



Melissa Conference, Nov 4, 2020



***Impact of closed life support system
on human microbiome and health
- managing symbiosis -***

Joël Doré & Hugo Roume

Micalis & MetaGenoPolis, INRA Jouy-en-Josas, France



frontiers
in Physiology

ORIGINAL RESEARCH
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Responses of Intestinal Mucosal Barrier Functions of Rats to Simulated Weightlessness

Mingliang Jin¹, Hao Zhang¹, Ke Zhao², Chunlan Xu¹, Dongyan Shao¹, Qingsheng Huang¹, Junling Shi¹ and Hui Yang^{1*}

THE FASEB JOURNAL • RESEARCH • www.fasebj.org 2017

Intestinal microbiota contributes to colonic epithelial changes in simulated microgravity mouse model

Junxiu Shi,^{*} Yifan Wang,^{*} Jian He,[†] Pingping Li,[‡] Rong Jin,^{*} Ke Wang,^{*} Xi Xu,[§] Jie Hao,^{*} Yan Zhang,^{*} Hongju Liu,[‡] Xiaoping Chen,[‡] Hounan Wu,^{†,1} and Qing Ge^{*,2}

Analytical Methods

From the journal:
Analytical Methods 2016

Human metabolic responses to microgravity simulated in a 45-day 6° head-down tilt bed rest (HDBR) experiment

[Pu Chen](#)^a, [Yanbo Yu](#)^a, [Chen Tan](#)^b, [Hongju Liu](#)^b, [Feng Wu](#)^b, [Hongyi Li](#)^a, [Jianying Huang](#)^a, [Haisheng Xiaoping Chen](#)^{*b} and [Bin Chen](#)^{*a}

The FASEB Journal • Research Communication 2015

Simulated microgravity disrupts intestinal homeostasis and increases colitis susceptibility

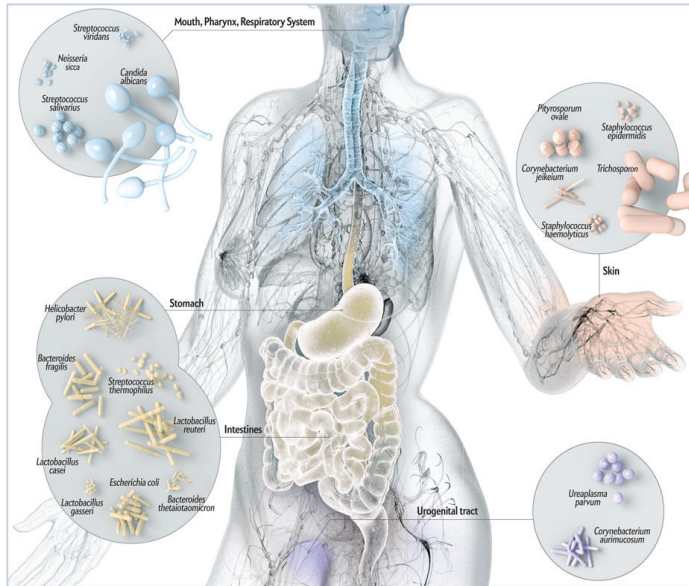
Pingping Li,^{*,1} Junxiu Shi,^{*,1} Peng Zhang,^{†,1} Ke Wang,^{*} Jinglong Li,[‡] Hongju Liu,[†] Yu Zhou,^{*} Xi Xu,^{*} Jie Hao,^{*} Xiuyuan Sun,^{*} Xuewen Pang,^{*} Yan Li,^{*} Hounan Wu,[§] Xiaoping Chen,^{†,2} and Qing Ge^{*,2}

Simulated microgravity
alters gut permeability
and intestinal
immune homeostasis ;
this will impact the microbiome...

will it be resilient or
may the alteration be durable ?

