

top ten

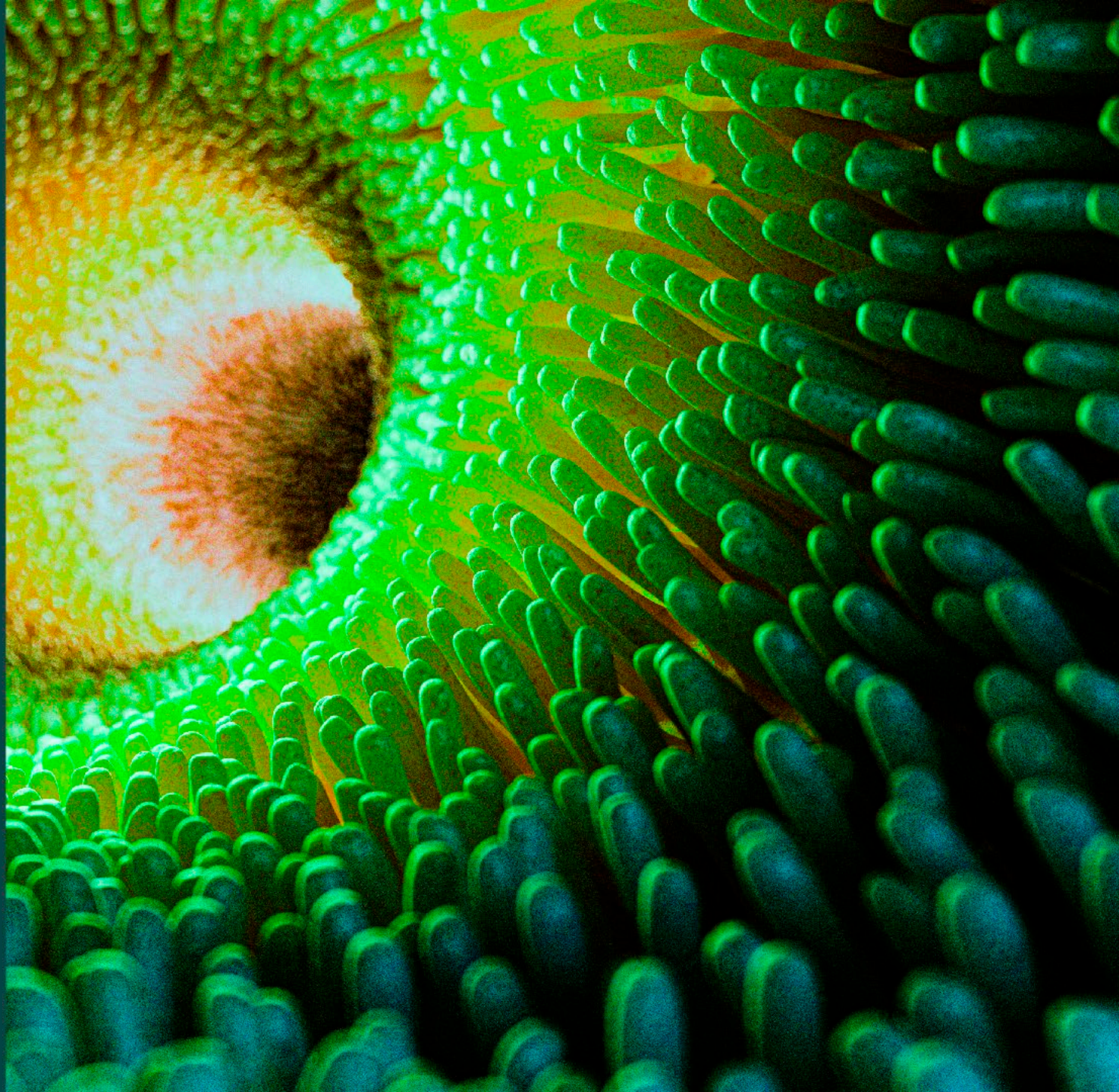
in gastroenterologia

14[^] EDIZIONE

24-25 NOVEMBRE 2023

BERGAMO

HOTEL EXCELSIOR SAN MARCO
Piazza della Repubblica, 6

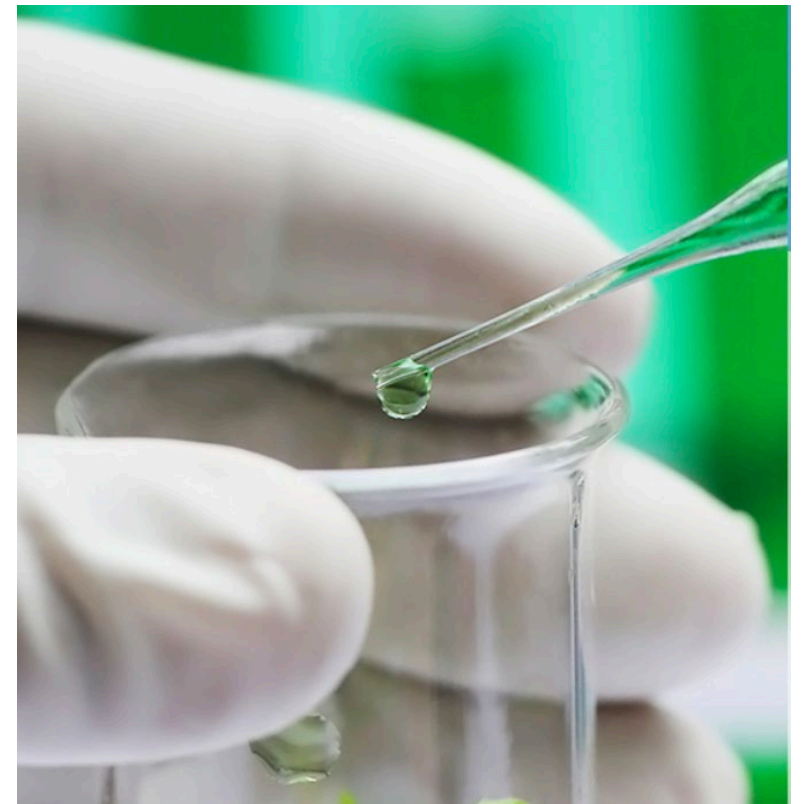


LA TERAPIA POSTBIOTICA



Sara Carloni, PhD

Sara.carloni@hunimed.eu
Humanitas University

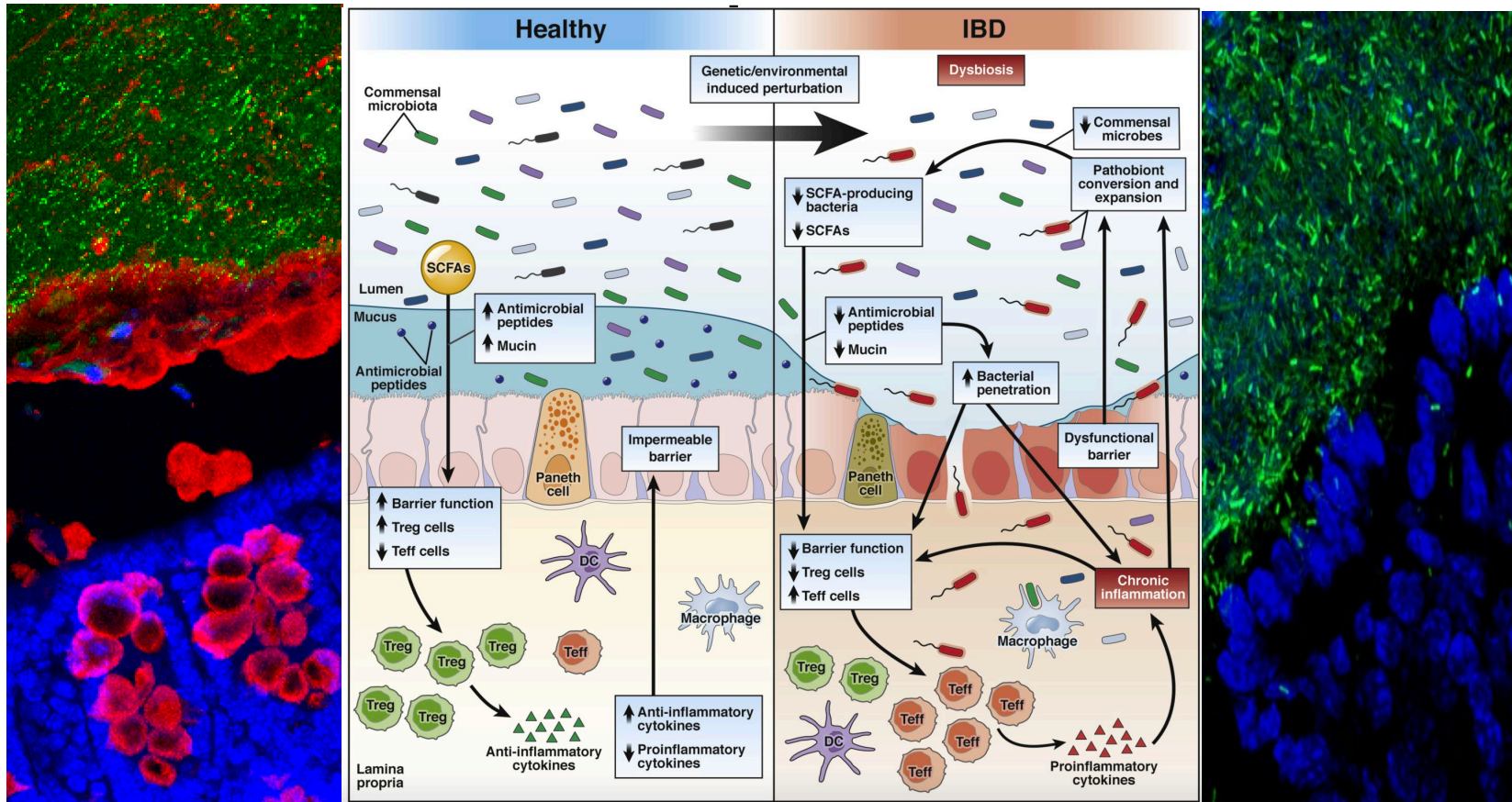


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Disclosure

- Research support: Postbiotica srl

Coinvolgimento della barriera mucosale nelle malattie infiammatorie intestinali (IBD)



