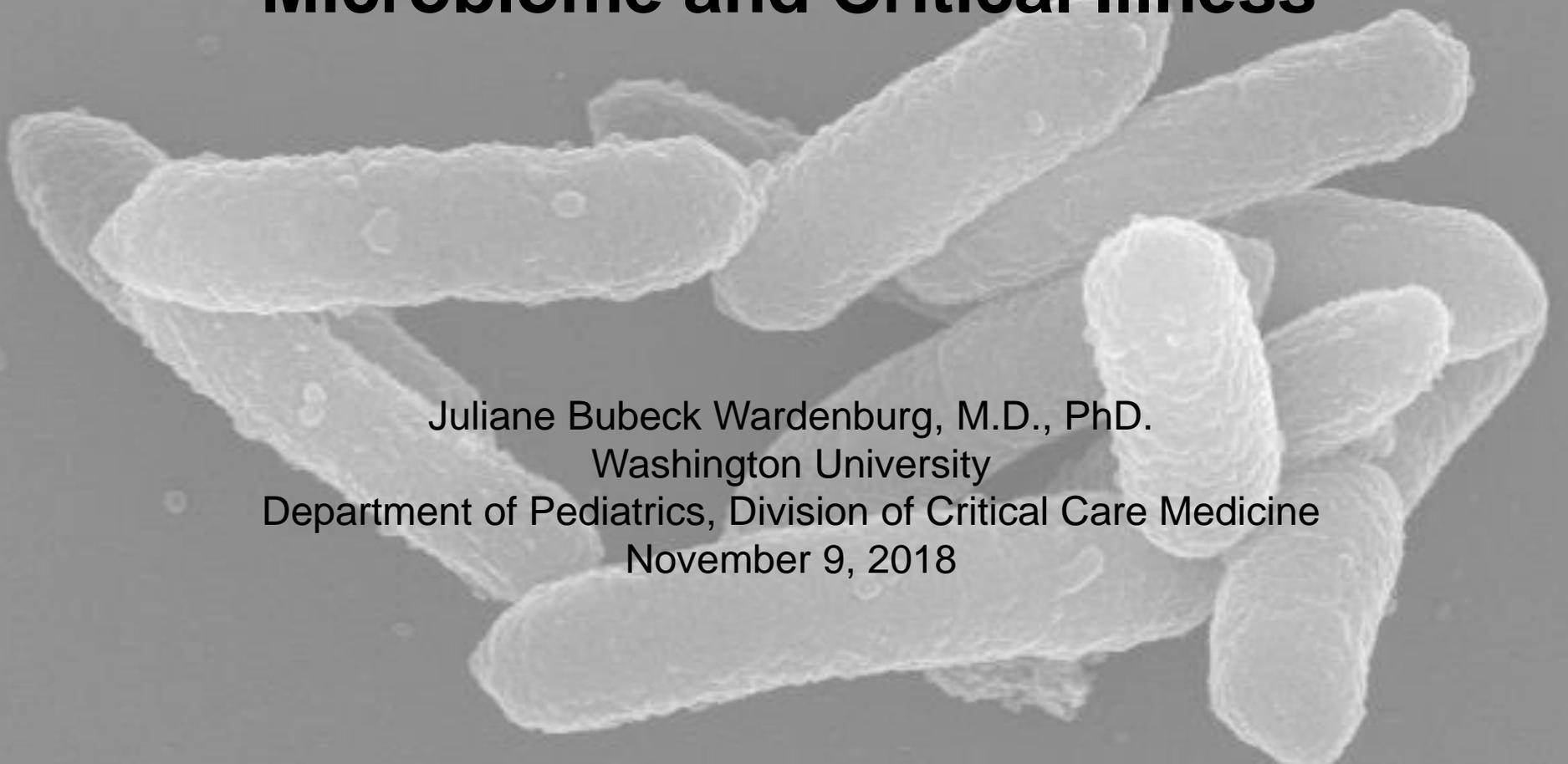


Microbiome and Critical Illness

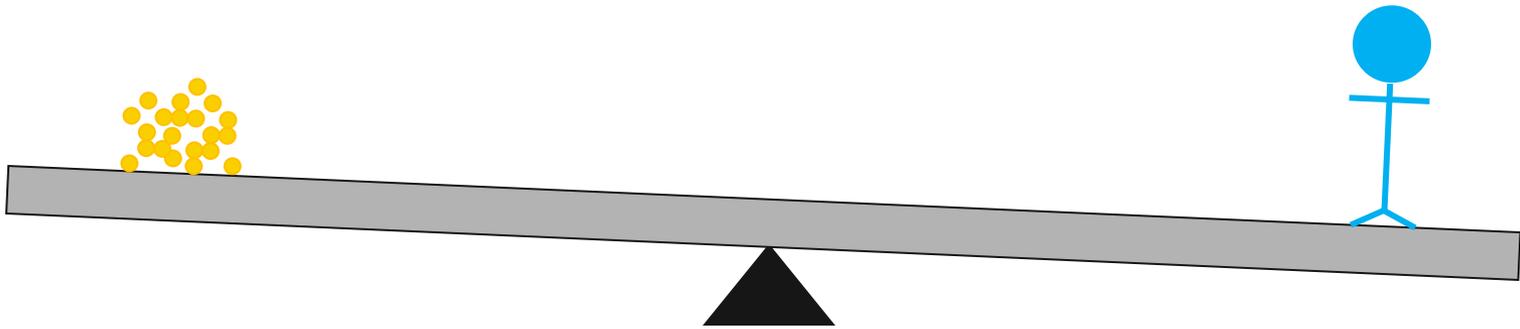


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Department of Pediatrics, Division of Critical Care Medicine
November 9, 2018

Disclosures

I have a financial agreement with Aridis Pharmaceuticals related to patents owned by the University of Chicago.