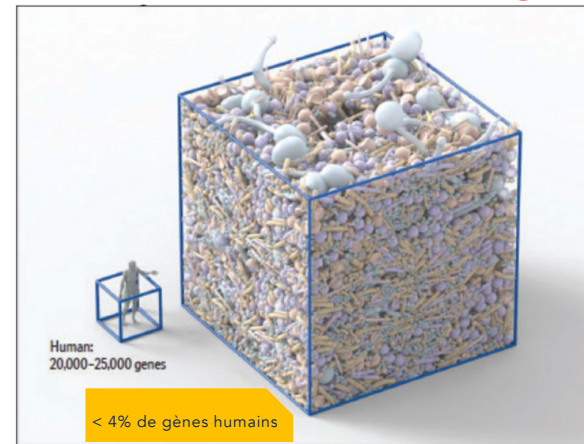
The human is microbial, ecosystem and symbiosis

~50 000 000 000 000 bacteria : as many as human cells in our body



our microbiomes are 'autochthonous' and specific to ecological niches they occupy

600 000 microbial genes * :
25 X the number of human genes



Microbiome science changes the landscape

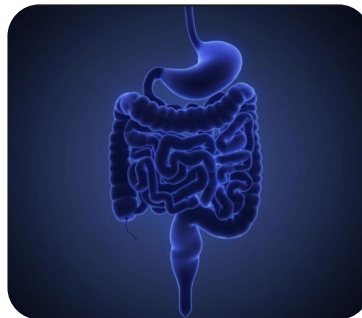
* per individual

Qin et al MetaHIT Consortium, Nature 2010
Grice et al, Annu Rev Genomics Hum Genet 2012
HMP Consortium et al., Nature 2012

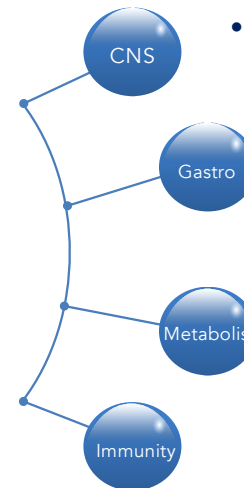
The common thread in chronic conditions

Dysbiosis: an alteration of host-microbes symbiosis

Alteration of the microbiota
+
Intestinal hyper-perméabilité
+
Inflammation
+
Oxydative stress

