HOW TO PREVENT AND/OR MINIMIZE THE PROBLEM OF MULTI-RESISTANCE

Intestinal Reservoir

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"THE CHALLENGE OF MDR AND XDR INFECTIONS"
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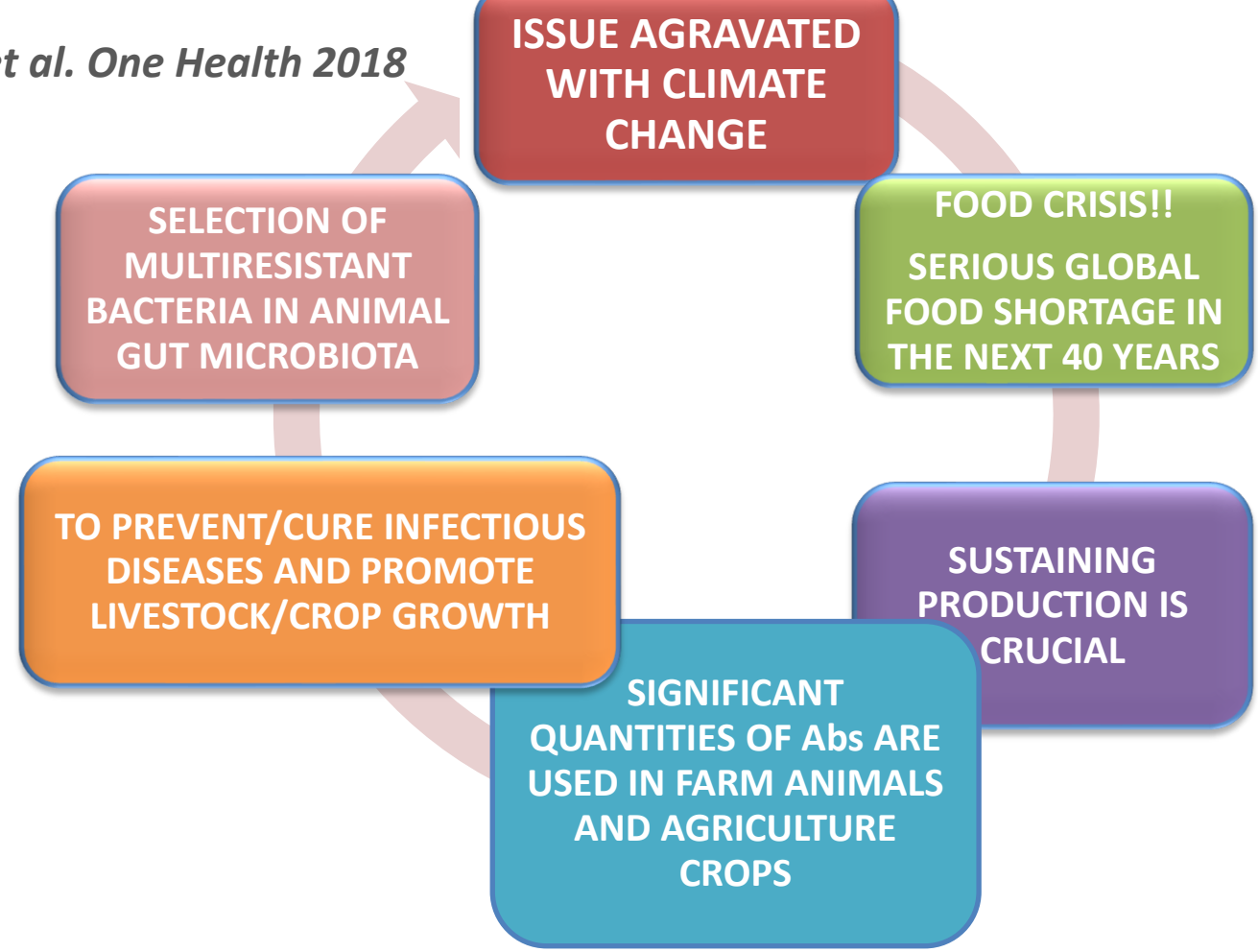
FLS SCIENCE

Berrian AM, et al. One Health 2018



The phenomenon of antibiotic resistance is, according to the General Assembly of the United Nations, a priority topic for human development, being on par with global warming!!!!!

Extended antibiotic treatment in salmon farms select multiresistant gut bacteria with a high prevalence of antibiotic resistance genes

Sebastián Higuera-Llantén[1], Felipe Vásquez-Ponce[1], Beatriz Barrientos-Espinoza[1], Fernando O. Mardones[2], Sergio H. Marshall[1], Jorge Olivares-Pacheco[1,3]*