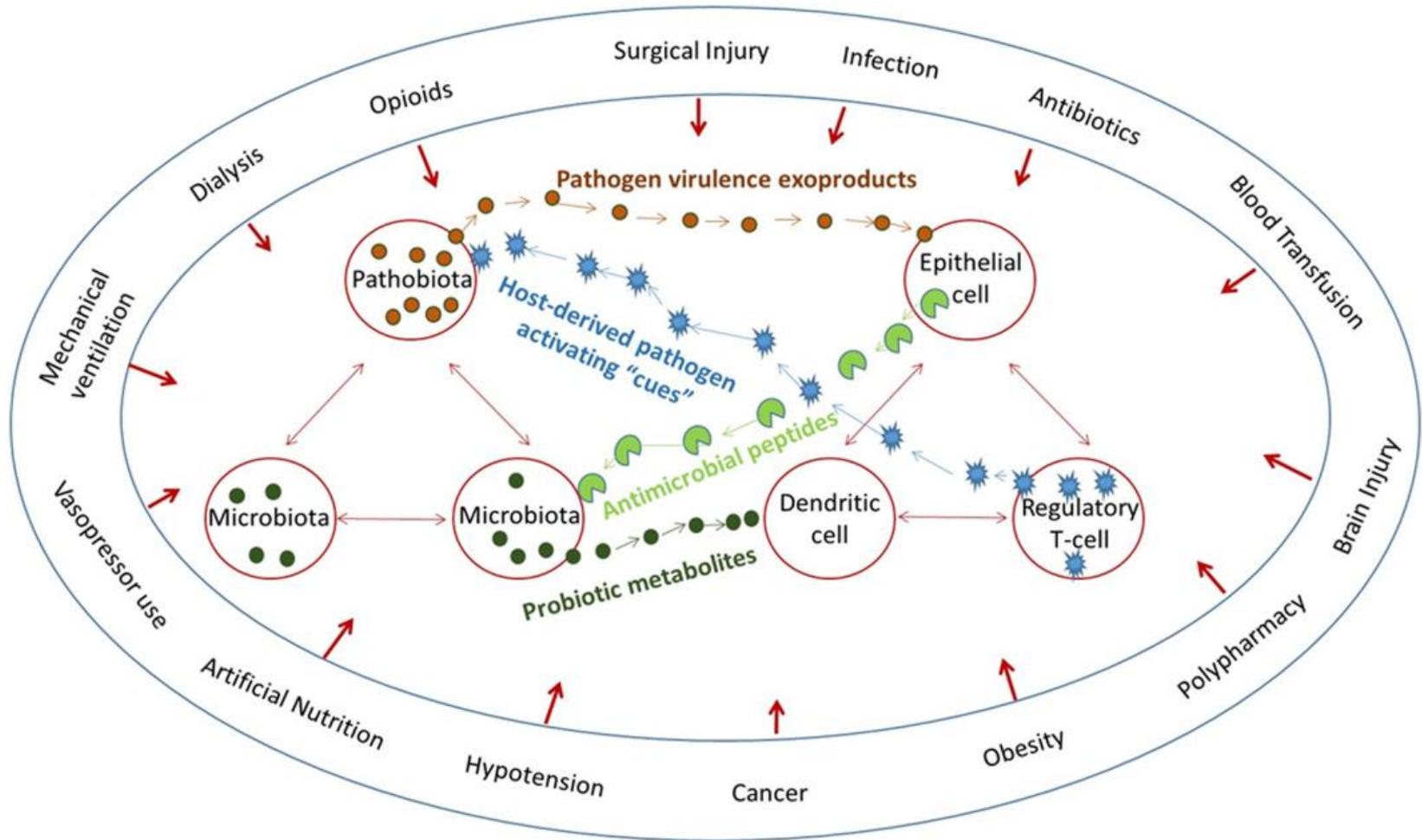
The host-microbe interaction



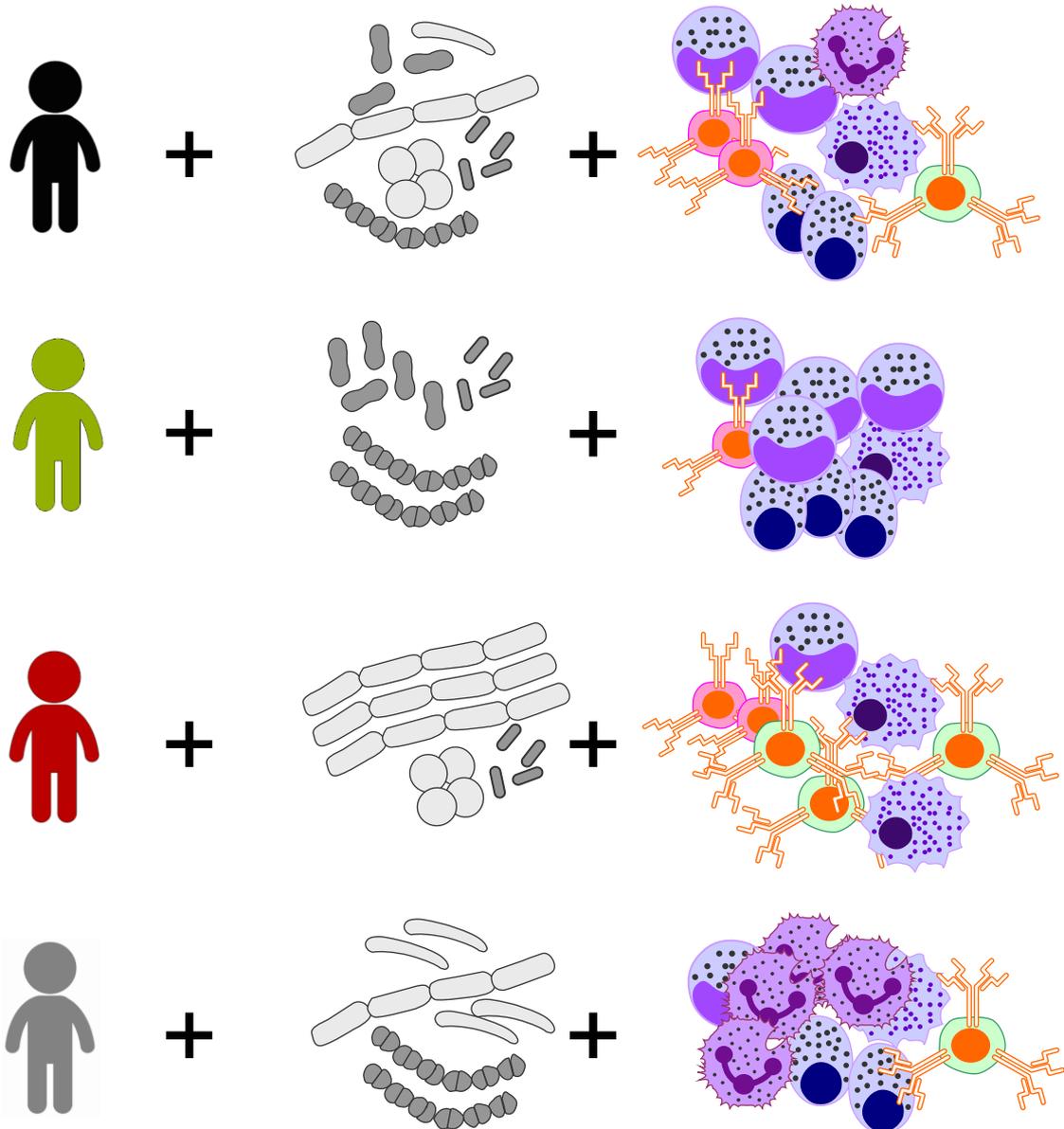
microbial niche establishment
niche competition
virulence factors
regulation of gene expression

state of health
immunologic competence
virulence factor susceptibility