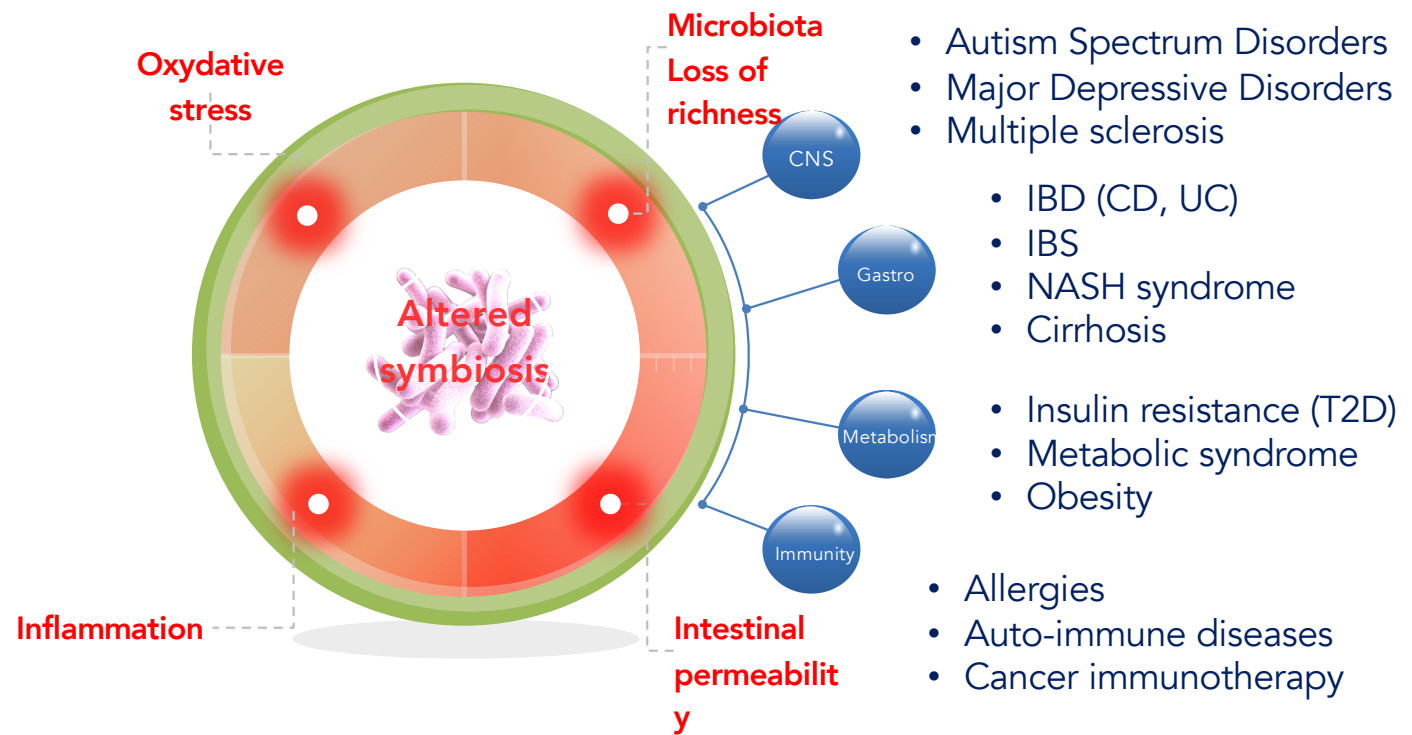


No prevention
& no treatment



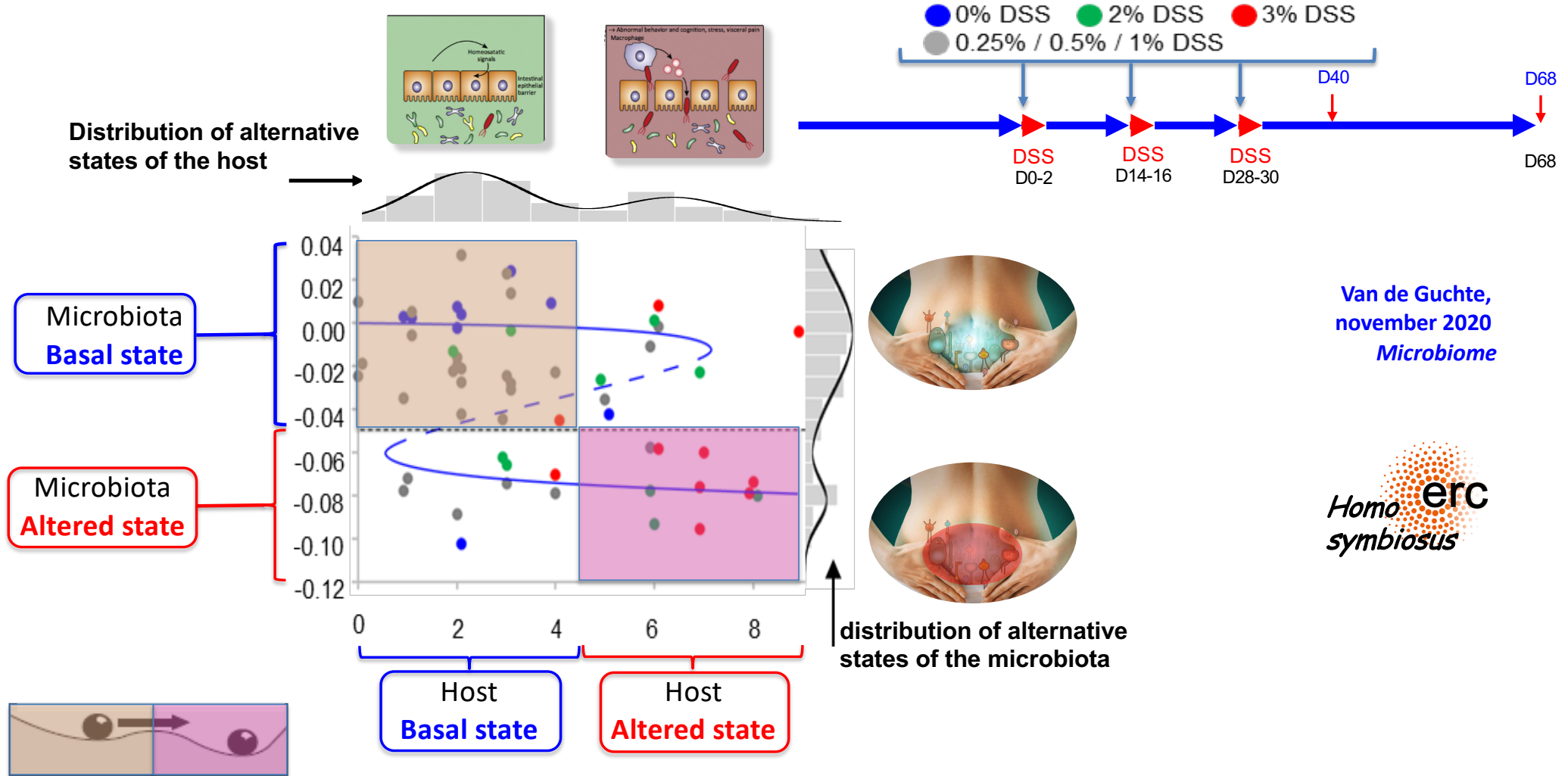
- Autism Spectrum Disorders
- Major Depressive Disorders
- Multiple sclerosis
- IBD (CD, UC)
- IBS
- NASH syndrome
- Cirrhosis
- Insulin resistance (T2D)
- Metabolic syndrome
- Obesity
- Allergies
- Auto-immune diseases
- Cancer immunotherapy