Nuclei epithelial cells
Mucine (mucous)
Bacteria

Mirae Lee et al., Gastroenterology, 2021

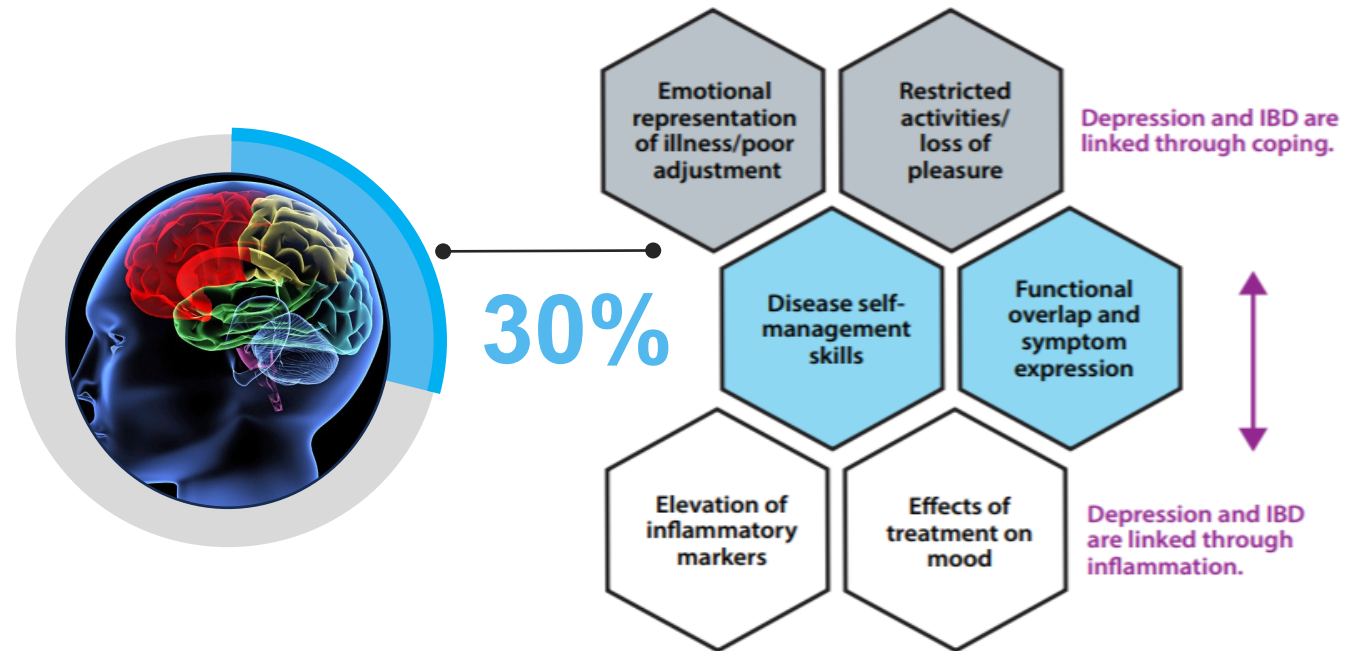
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Manifestazioni Extra-intestinali in pazienti IBD

"La depressione nei pazienti con malattie infiammatorie intestinali è considerata una conseguenza per far fronte alla cronicità del disturbo."



Siddharth et al., *Inflammatory Bowel Diseases* (2013)



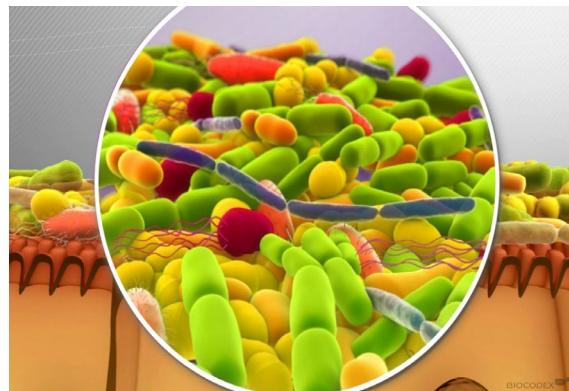
Keefe et al., *Gastroenterol. Hepatol.* 2017

Strategie per modulare il microbiota



PREBIOTIC

Prebiotics are substances (non-digestible fiber) that induce the growth or activity of microorganisms that contribute to the well-being of their host.



PROBIOTIC

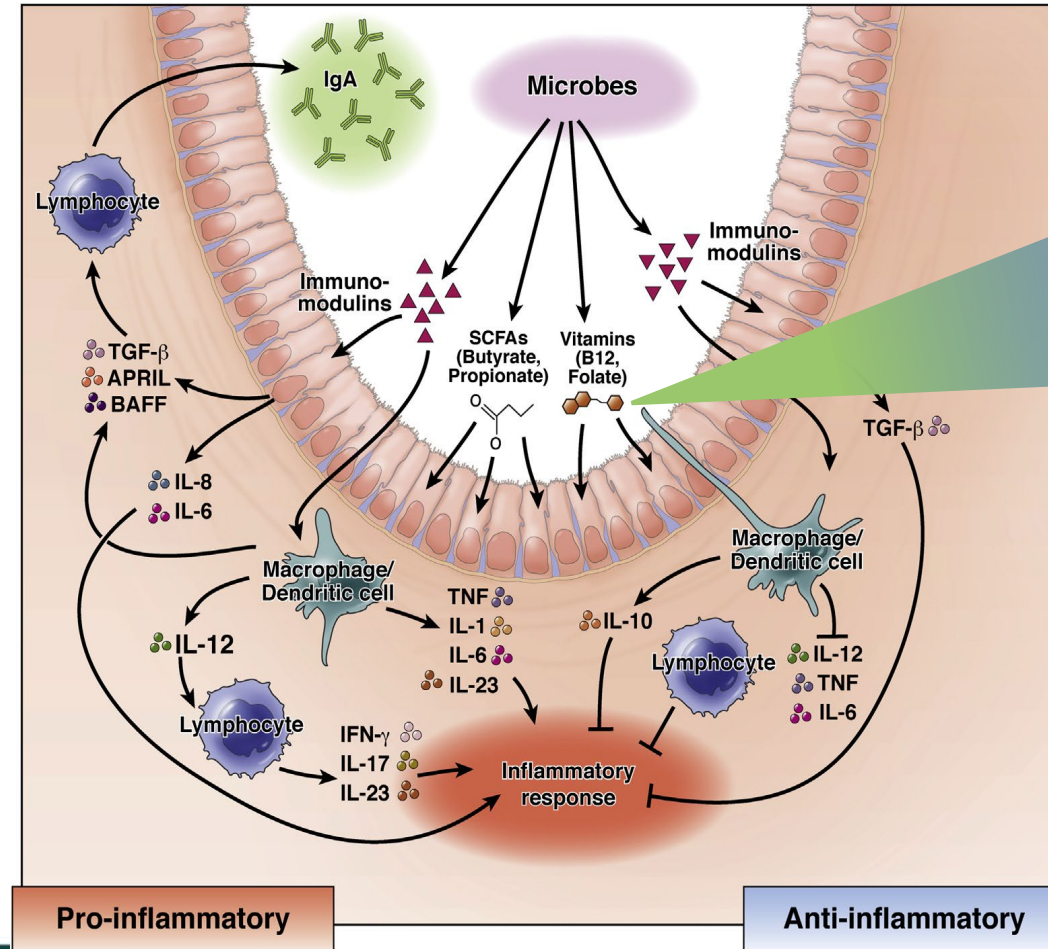
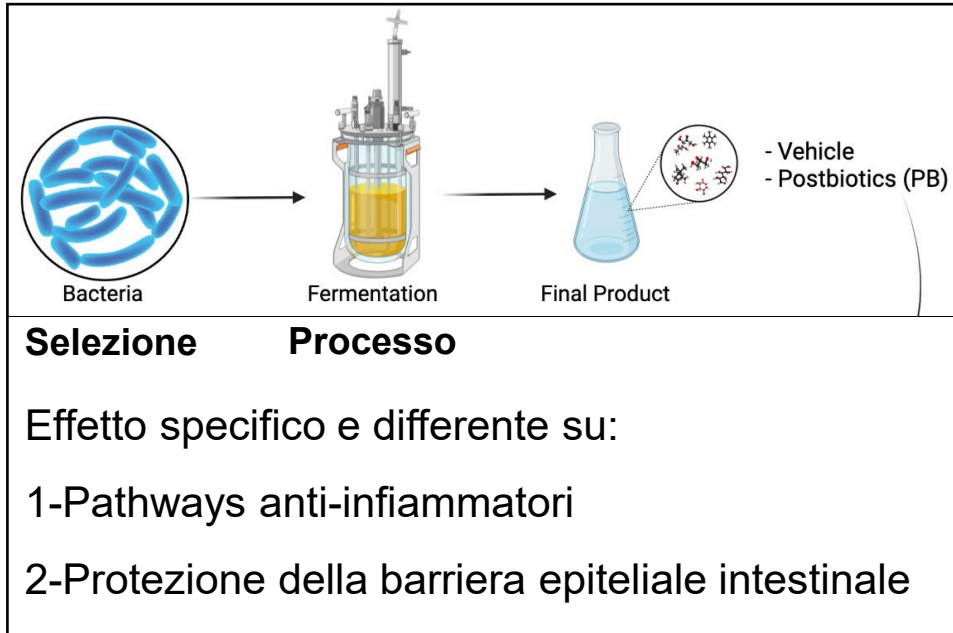
Probiotics are "live" microorganisms which, when administered in adequate amounts, confer a health benefit on the host"
FAO/WHO



POSTBIOTIC

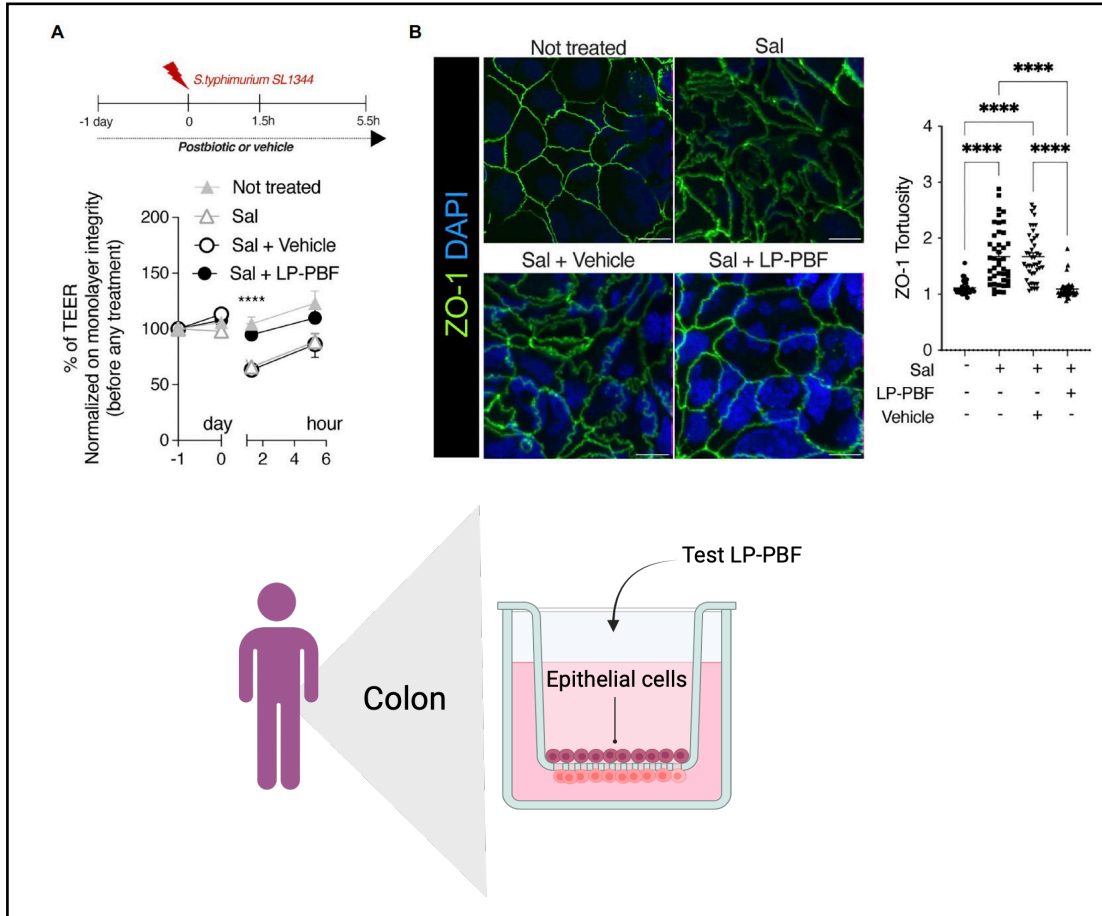
Postbiotics are substances generated by probiotics metabolism, key factors in maintaining long-term health benefit