tissue-specific regulation

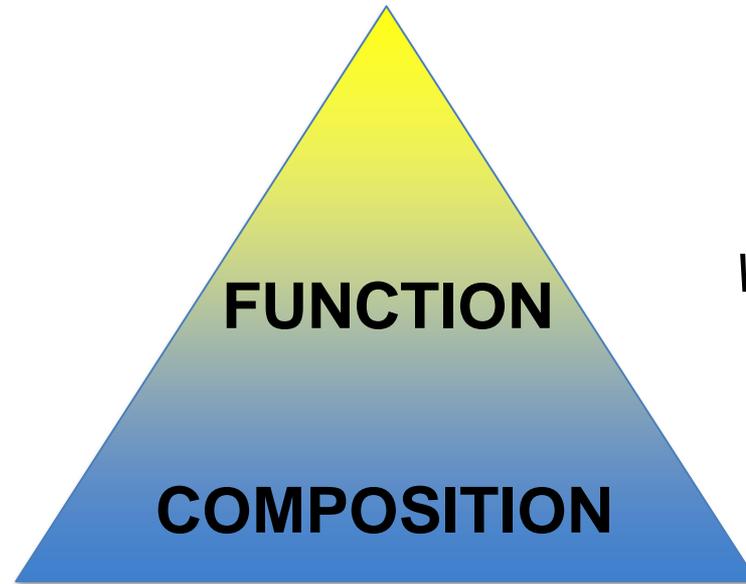
Critical care and the microbiome



Critical Illness: a complex system



What is the basis for microbial impact on human health?

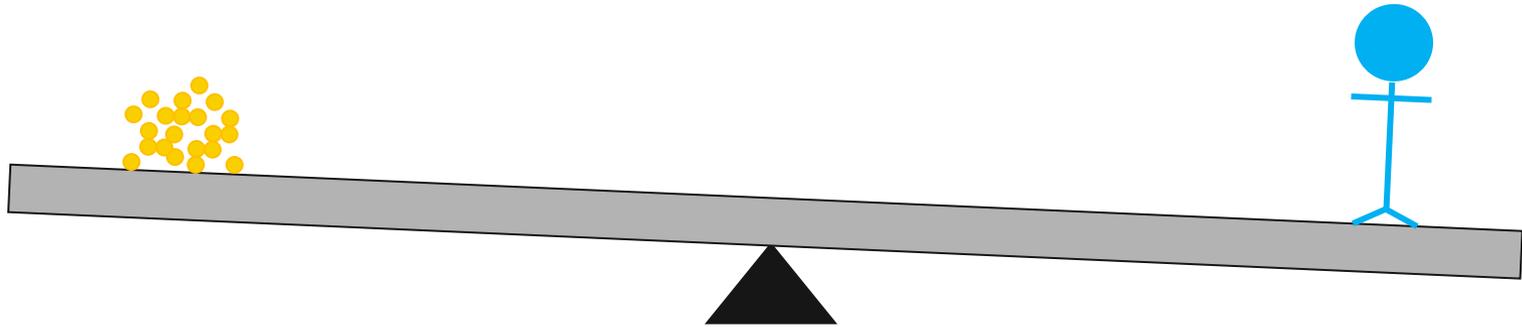


*WHAT CAN THEY DO?
ARE THEY ACTIVE?*

WHO IS THERE?