PLOS ONE | https://doi.org/10.1371/journal.pone.0203641 September 11, 2018

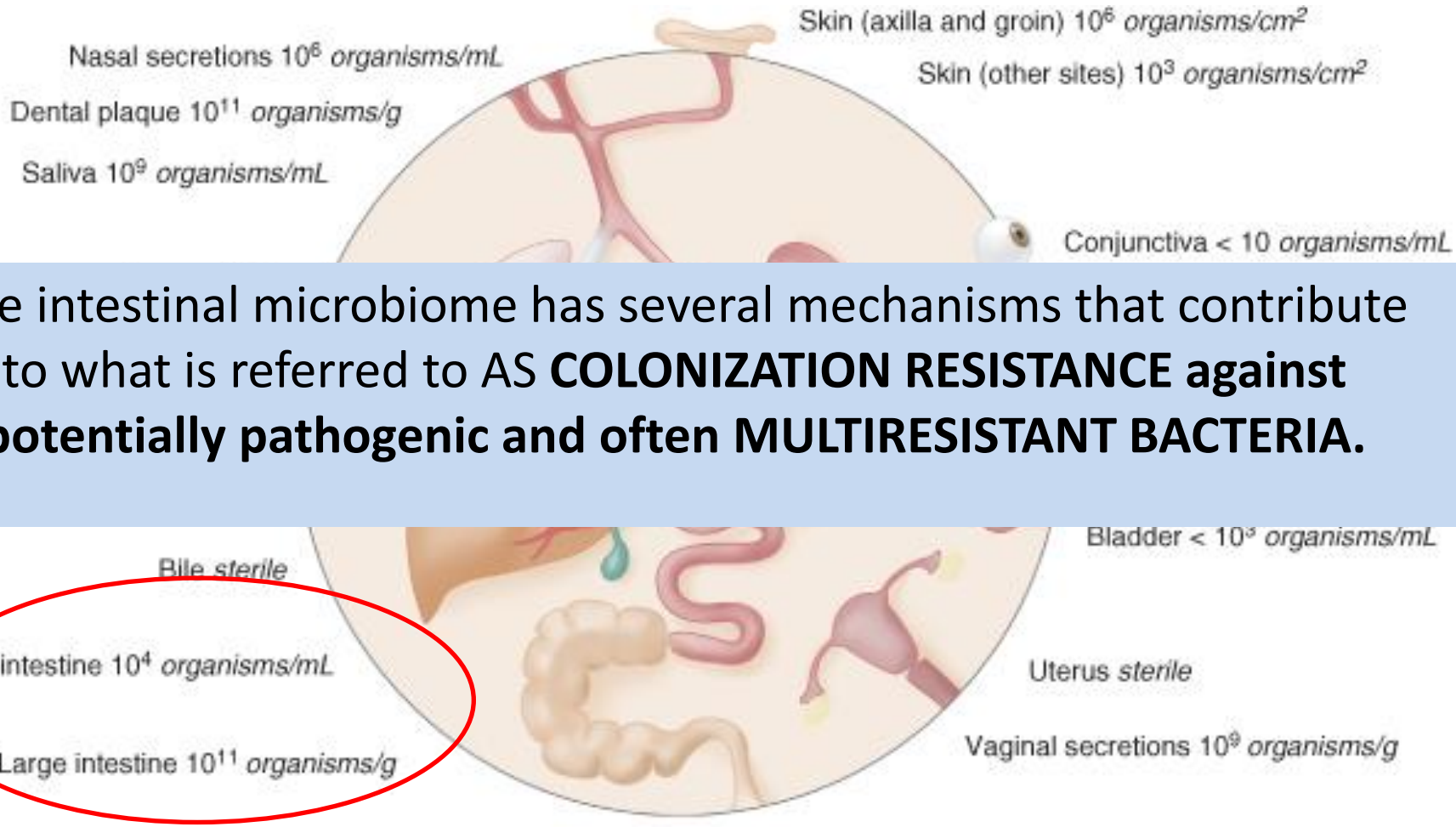
- The primary aim of this study was to characterize the antibiotic-resistant bacteria present in the intestinal microbiota of farmed Atlantic salmon treated with high antibiotic doses
- 15 healthy fish were selected from 4 Salmon farms that used similar amounts of Abs and were euthanised in order to isolate the bacteria

It was demonstrated that the high use of the antibiotics florfenicol and oxytetracycline leads the selection of multiresistant bacteria in the gut microbiota of farmed fish of the *Salmo salar* species at the seawater stage. Also, the phenotypic resistance of these bacteria can be correlated with the presence of antibiotic resistance genes.

antibiotics and were considered as “SUPERRESISTANT BACTERIA”