Altered host-microbes symbiosis in chronic conditions



With circular causalities >> impacts?

Inflammation alone may induce durably altered symbiosis – a rat model

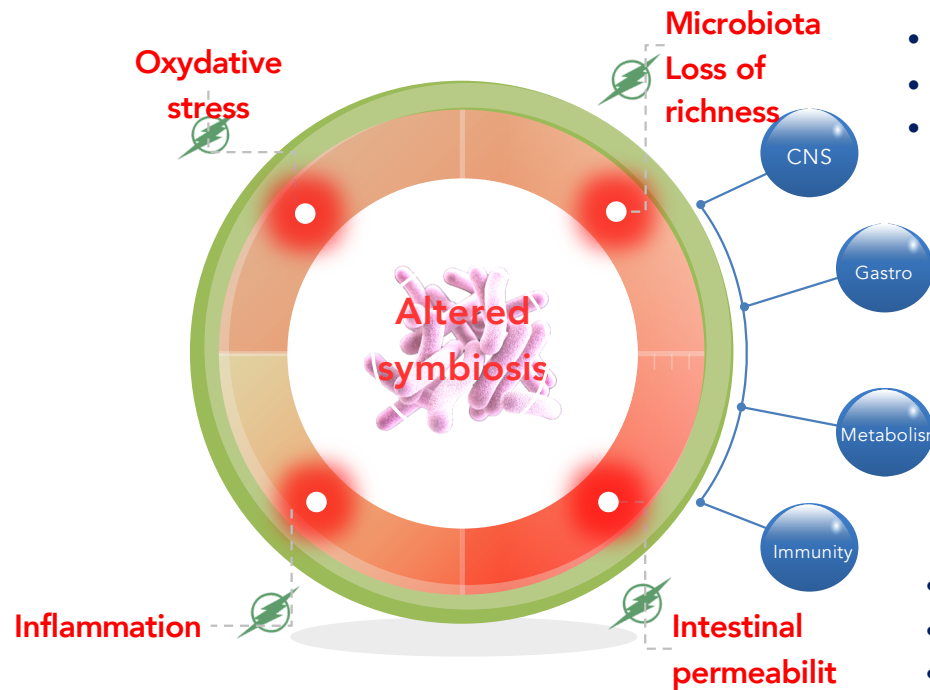


Altered host-microbes symbiosis in chronic conditions

with circular causalities

... at least
4 actionable
levers
for :

- diagnostic,
- prediction,
- prevention
- therapy



- Autism Spectrum Disorders
- Major Depressive Disorders
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- Cancer immunotherapy

Where nutrition targeted microbiota ...

Where medicine targeted symptoms and mainly inflammation...