Understanding BOTH composition and function will be essential to enable prophylactic and therapeutic intervention

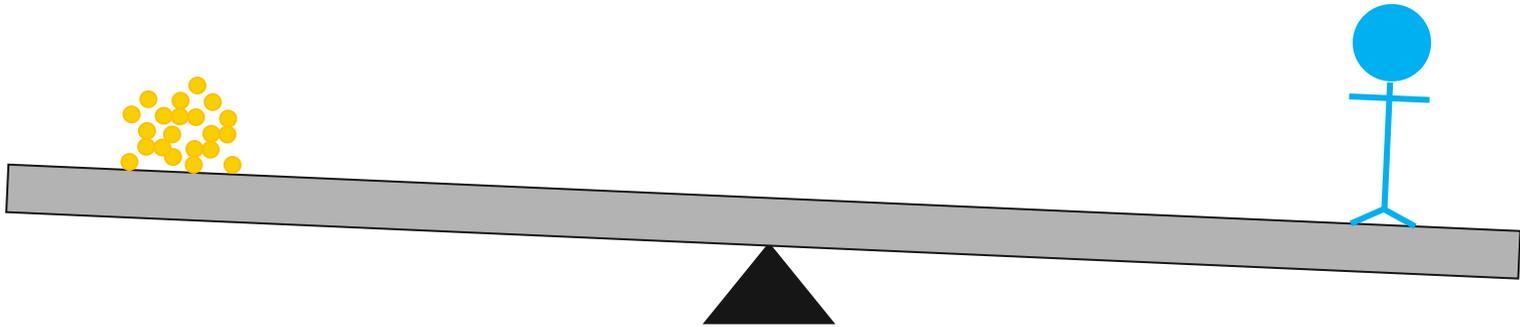
The host-microbe interaction



Key Questions:

- 1) Does the microbiome cause critical illness?
- 2) Does the microbiome modulate outcome in critical illness?
- 3) Can the microbiome be harnessed to protect against critical illness?

The host-microbe interaction

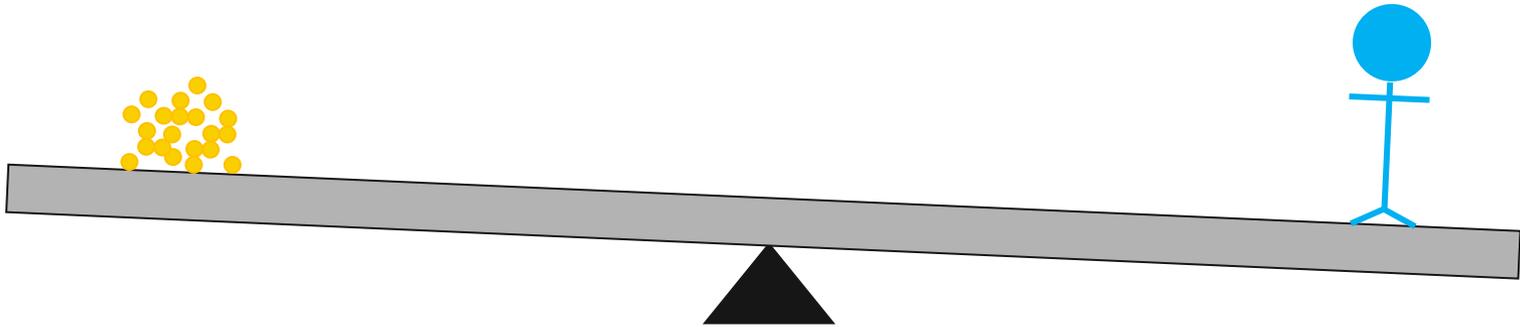


1) Does the microbiome cause critical illness?