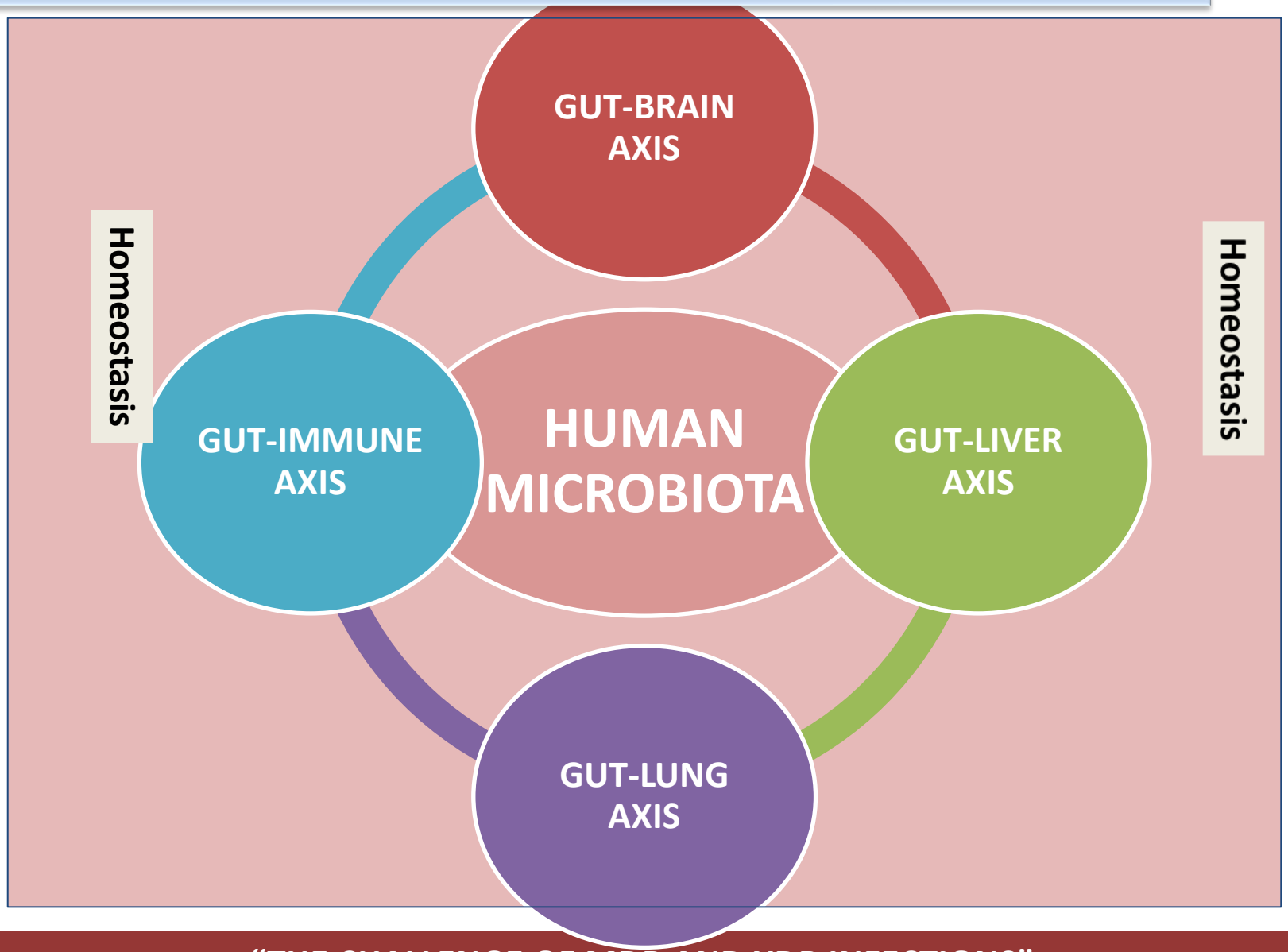
- 77% of antibiotic resistant bacteria showed at least one gene resistant to florfenicol and 89% showed at least 1 gene resistant to oxytetracycline

Human Microbiota

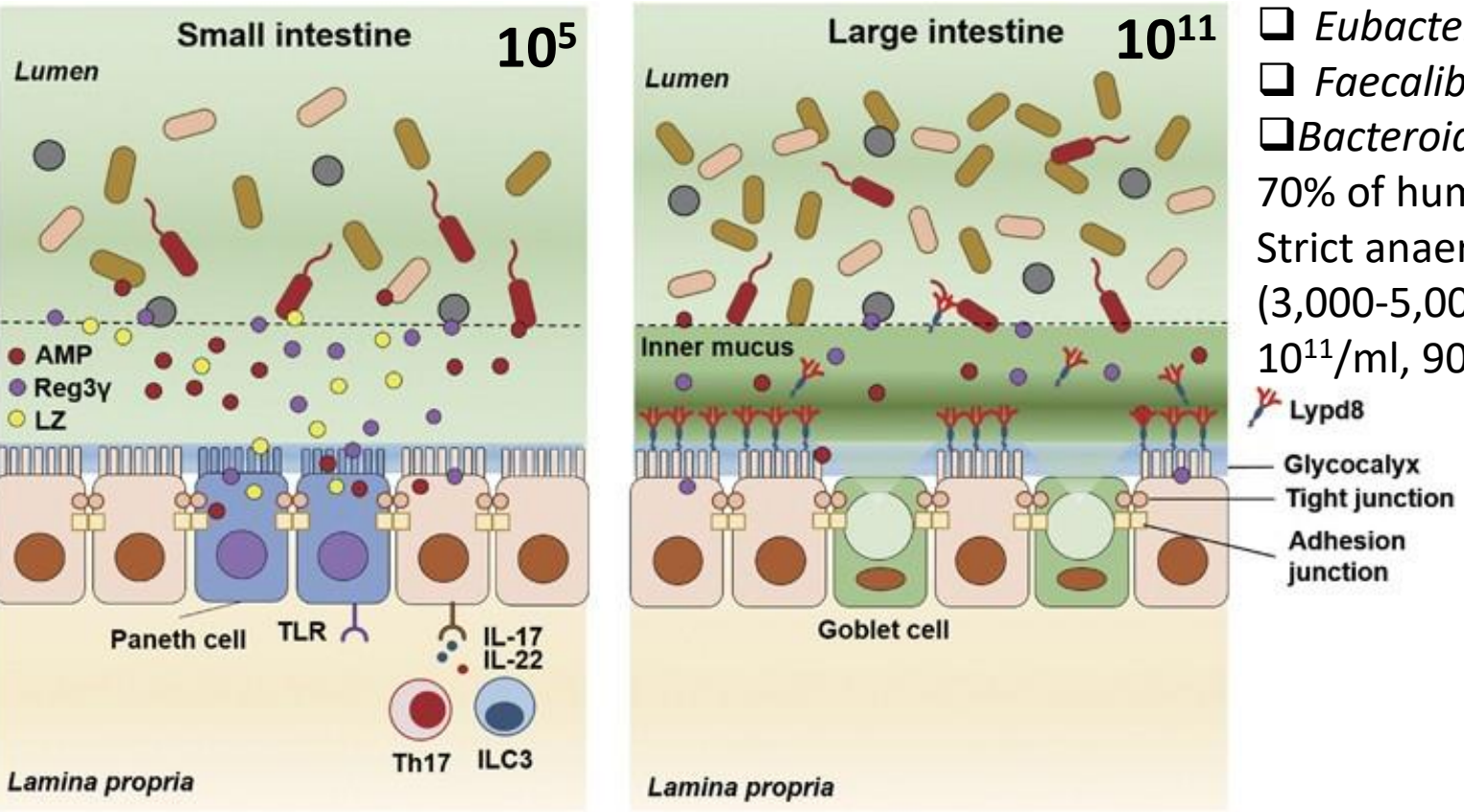


The intestinal microbiome has several mechanisms that contribute to what is referred to AS **COLONIZATION RESISTANCE against potentially pathogenic and often MULTIRESISTANT BACTERIA.**