Postbiotici: Componenti chiave dell'interazione tra ospite e microbi



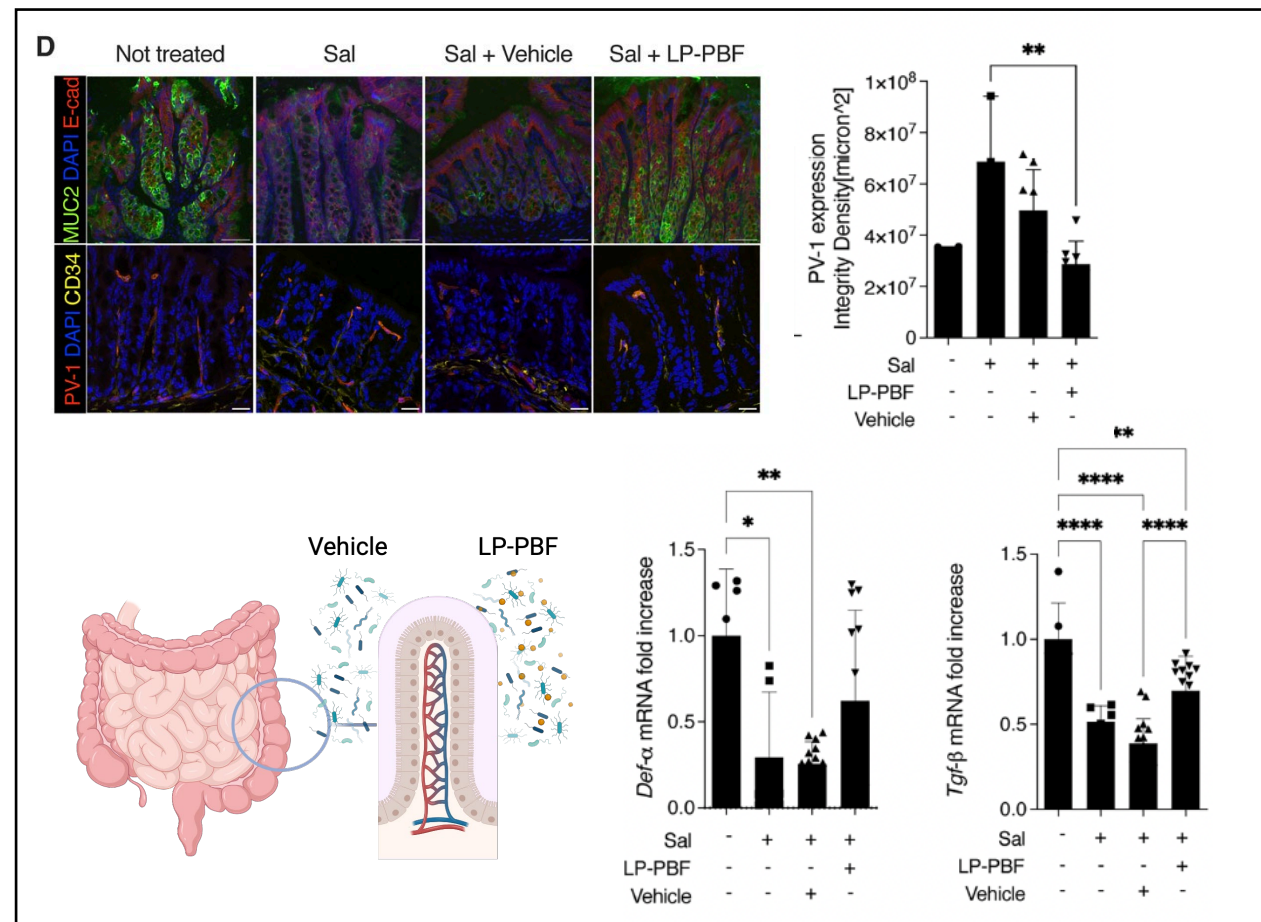
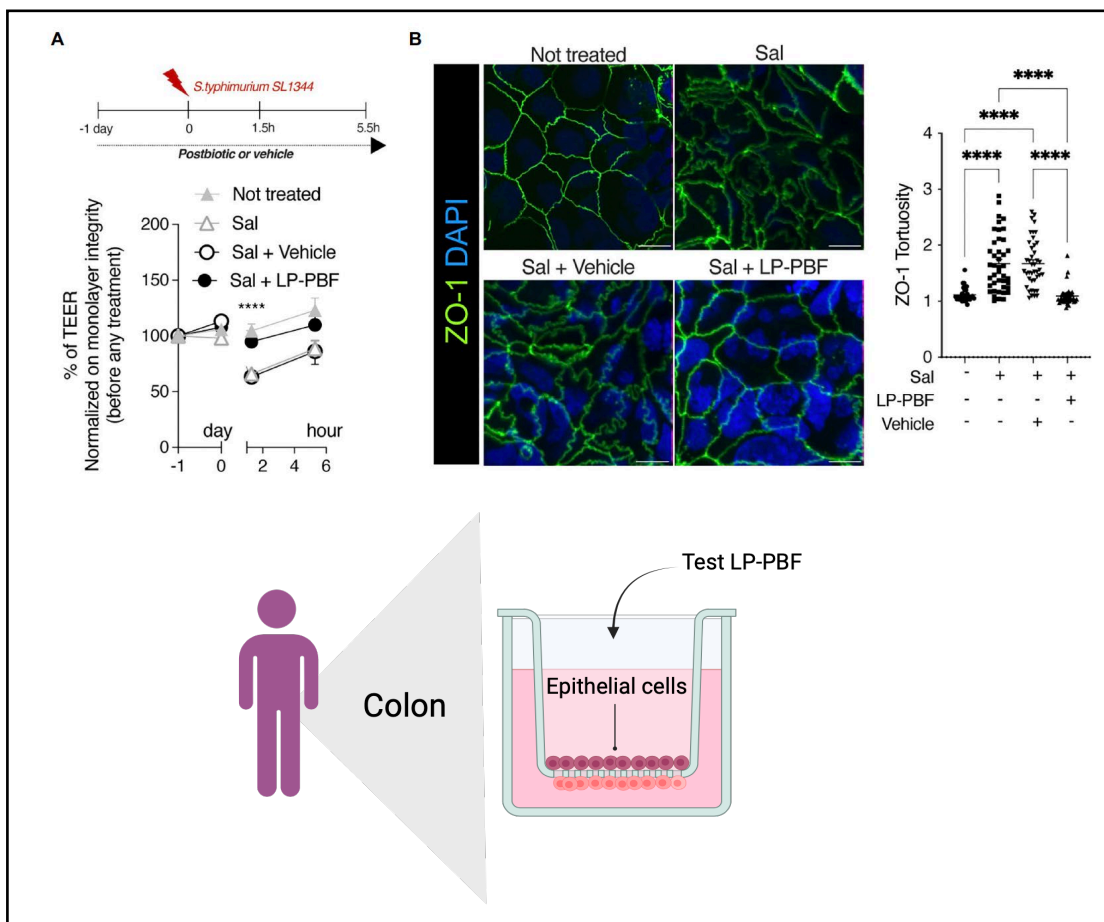
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Il postbiotico derivato da *Lactobacillus paracasei* CNCM I-5220 protegge dall'insorgenza della permeabilità intestinale



Algieri, Tanaskovic et al. Frontiers Microbiology 2023

Il postbiotico derivato da *Lactobacillus paracasei* CNCM I-5220 protegge dall'insorgenza della permeabilità intestinale

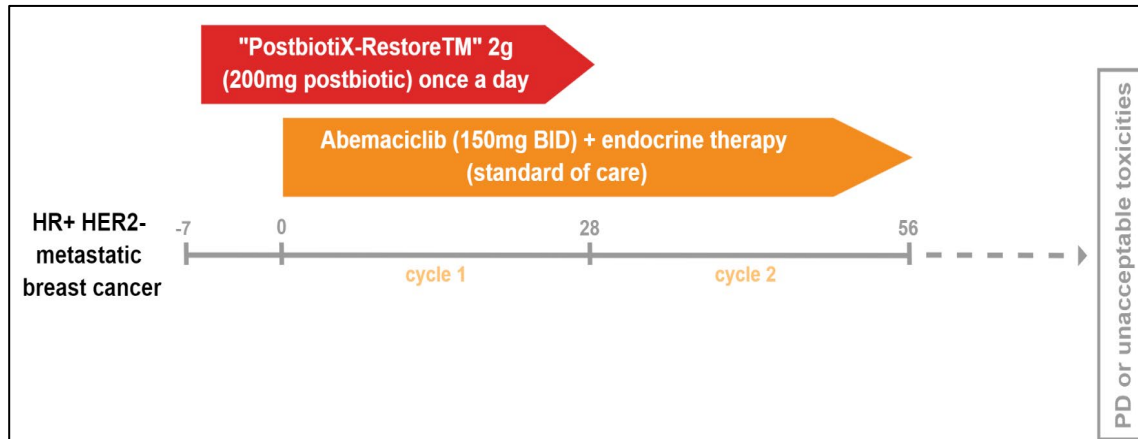


Algieri, Tanaskovic et al. Frontiers Microbiology 2023

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La terapia postbiotica in profilassi stabilizza la diarrea indotta da ademaciclin: dati preliminari

- Abemaciclib è un **CDK 4/6 inhibitor** for the treatment of HR+/HER2- advanced breast cancer;
- **Abemaciclib-induced diarrhea** can affect patients' quality of life and cause treatment discontinuation and/or dose modifications
- Diarrhea could be induced by **microbiota** alterations



Clinical Study:

- A prospective, observational, open-label study planned to enroll 30 HR+/HER2- advanced breast cancer patients at IRCCS Humanitas Research Hospital, Italy;
 - The **primary endpoint** was the **median time to diarrhea onset**;
 - The **secondary objectives** were **incidence, severity, and duration** of diarrhea.