S. aureus
S. pneumoniae
E. coli
K. pneumoniae
P. aeruginosa
C. albicans
B. fragilis

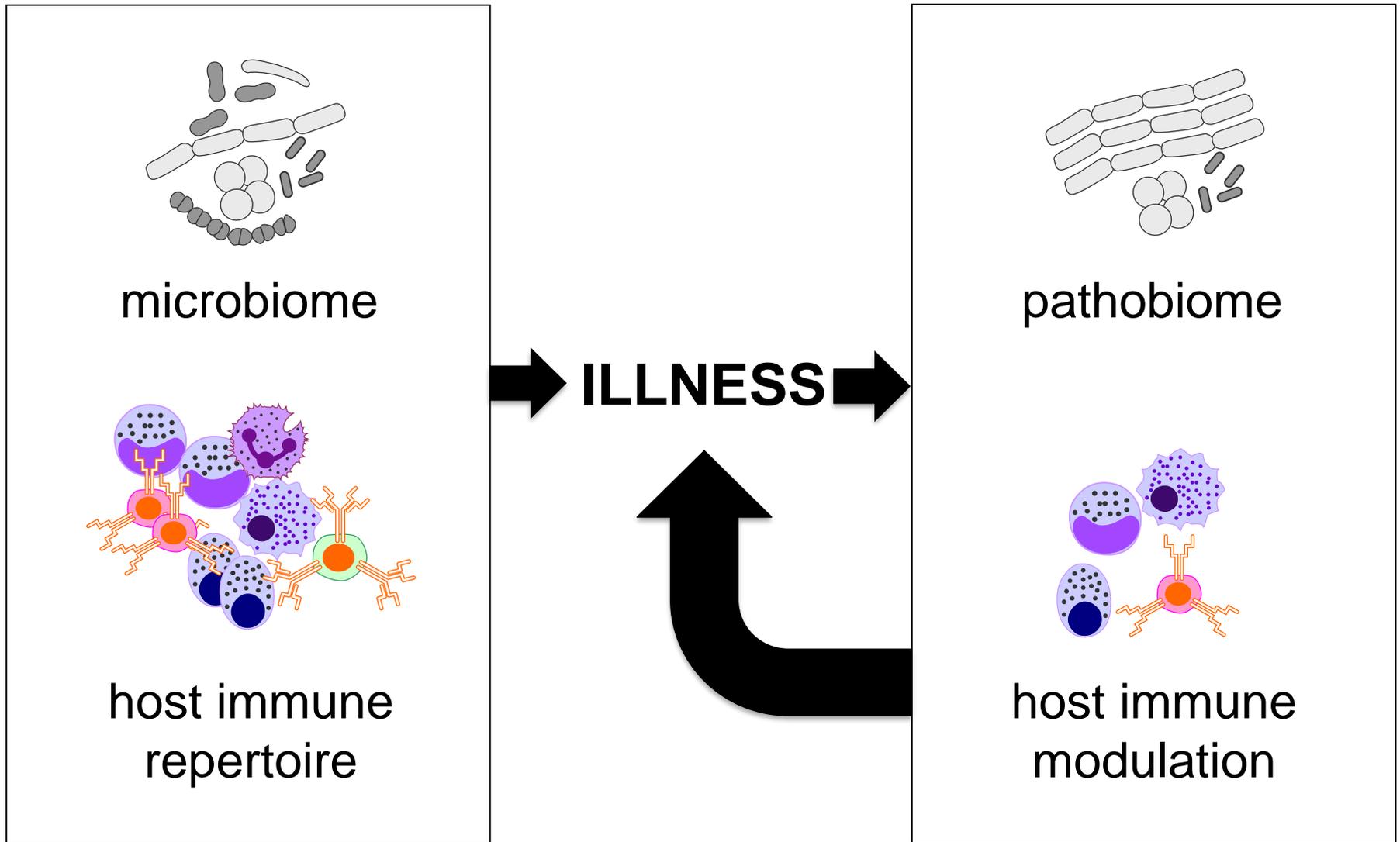
PATHOBIONTS

The host-microbe interaction



2) Does the microbiome modulate outcome in critical illness?