But, which is the role of Human microbiota?



Spatial organization of intestinal microbiota in healthy humans



- ❑ *Eubacterium rectale*
- ❑ *Faecalibacterium praunitzii*
- ❑ *Bacteroides group*

70% of human flora

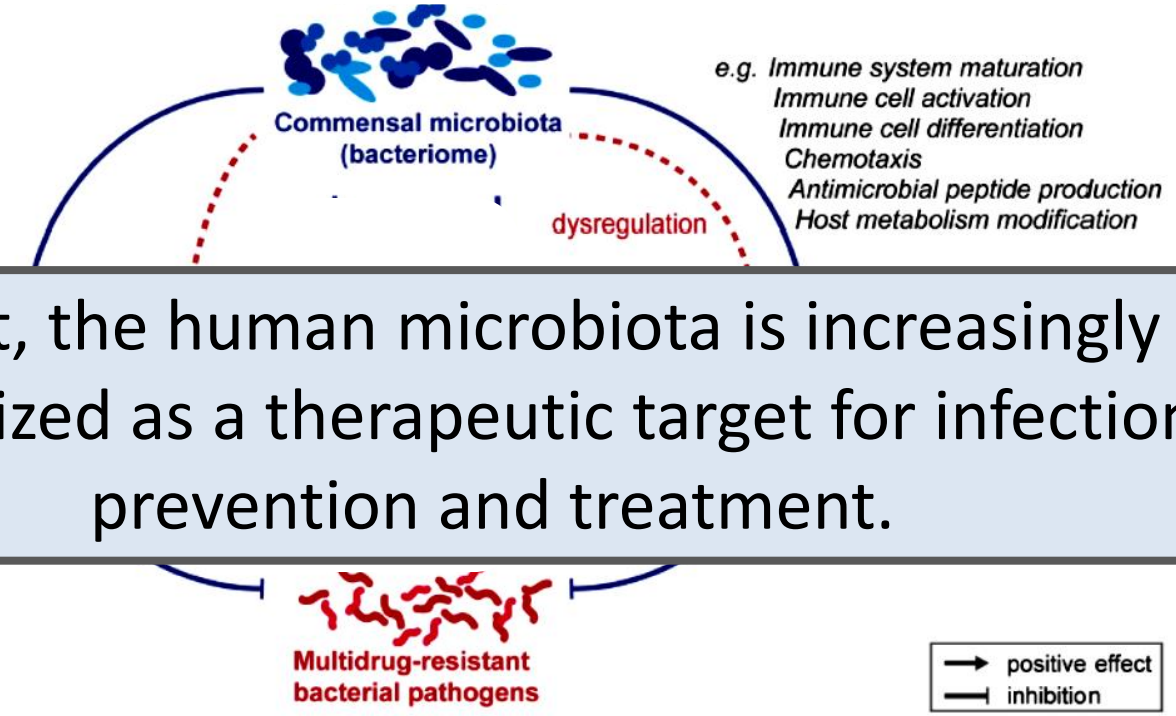
Strict anaerobes predominate (3,000-5,000 diferent species)

10^{11}/ml, 90% fecal mass

Modified from Okumura R and Takeda K. Exp Mol Medicine 2017

Swidsinski A, Loening-et al, in "Spatial organization of intestinal microbiota in healthy humans" in UpToDate, Dec 2022.