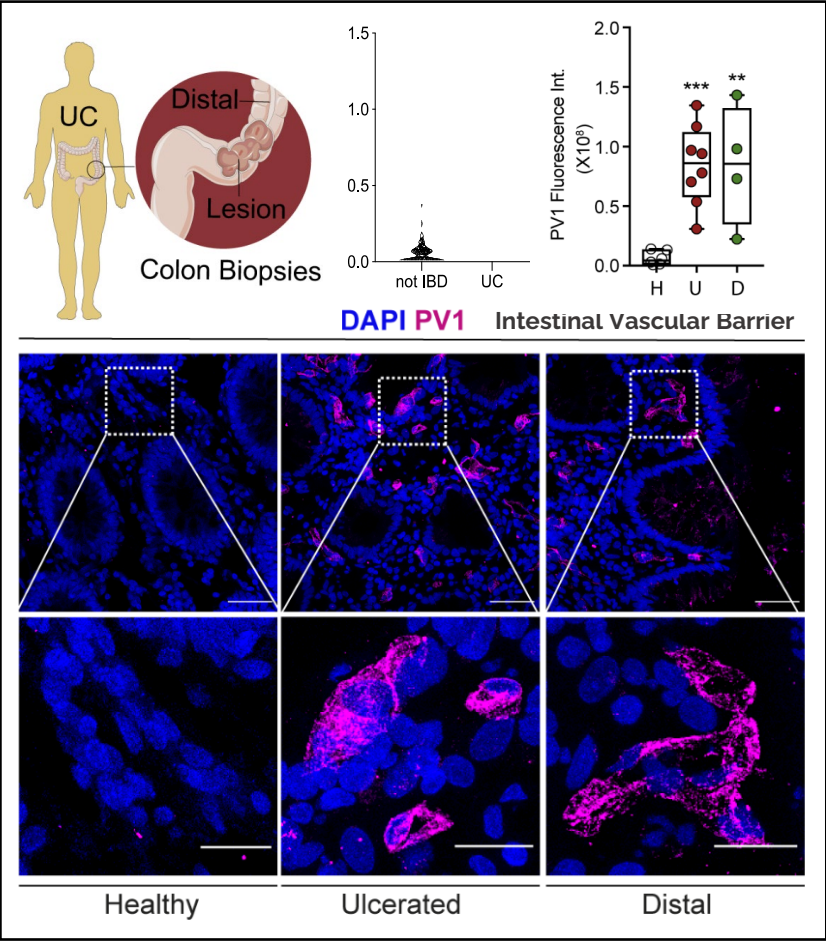
Regularization of bowel movements (frequency and consistency) in the first week of PostbioticX-RestoreTM alone;

Compared to the Monarch1 trial³, we observed a **lower degree of toxicity**, no cases of severe diarrhea (**G3/G4** 0 vs 20%), **G1** (90% vs 42%) and **G2** (10% vs 30%), and a **shorter duration of diarrhea (median time 6 days)**.

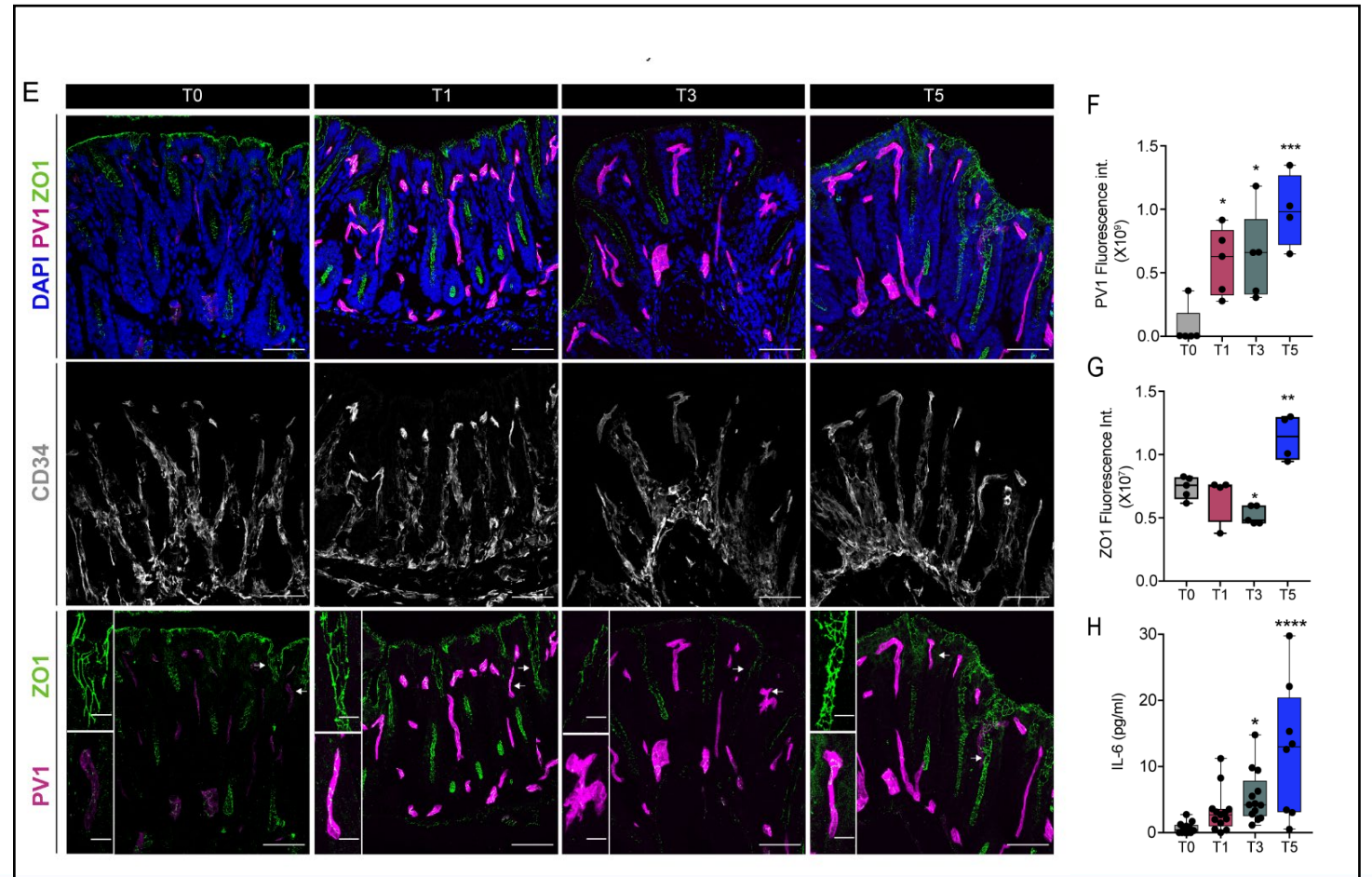
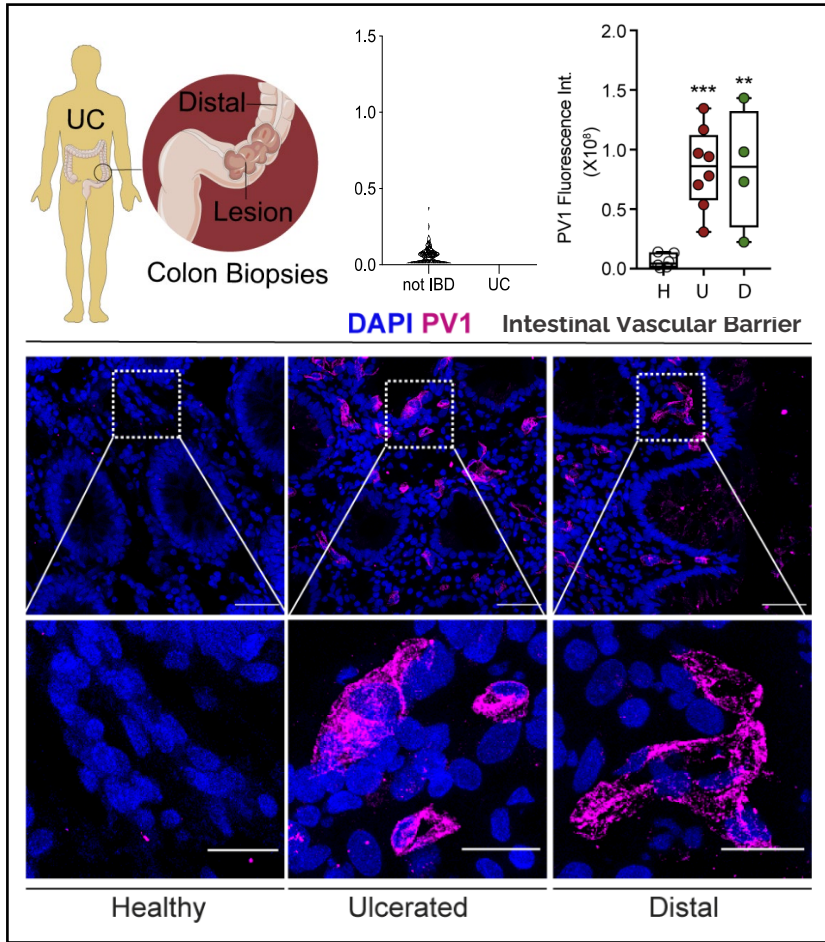
No case of **treatment discontinuation** due to diarrhea.