The microbiome and disease: a vicious cycle

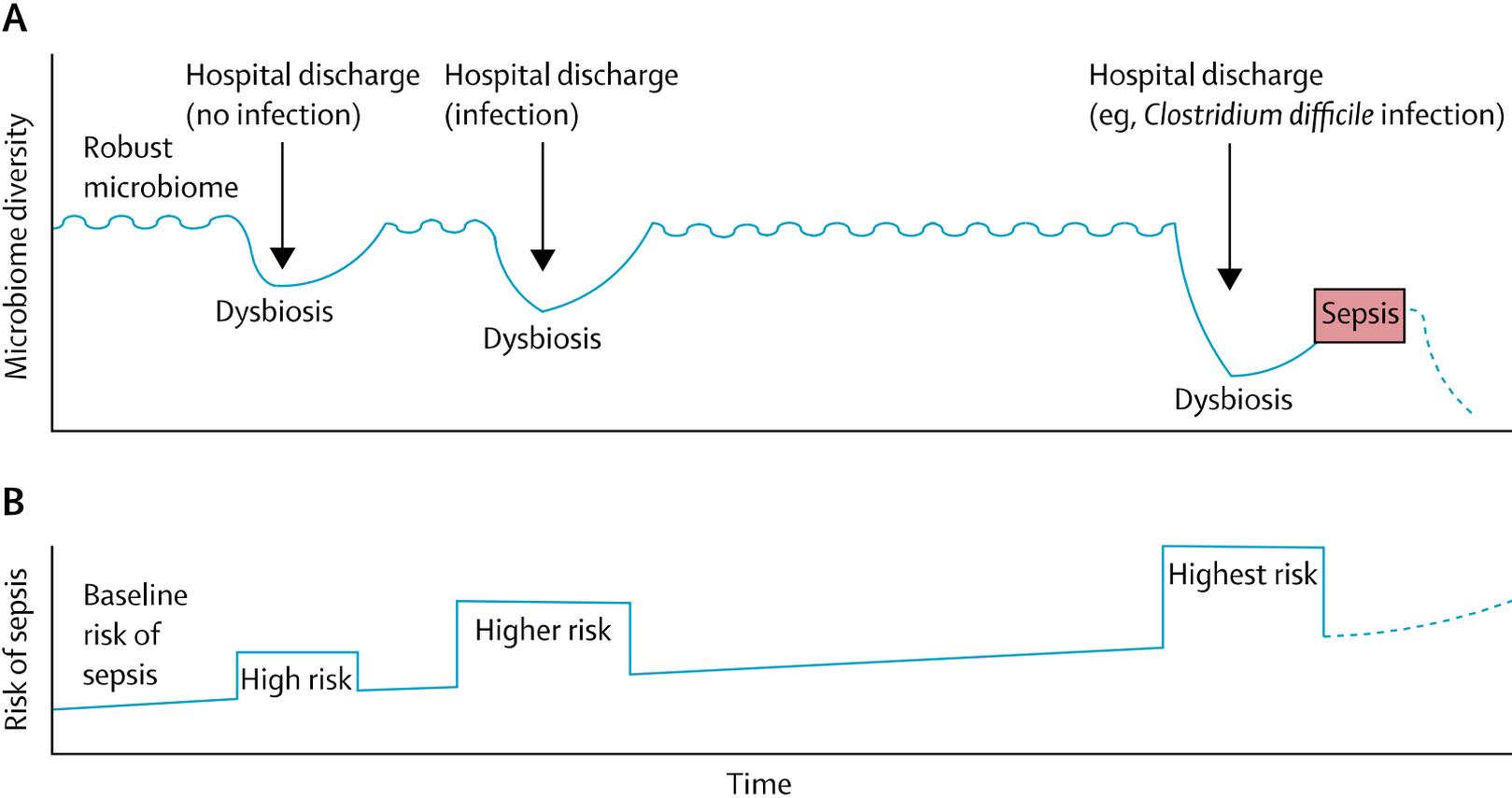


Haack and Wiersinga, Lancet Gastroenterol Hepatol, 2017

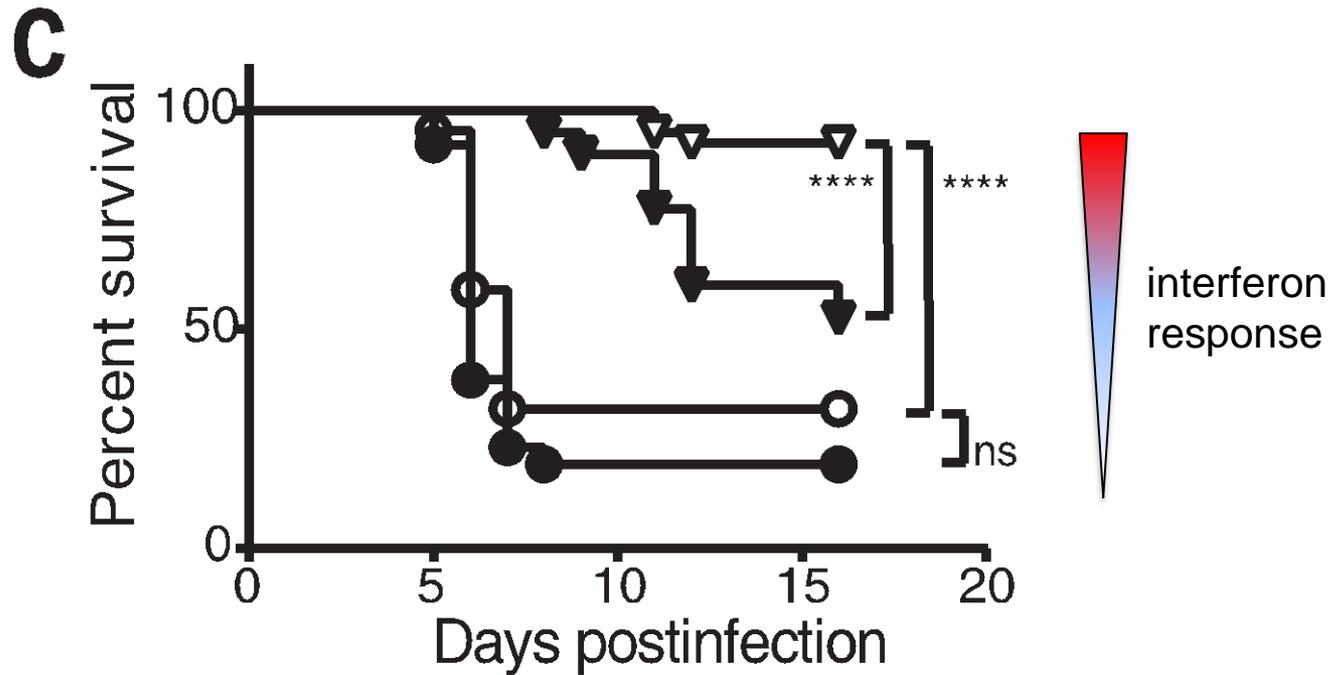
Fay, et al, BBA Molecular Basis of Disease, 2017