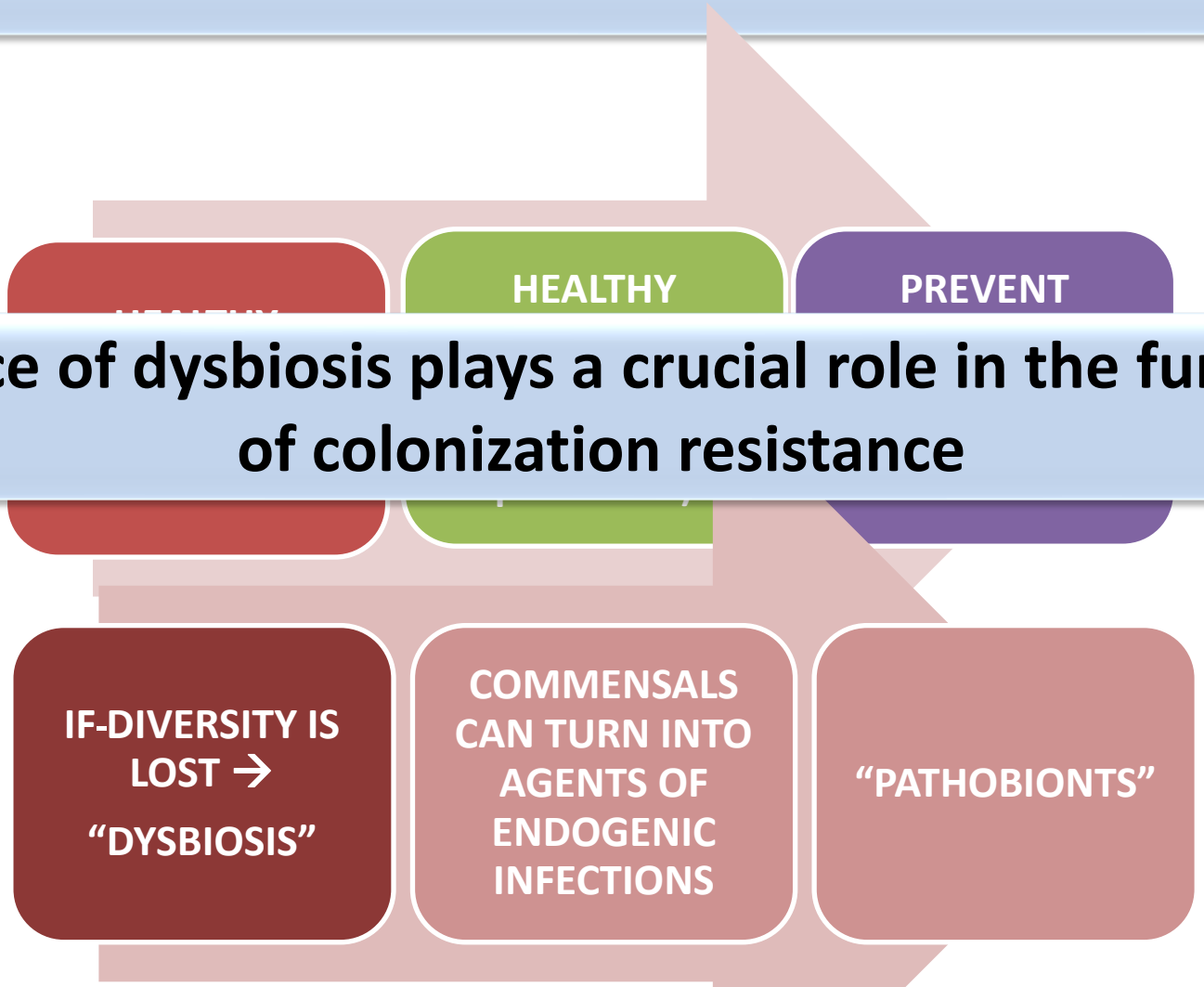
DIRECT EFFECTS OF INTESTINAL MICROBIAL COMMENSALS ON BACTERIAL INFECTION



In fact, the human microbiota is increasingly recognized as a therapeutic target for infection prevention and treatment.

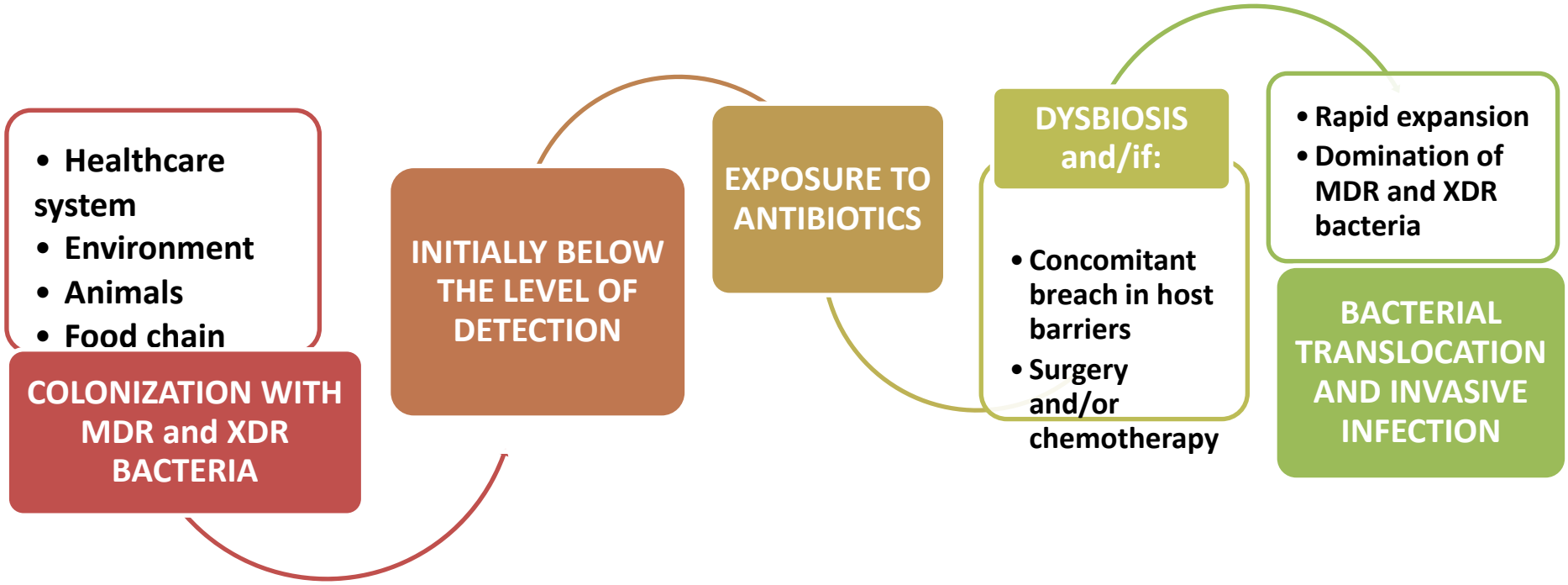
Wuethrich I, et al. Gut Microbes 2021

“Colonization resistance and pathobionts”
are the main direct effects of microbial intestinal commensals