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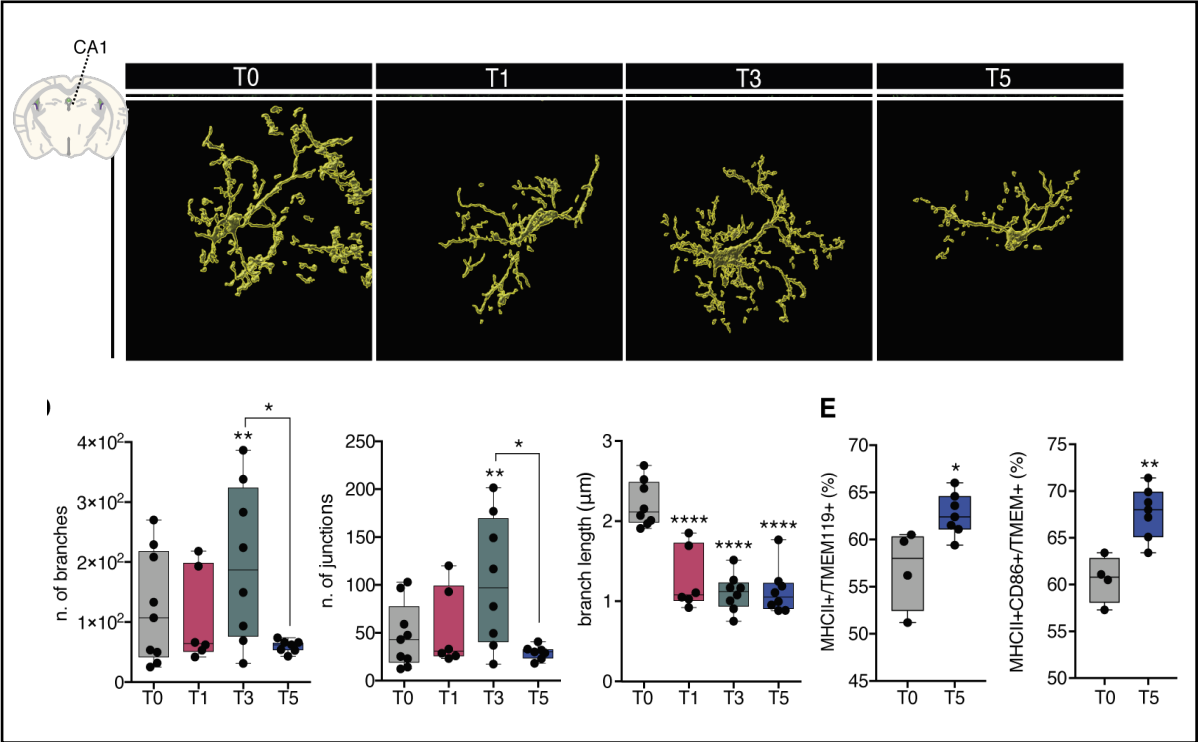
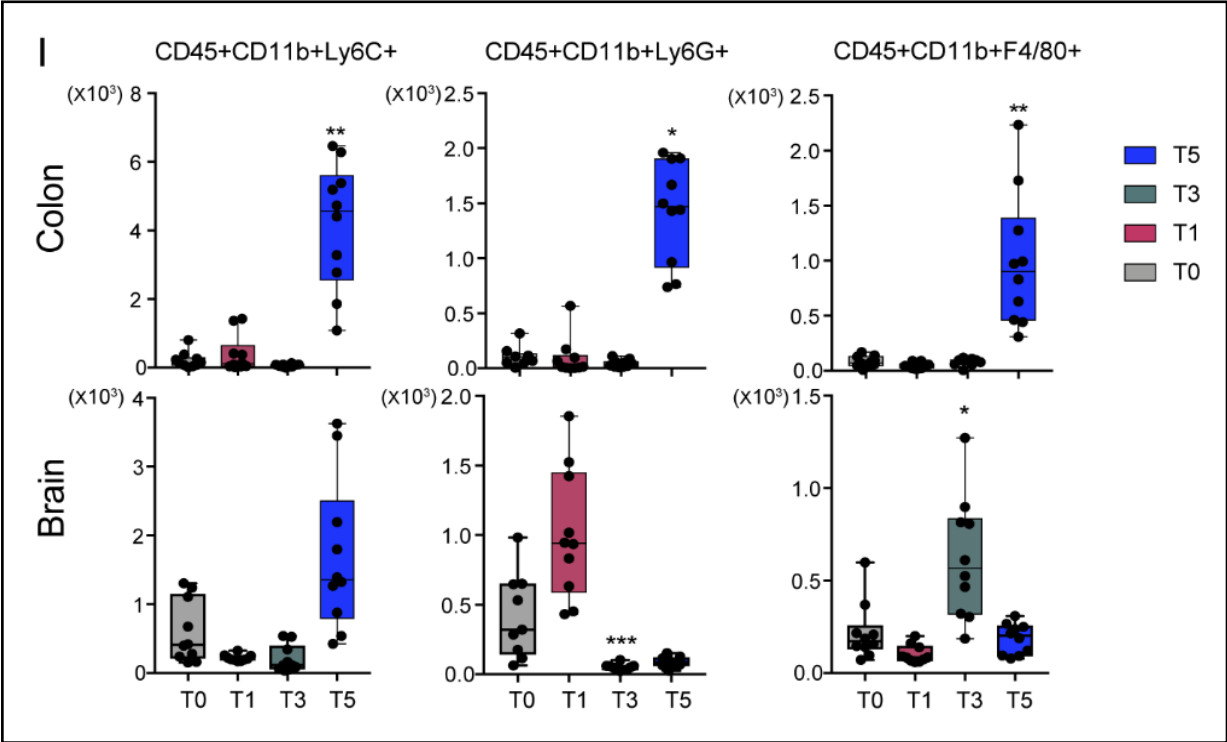
La barriera intestinale risulta essere compromessa in pazienti e modelli UC



La barriera intestinale risulta essere compromessa in pazienti e modelli UC

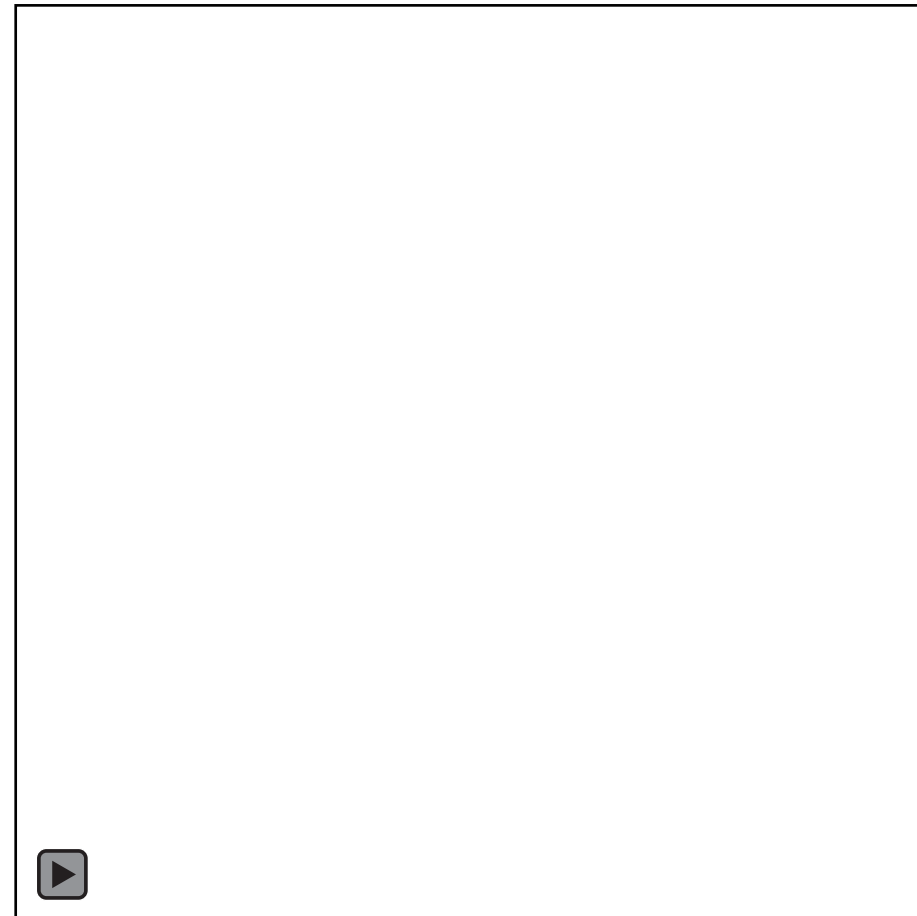
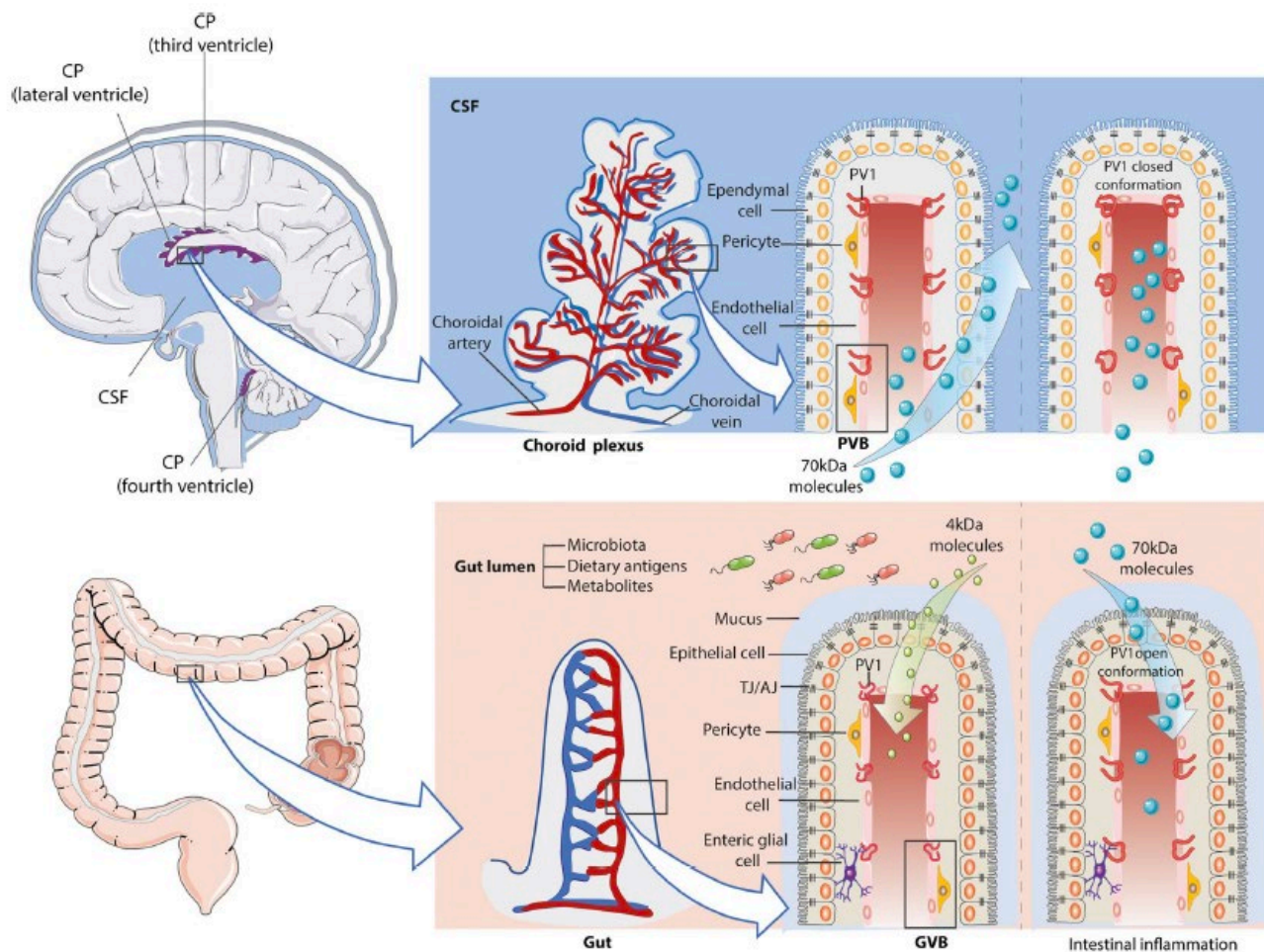