Alverdy and Luo, Front Microbiol, 2017

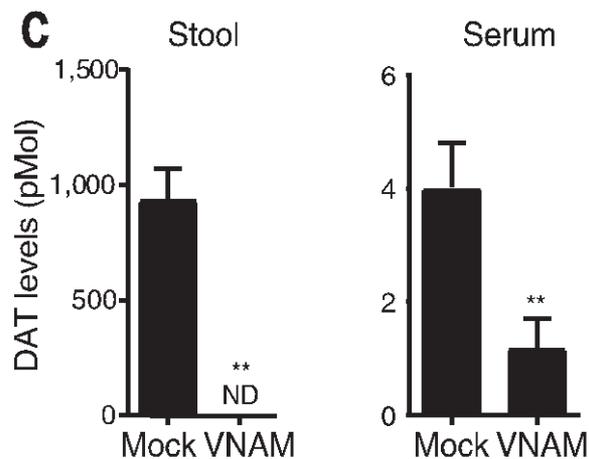
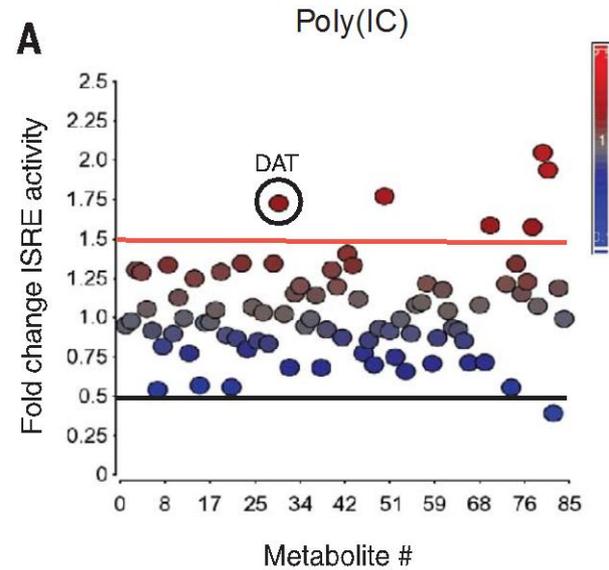
Microbiome health and risk of sepsis



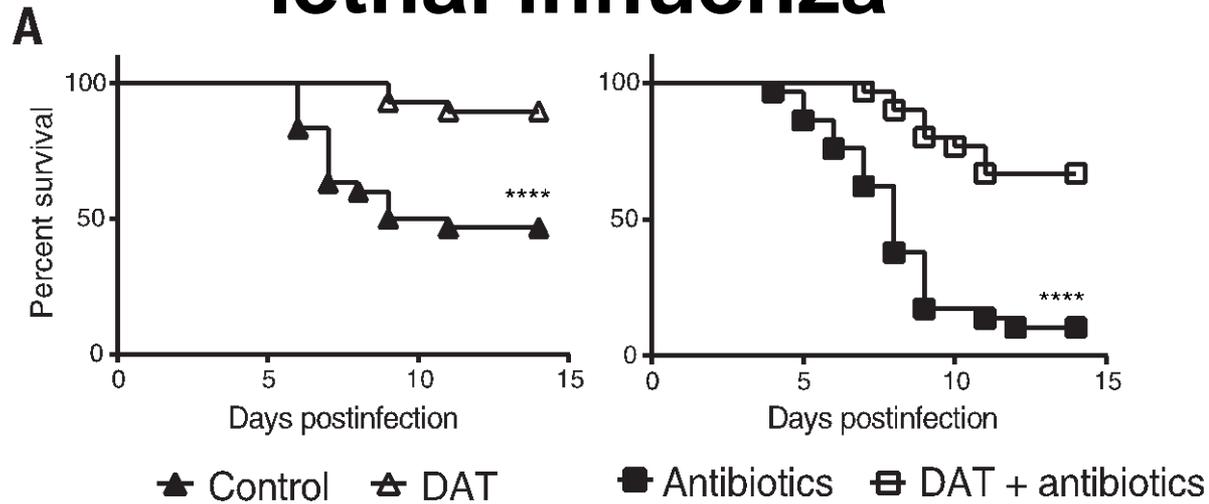
Interferon response is required for protection against lethal influenza



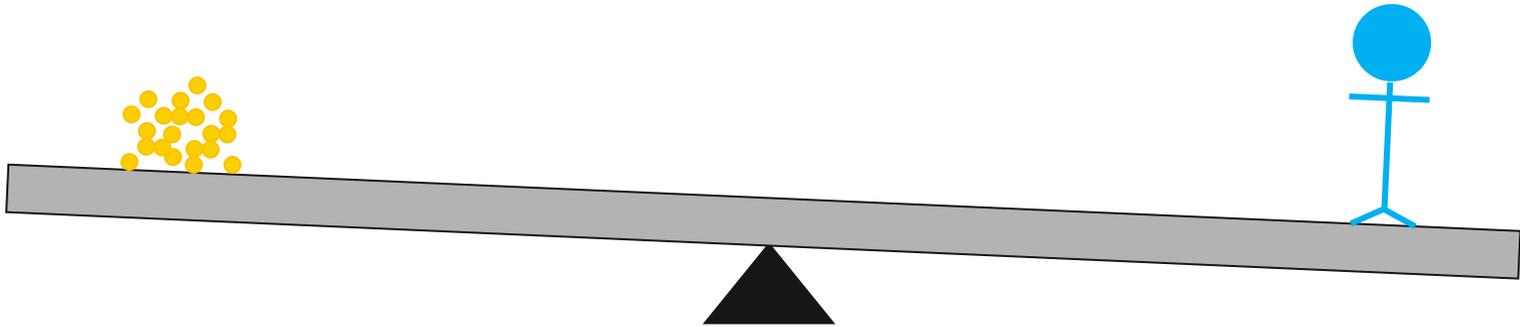
Identification of microbial metabolites that influence interferon response