The absence of dysbiosis plays a crucial role in the functionality of colonization resistance

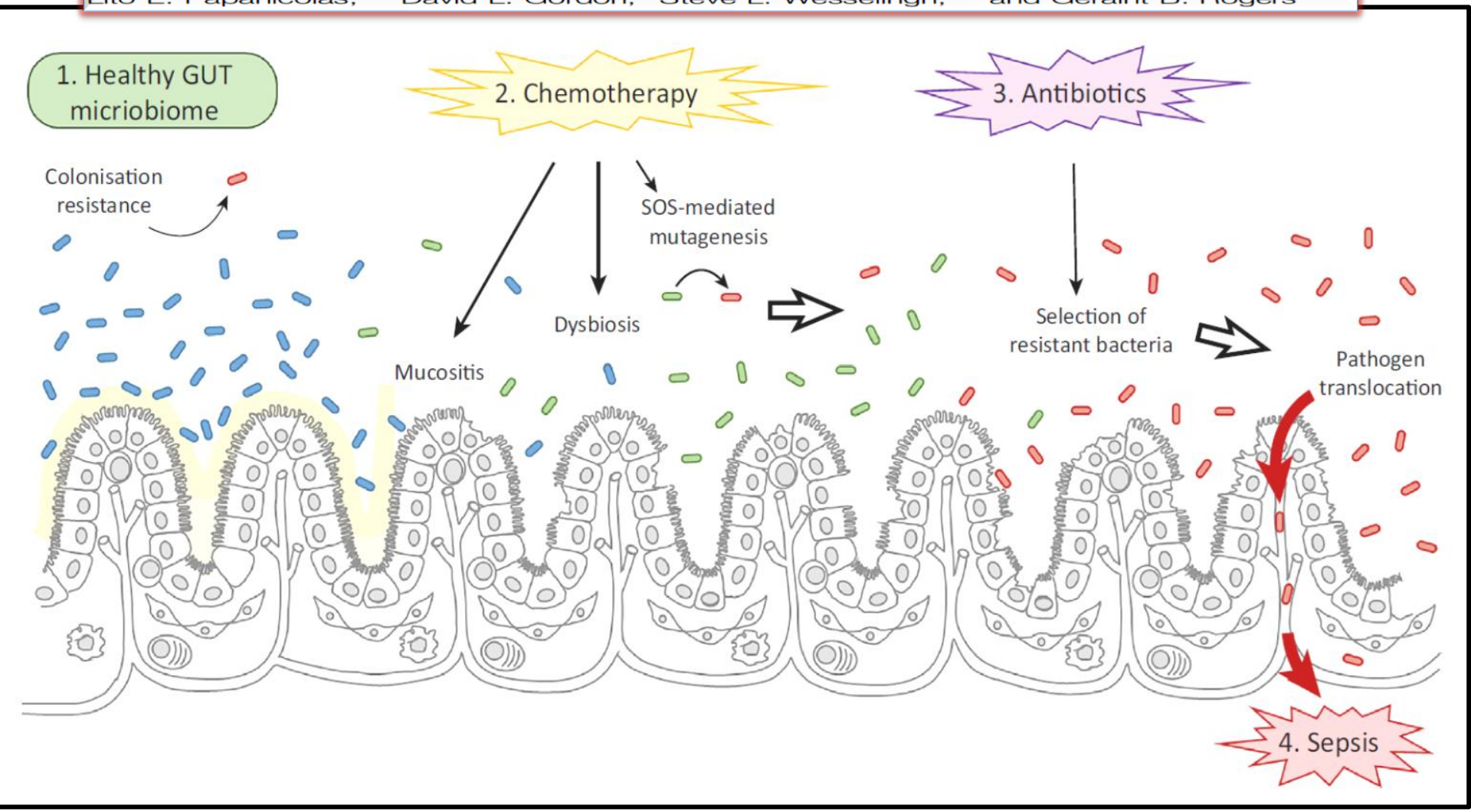
Direct effects of microbial commensals "Colonization resistance and pathobionts"



Not Just Antibiotics: Is Cancer Chemotherapy Driving Antimicrobial Resistance?

Trends Microbiol 2018;26:393-400

Lito E. Papanicolas,[1,2] David L. Gordon,[3] Steve L. Wesselingh,[1,2] and Geraint B. Rogers[1,2,*]