L'infiammazione intestinale si traduce in neuro-infiammazione

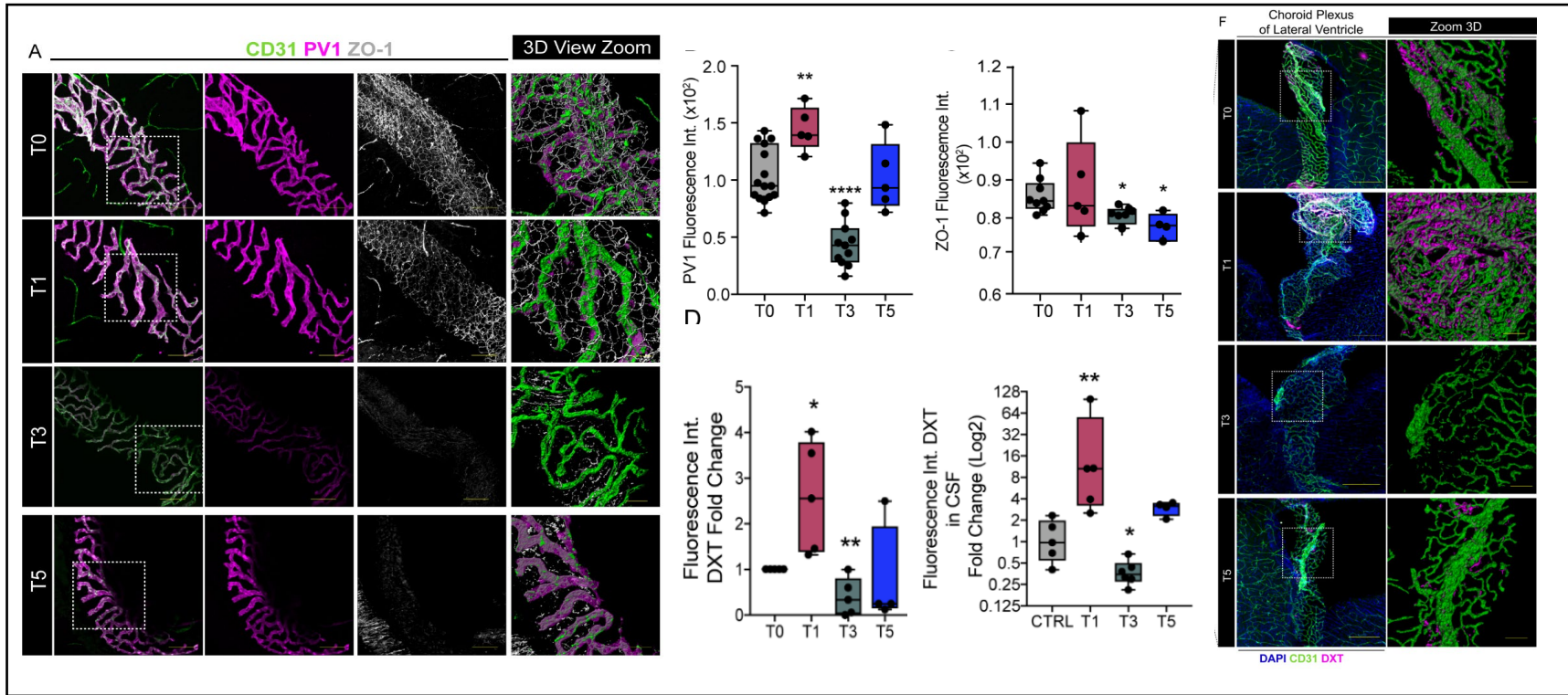
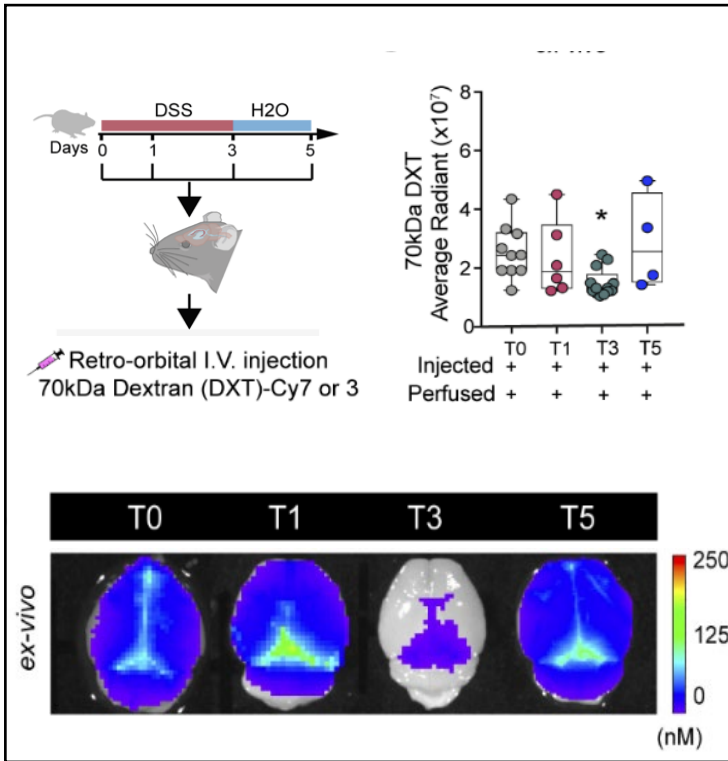


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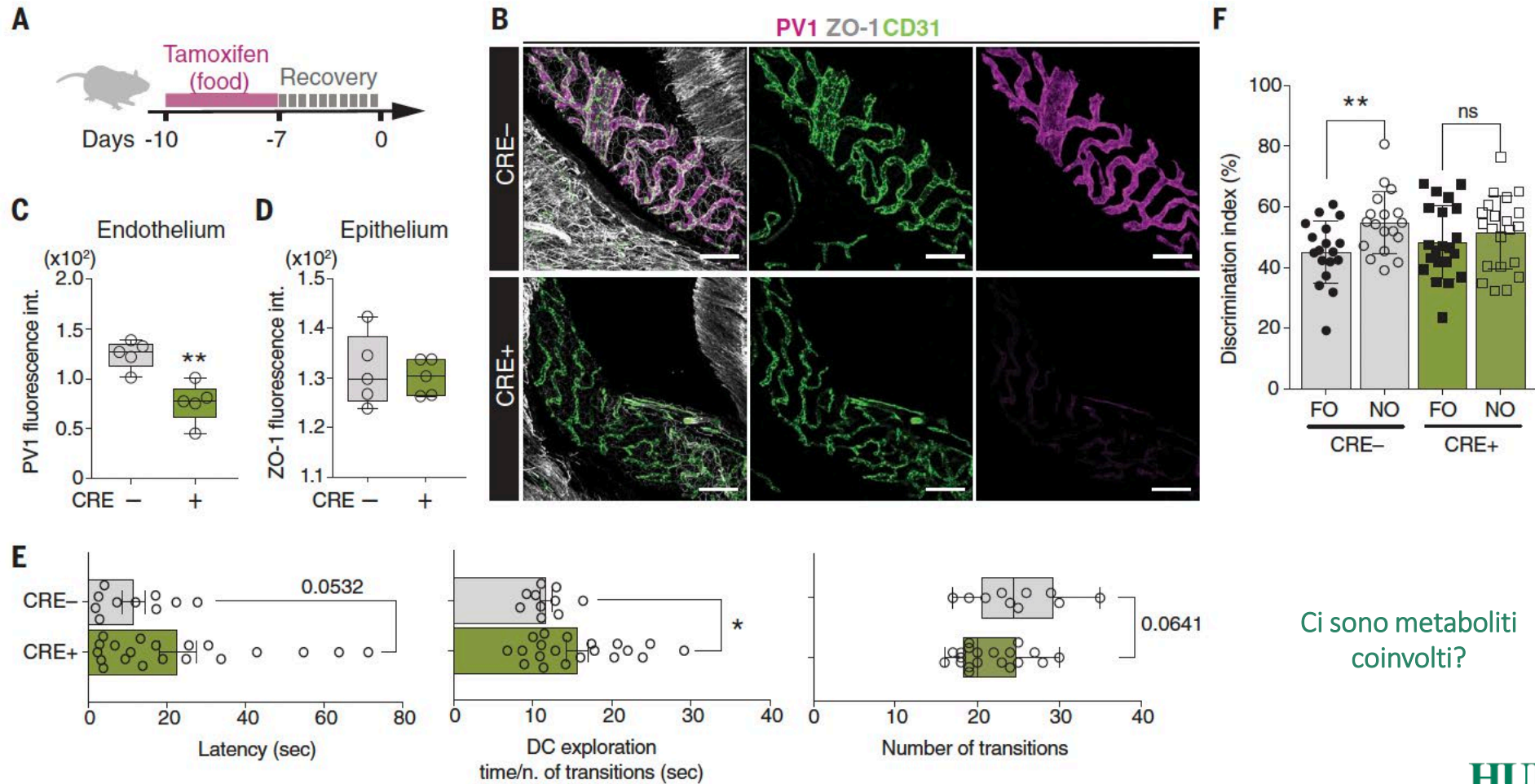
Una nuova barriera collega l'asse intestinale-circolatorio-cerebrale: la barriera vascolare del plesso coroideo (PVB)



