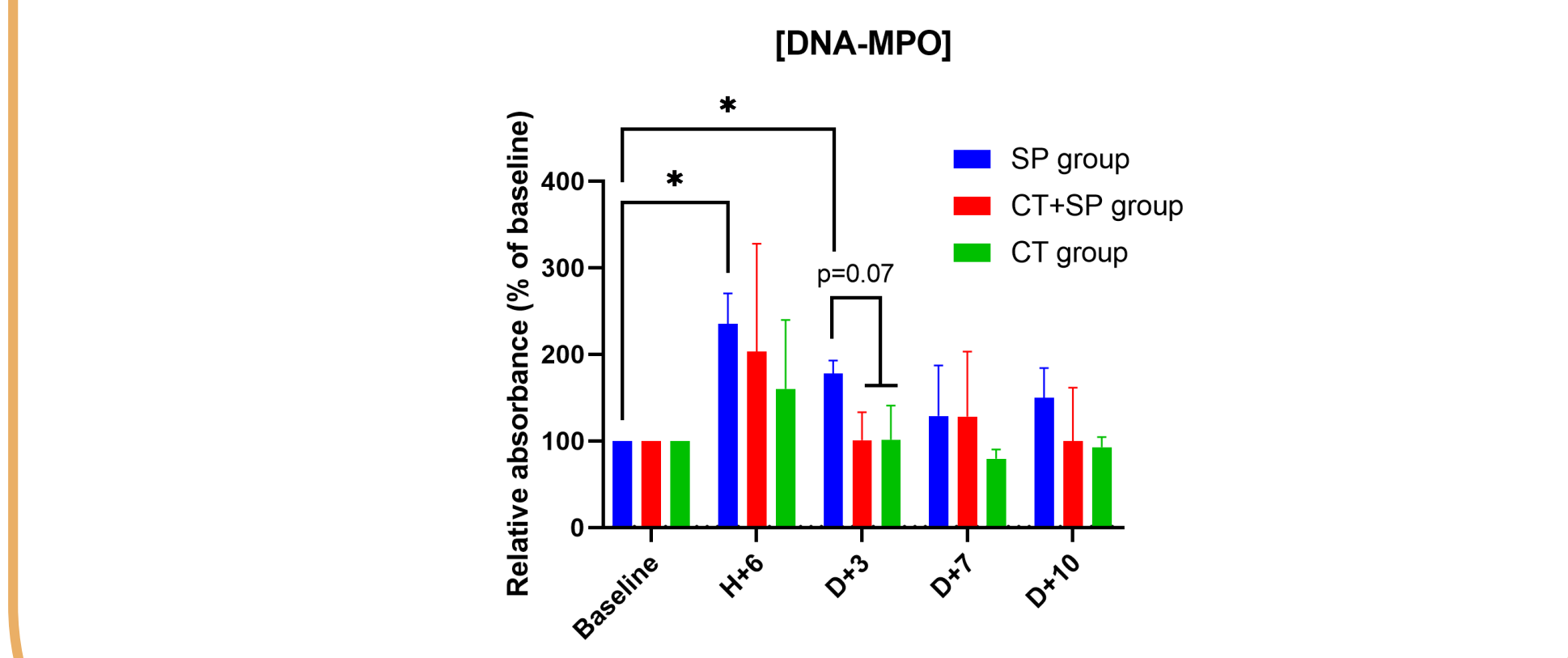
RESULTS:



Heatmap representing the modulation of cytokine concentration (increase and decrease) in cervicovaginal fluids of all females over time after one or 4 inoculations of seminal plasma (SP) or PBS.



Heatmap representing the modulation of cytokine concentration (increase and decrease) in cervicovaginal fluids of all females over time in the SP, *Chlamydia trachomatis* (CT) and SP +CT group.



NET formation by measuring myeloperoxidase (MPO)/DNA complex in cervicovaginal fluids.

CONCLUSIONS:

- ❖ Environmental factors → variation according to menstrual cycle
- ❖ No persistent infection & increased of serum CT specific IgG levels in *L. crispatus* treated animals
- ❖ Increase of mature/activated neutrophils in the blood & modification of the vaginal microbiota composition after CT infection in all animals
- ❖ Tolerance of SP after several expositions; SP expositions with or w/o CT infection lead to different cervicovaginal cytokine profiles
- ❖ NET formation is increased in the group exposed to SP alone

Complex interactions between vaginal microbiota, inflammation, and CT infection
Useful informations for the development of preventive or therapeutic approaches against STIs and to optimize reproductive health in women