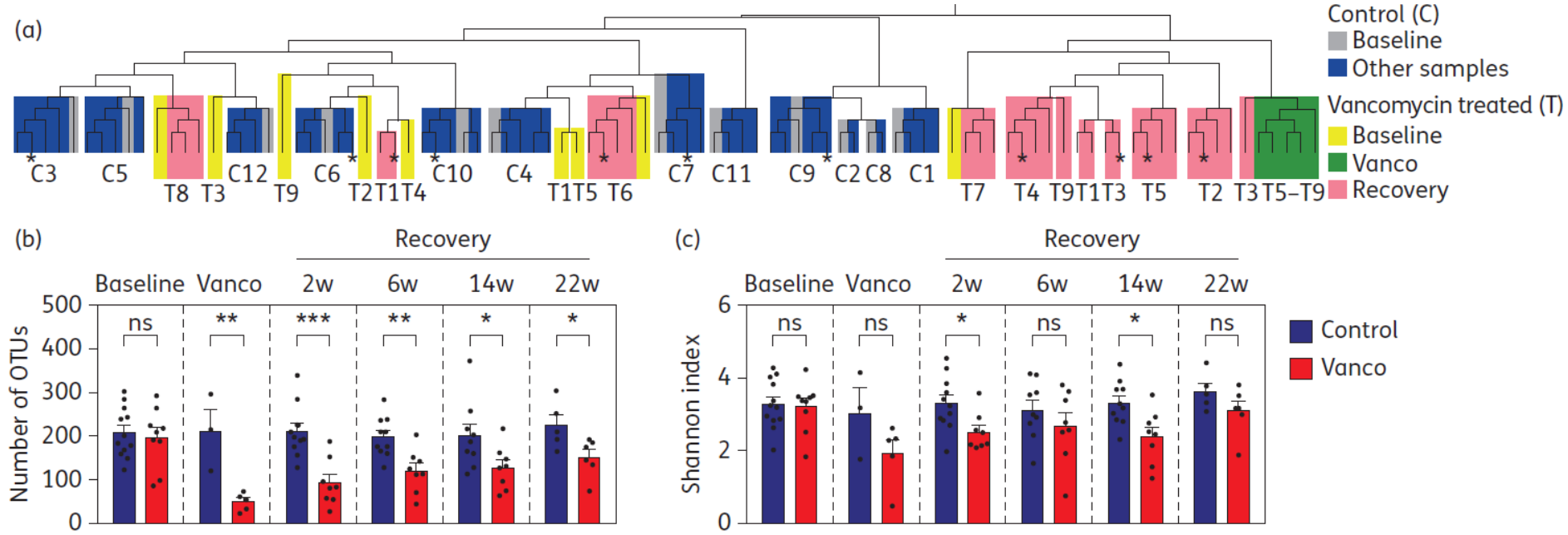


J Antimicrob Chemother 2017; **72**: 128–136
doi:10.1093/jac/dkw383 Advance Access publication 5 October 2016

Journal of Antimicrobial Chemotherapy

Short- and long-term effects of oral vancomycin on the human intestinal microbiota

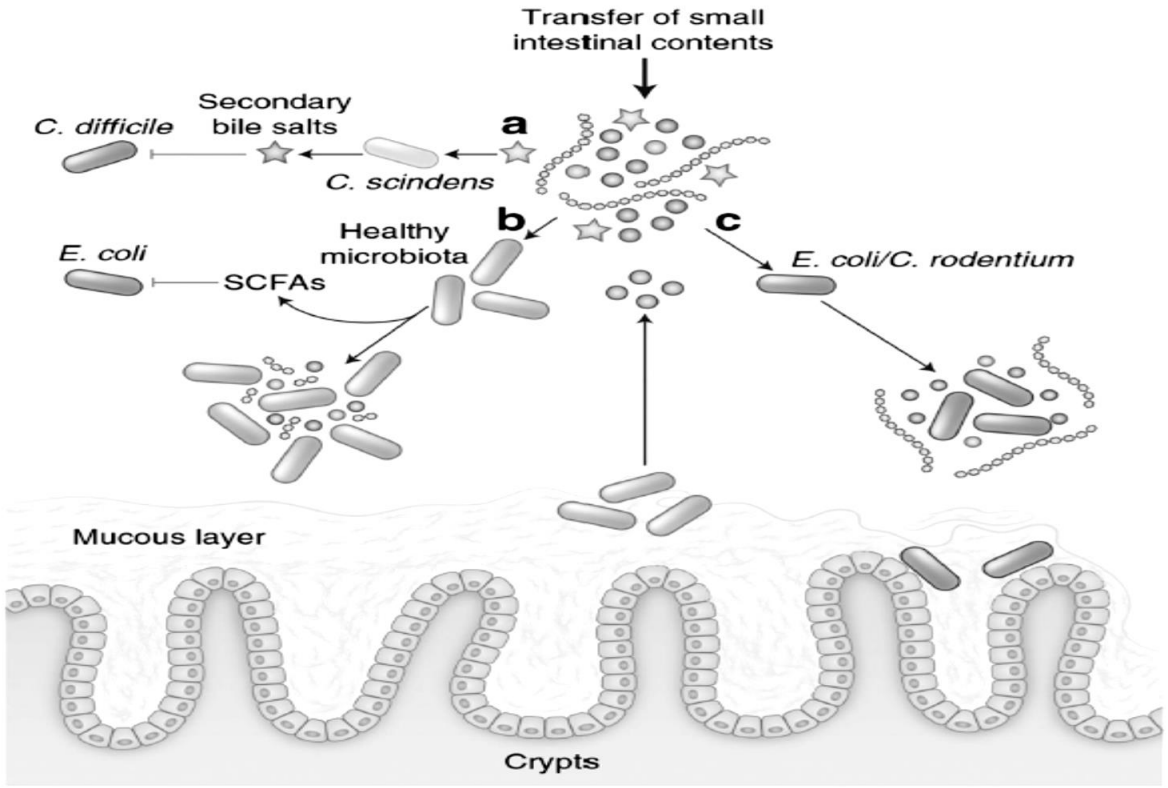
Sandrine Isaac[1]†, Jose U. Scher[2]†, Ana Djukovic[1], Nuria Jiménez[1], Dan R. Littman[3,4], Steven B. Abramson[2], Eric G. Pamer[5,6] and Carles Ubeda[1,7]*



Mucosal Immunol. 2019 January ; 12(1): 1–9. doi:10.1038/s41385-018-0053-0.