La PVB nel modello di UC risulta chiusa



La chiusura della PVB induce uno stato ansioso depressivo

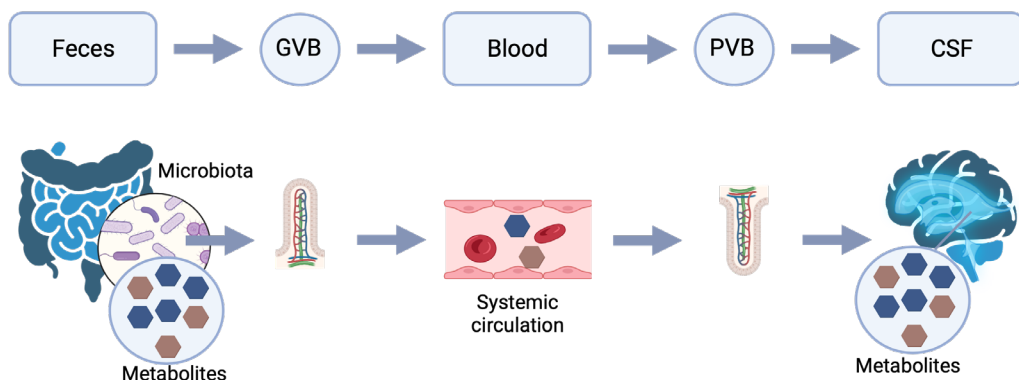
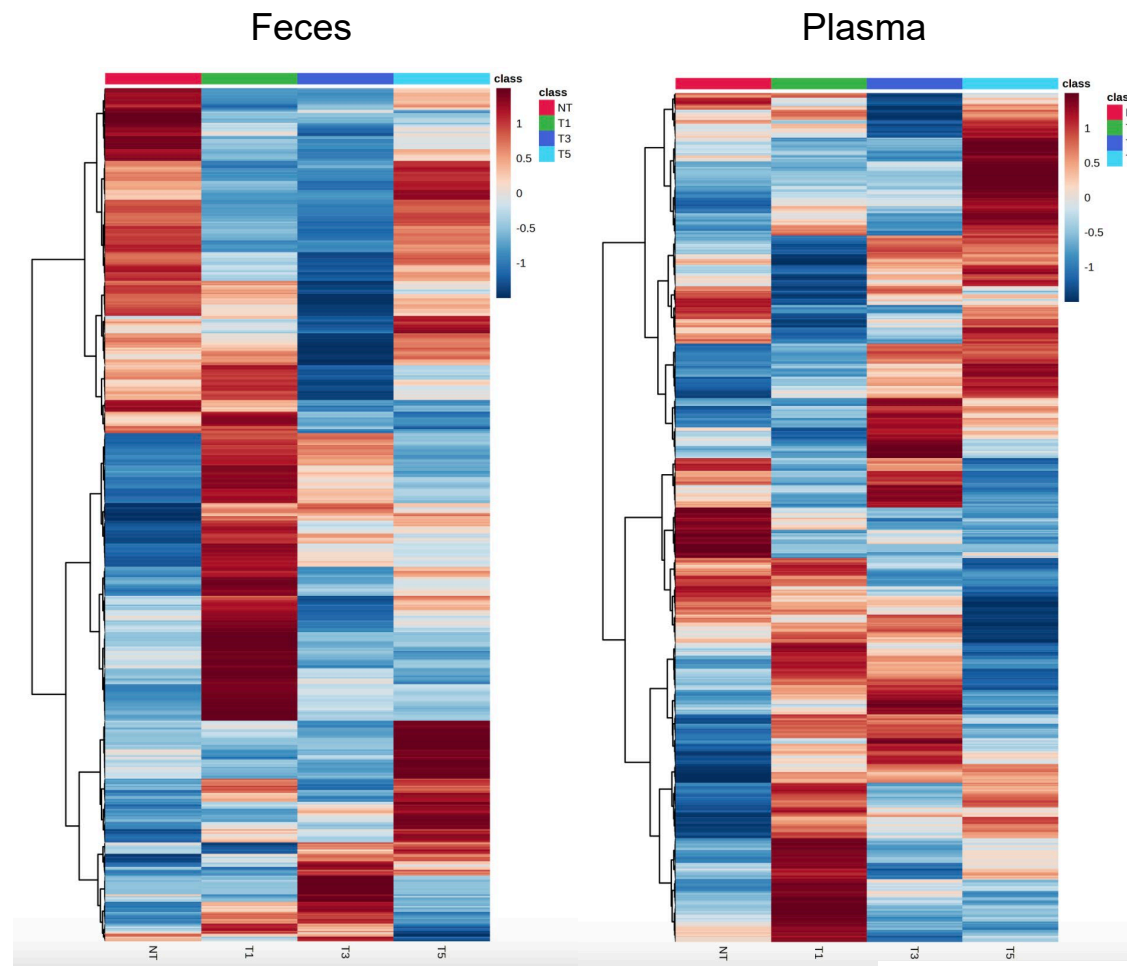
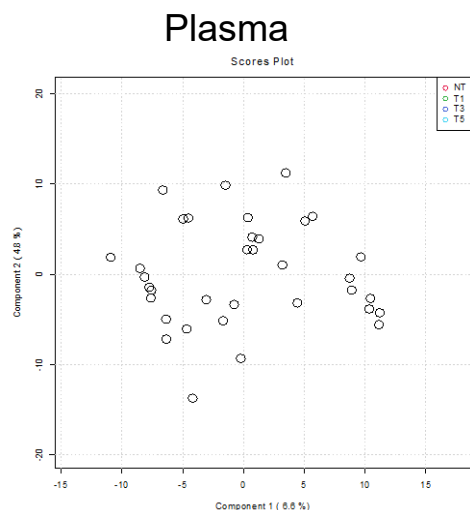
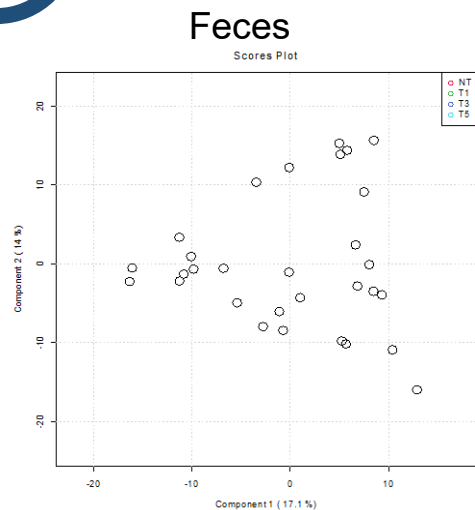


Ci sono metaboliti coinvolti?

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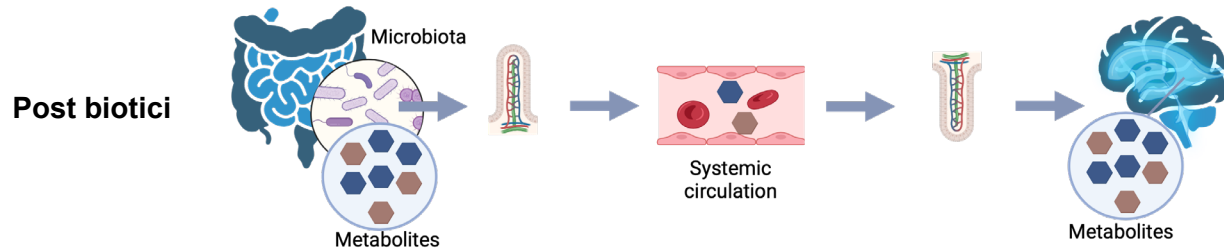
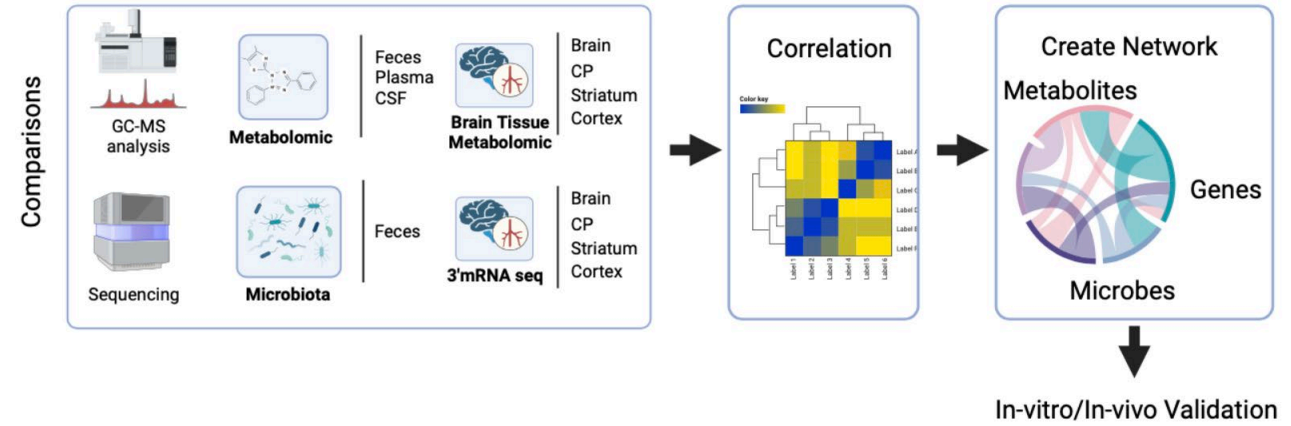
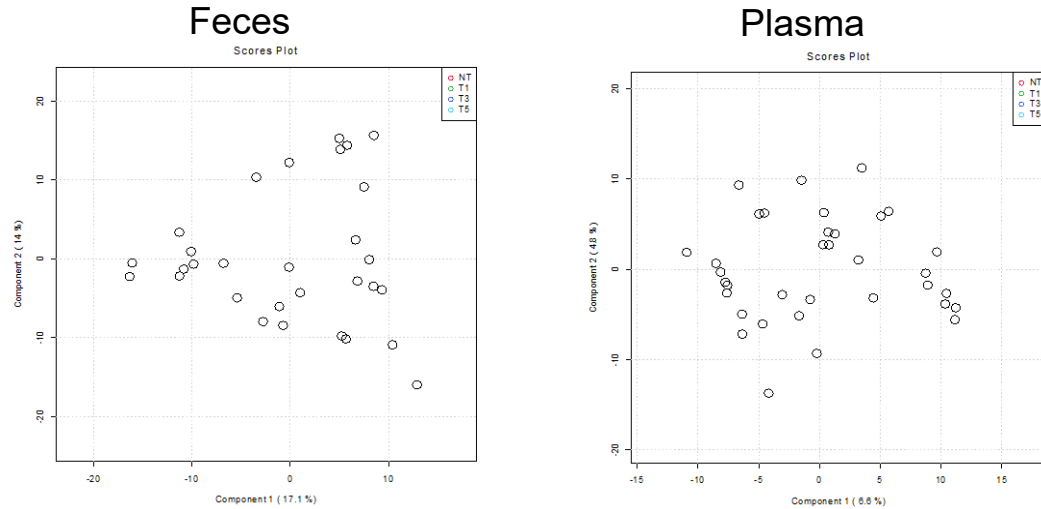
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Nel modello di UC si ha una signature metabolica intestinale e circolatoria



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Nel modello di UC si ha una signature metabolica di derivazione batterica intestinale e circolatoria



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Identificazione delle specie batteriche commensali associate alla risposta anti-PD1