... a change in paradigm is possible ; towards a personalized holistic approach

Doré *Thérapie* 2017

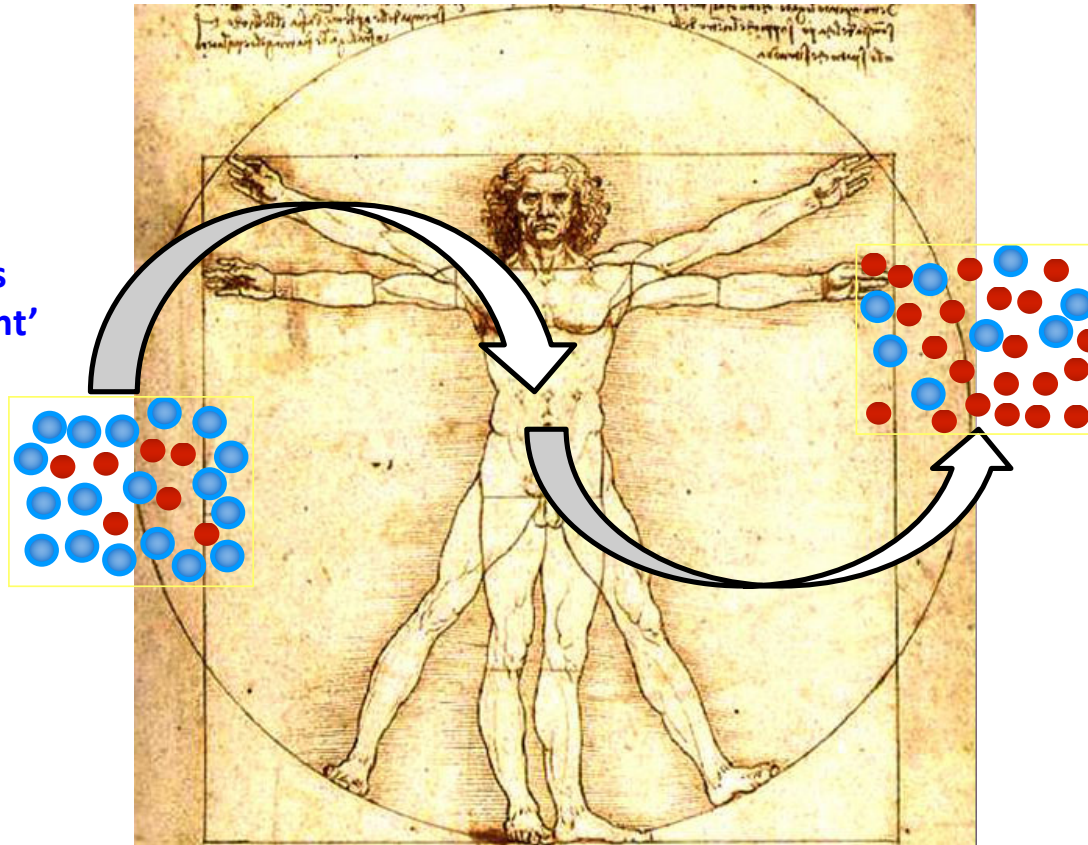
Van de Guchte *Microbiome* 2018

Van de Guchte *Microbiome* 2020

Symbiosis preservation / restoration

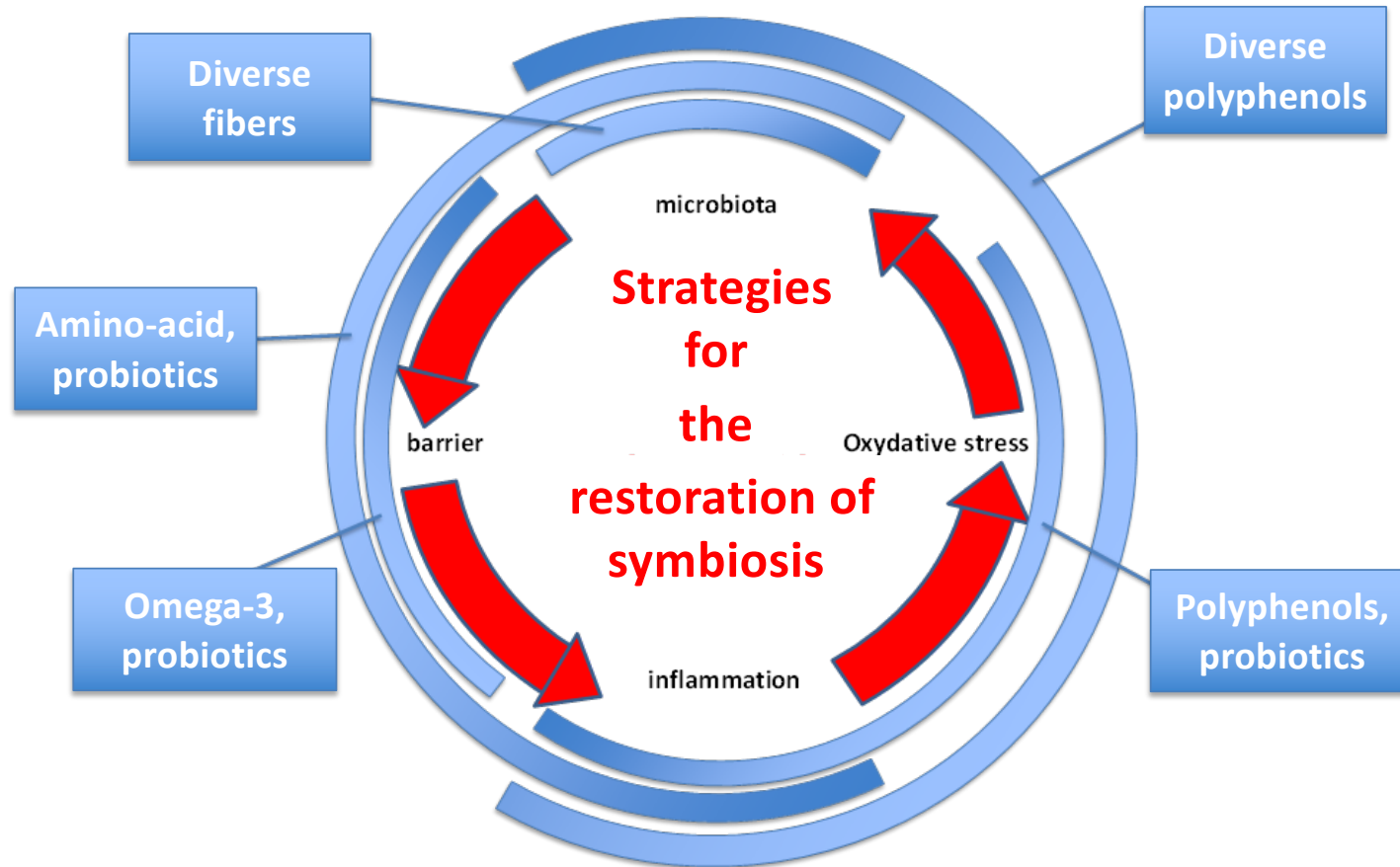