Interbacterial mechanisms of colonization resistance and the strategies pathogens use to overcome them

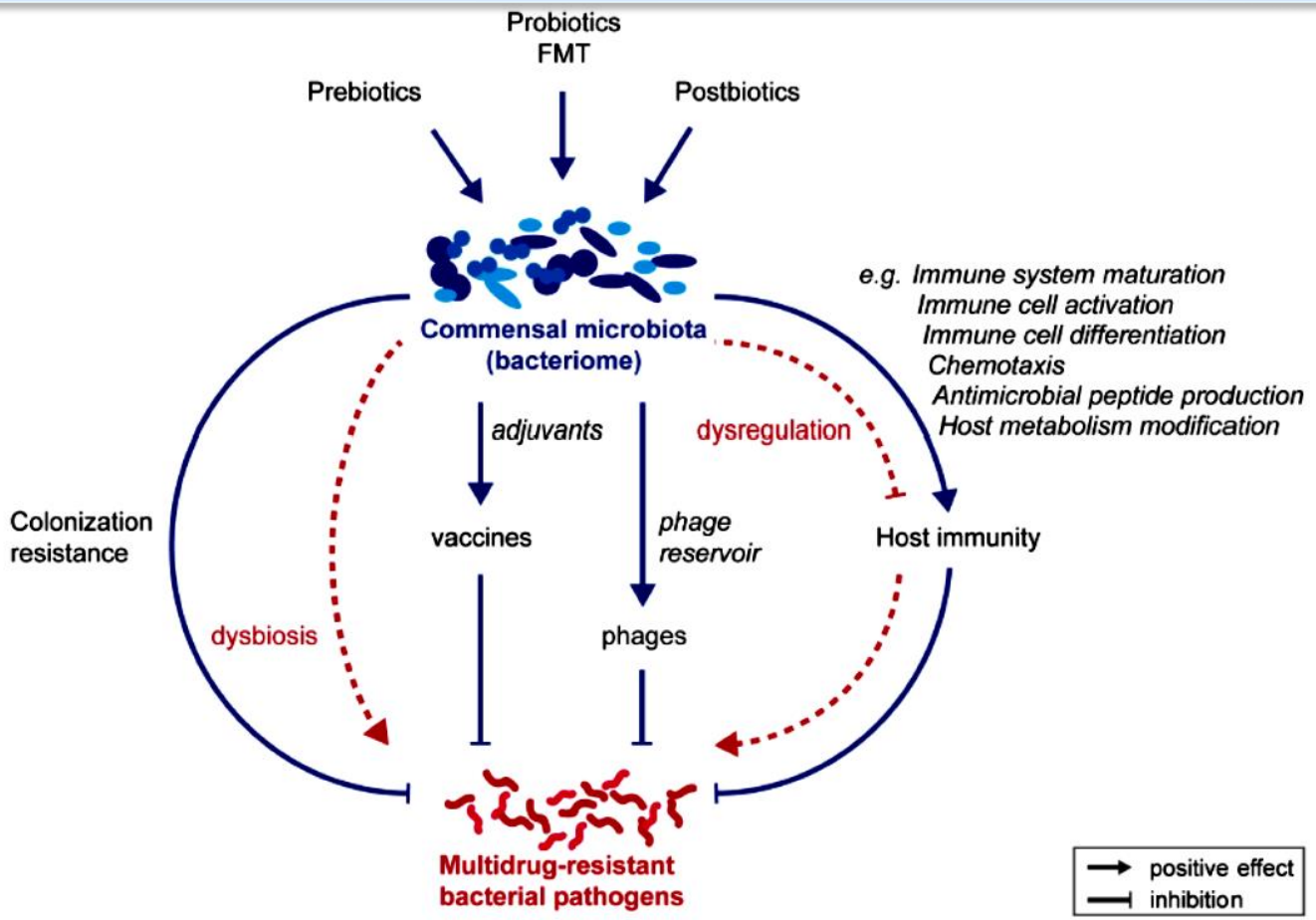
Matthew T. Sorbara[1] and **Eric G. Pamer**[1,2]



Indirect effects of microbial commensals on bacterial infection

- Immune system regulation
- Alternative interventions against MDR pathogens
  - Microbiota-based treatments
  - Fecal microbiota transplantation
  - Probiotics and live biotherapeutics
  - Prebiotics and postbiotics
  - Phage-mediated therapies
  - Vaccines and antibodies
  - Mitigating antibiotic collateral damage
  - Antimicrobial stewardship

INDIRECT EFFECTS OF INTESTINAL MICROBIAL COMMENSALS ON BACTERIAL INFECTION



Wuethrich I, et al. Gut Microbes 2021

To sum up….

- The phenomenon of antibiotic resistance is a priority topic for human development, on par with global warming.
- We cannot rely on classic antibiotics alone to suppress the rise of MDR bacterial pathogens.
- Significant quantities of antibiotics are used in farm animals, aquaculture and agricultural crops in order to significantly increase animal protein production.
- Contact with animals, food chain and hospital settings can lead to low levels of MDR intestinal colonization.

- **Exposure to antibiotics and/or chemotherapy can lead to human intestinal dysbiosis which in turns plays a crucial role in high level colonization and gut MDR dominance.**
- **The concomitant breach of gut mucous barrier caused by surgery or chemotherapy-induced mucositis trigger bacterial translocation and invasive infection.**
- **Strategies aimed at enhancing intestinal microbiota diversity and a healthy immune system to ensure colonization resistance in the intestinal reservoir are warranted and must be evaluated in controlled trials.**