A single microbial metabolite protects against lethal influenza

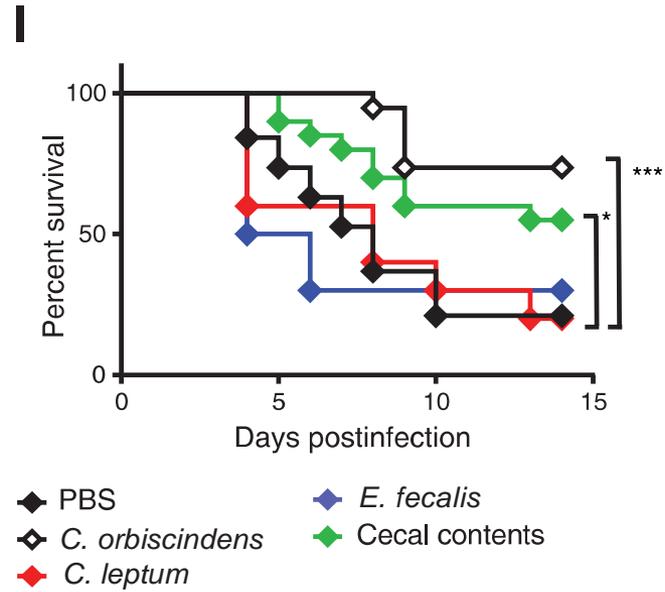


The host-microbe interaction

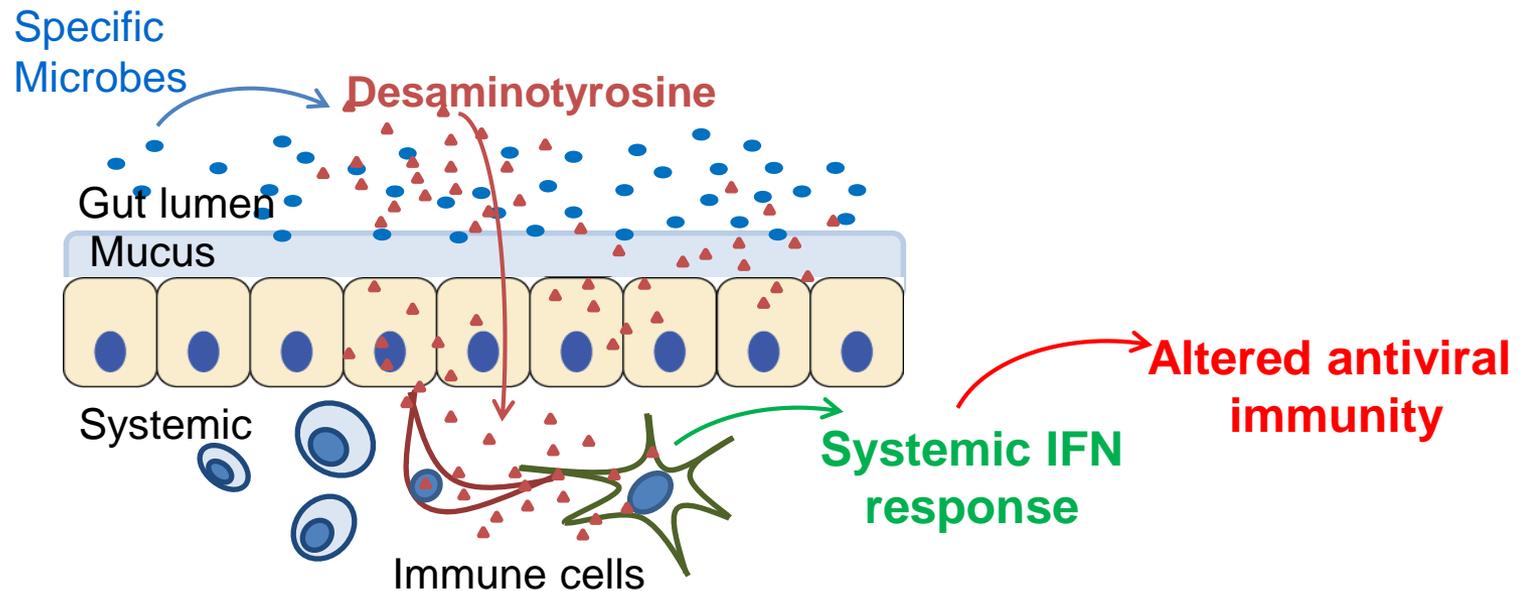


3) Can the microbiome be harnessed to protect against critical illness?

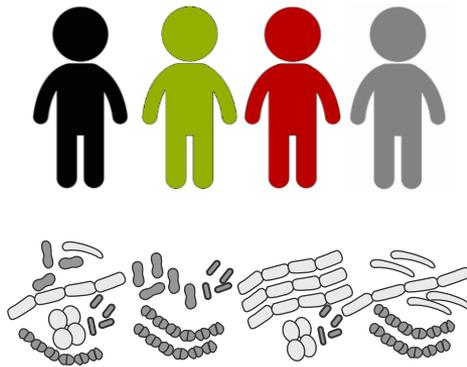
Microbial specificity of survival benefit



Mechanistic insight on disease protection



The microbiome in critical illness



Unique host and microbiome

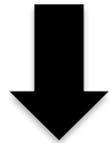
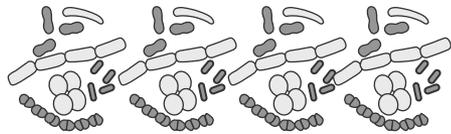
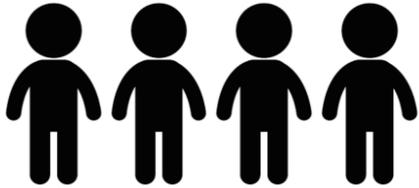
Both early imprinting and events in life shape microbiome

NOT STATIC!

Understanding risk and designing prevention and therapy will require knowledge of functional impact of microbiome

How can we harness the microbiome?

NO



YES