- Dietary ingredients
- Supplements including probiotics
- Intestinal 'transplant'

Health-prone microbiota



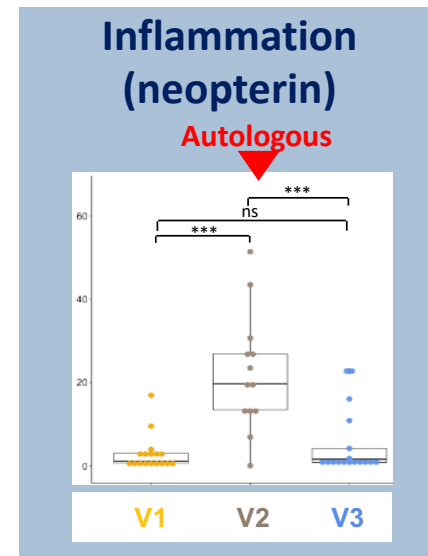
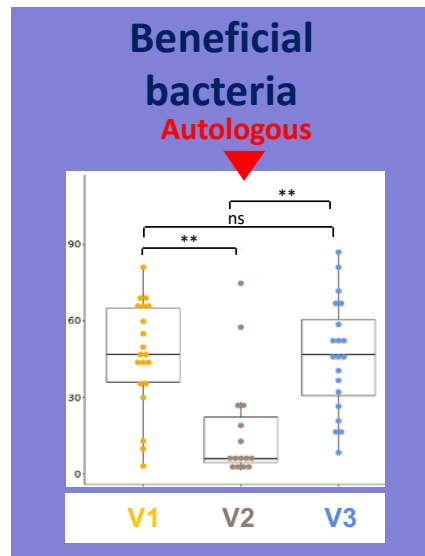
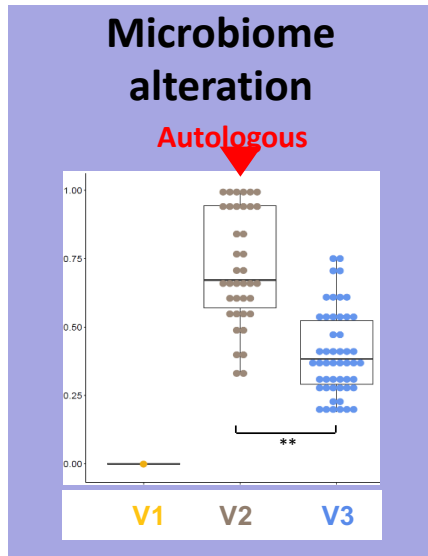
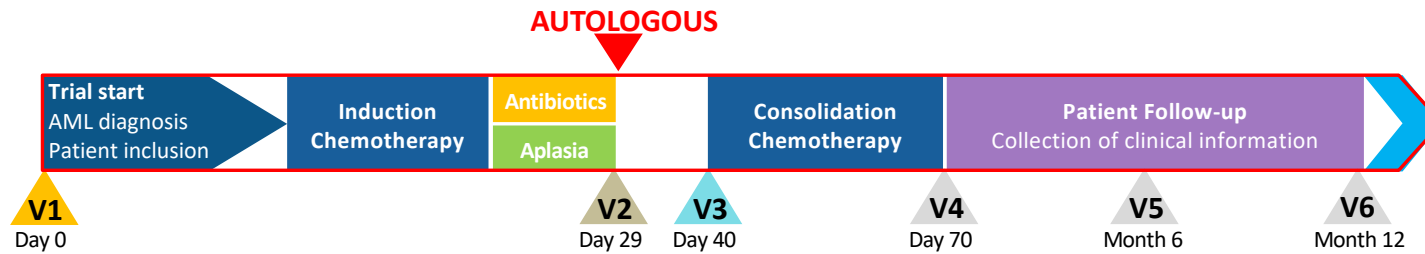
Risk-associated microbiota

Mitigating the risk of altered symbiosis using food-grade ingredients in a combinatorial approach



Correcting altered symbiosis using autologous fecal microbiota transfer

25 Acute Myeloid Leukemia patients administered a single autologous dose with 12 month follow up ([NCT02928523](#))

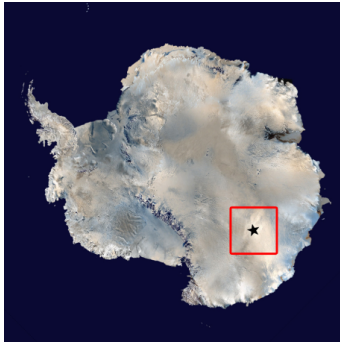


- **90%** recovery of Microbiota richness (Gene and Species level)
- Excellent safety profile with **84%** survival after one year

Dubuisson et al.
J Pharm Clin 2018

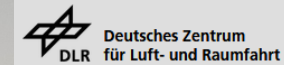
Mohty et al.
Blood 2018

Burz et al.
Sci Reports 2019



3500 m above sea level
1000 km off the coast

Antarctic CONCORDIA station



Project ICELAND: Immune and microbiome Changes in Environments with Limited Antigen Diversity (WO 17/18)



**12-13 participants for one year in Antarctica.
9 months locked on Concordia.**



**... During 3 winterover periods: doubleblind,
placebo- controlled randomized study *with BL1714* !**



Bifidobacterium longum 1714™ Strain Modulates Brain Activity of Healthy Volunteers During Social Stress

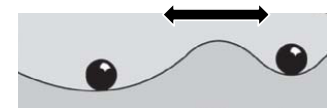
Huiying Wang, PhD^{1,2,3}, Christoph Braun, PhD^{2,4}, Eileen F. Murphy, PhD⁵ and Paul Enck, PhD¹

Am J Gastroenterol 2019;114:1152-1162. <https://doi.org/10.14309/ajg.000000000000203>



Take home messages :

- **dysbiosis is an altered state of host-microbes symbiosis**, which may be promoted by numerous triggers under space flight conditions.
- **new paradigm : a multi-target modulation should be considered** for personalized prevention and restoration countermeasures
- **Implications for early warning signals identification:** predictive markers of alteration and monitoring of countermeasures efficacy should combine microbiome and host parameters
- **Implications for the design of personalized countermeasures:** restoration or protection of host-microbes symbiosis will involve a combinatorial approach targeting gut permeability, inflammation, oxidative stress and microbiome, or rely on autologous intestinal microbiota restoration.





MELISSA



Micalis
Mico-robotique de l'AMT - installations au service de la santé

metagenopolis
mgps.eu



Thanks for your attention,
& take care of your symbiosis



joel.dore@inrae.fr

Micalis & MetaGenoPolis, INRAE Jouy-en-Josas, France