CANCER IMMUNOTHERAPY

Gut microbiome modulates response to anti-PD-1 immunotherapy in melanoma patients

V. Gopalakrishnan,^{1,2*} C. N. Spencer,^{2,3*} L. Nezi,^{3*} A. Reuben,¹ M. C. Andrews,¹

Ruminococcaceae
Bacteroides

CANCER IMMUNOTHERAPY

Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors

Bertrand Routy,^{1,2,3} Emmanuelle Le Chatelier,⁴ Lisa Derosa,^{1,2,3}

A. muciniphila

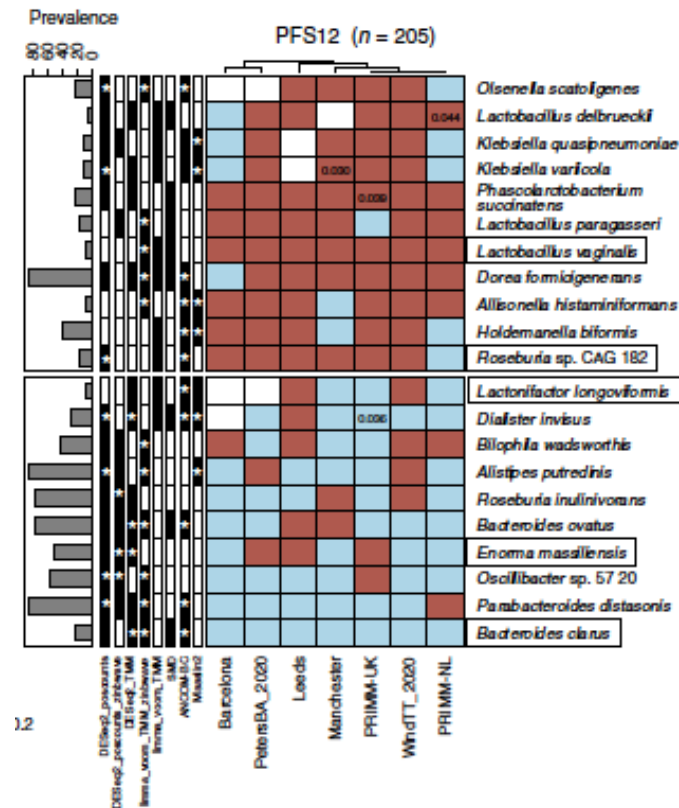
CANCER IMMUNOTHERAPY

The commensal microbiome is associated with anti-PD-1 efficacy in metastatic melanoma patients

Vyara Matson,^{1*} Jessica Fessler,^{1*} Riyue Bao,^{2,3*} Tara Chongsuwat,⁴ Yuanyuan Zha,⁴

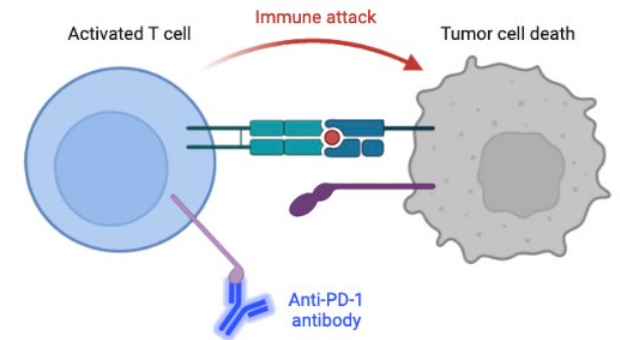
B. longum

Ci sono metaboliti coinvolti?

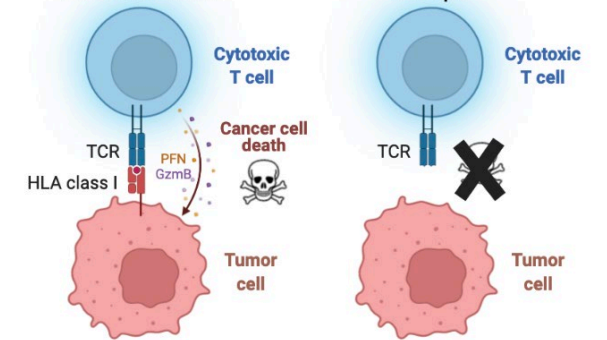


Lee et al. Nature Medicine 2023
www.nature.com/naturemedicine

Anti-PD-1 antibodies permit T cell activation



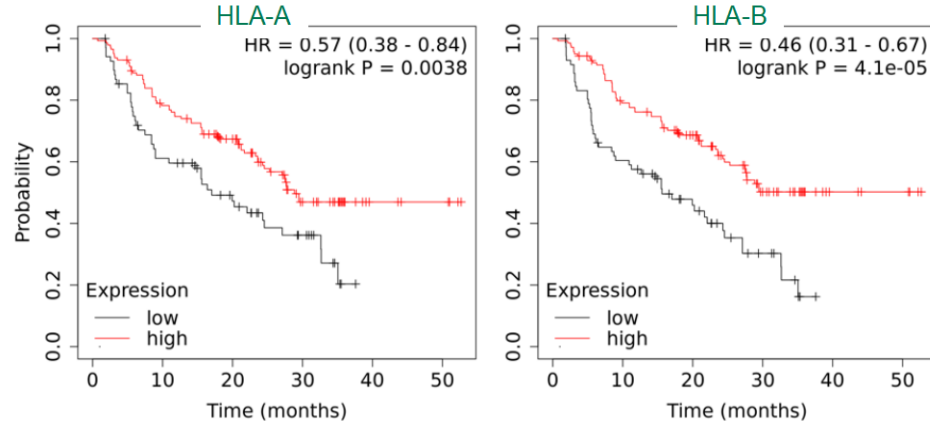
T cell cytotoxicity relies on proper presentation of peptides on HLA class I



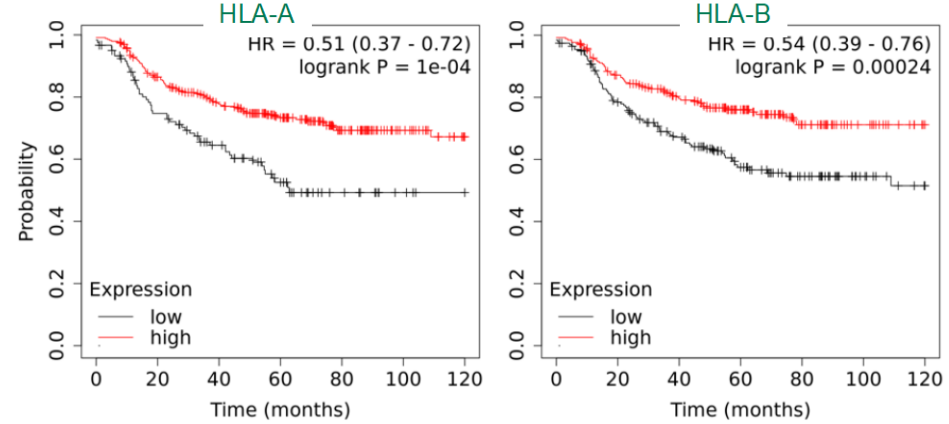
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La risposta dei pazienti oncologici dipende dall'espressione di HLA

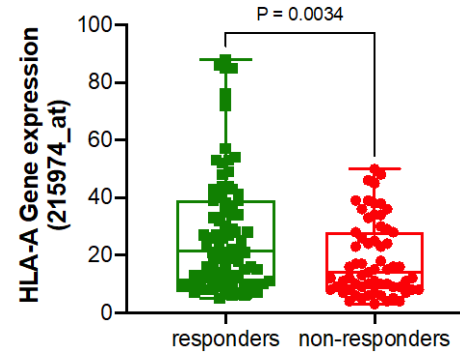
Melanoma – anti-PD-1 checkpoint inhibitors



Breast cancer – SoC chemotherapy

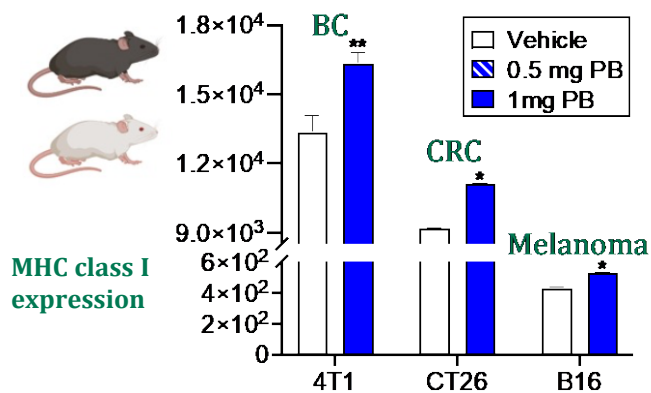
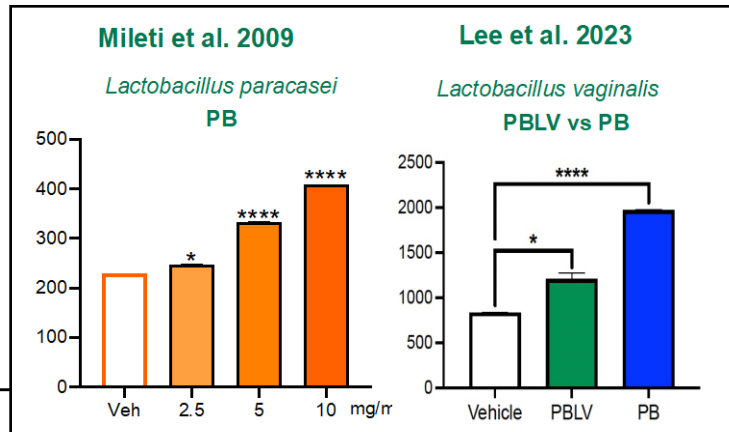
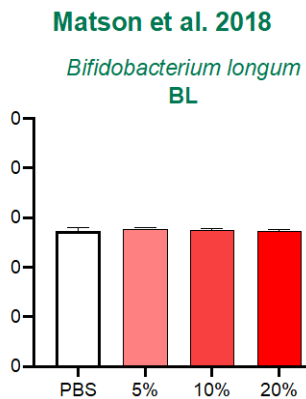
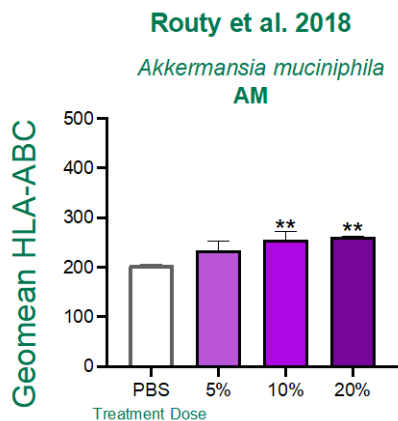


Colorectal cancer – SoC chemotherapy



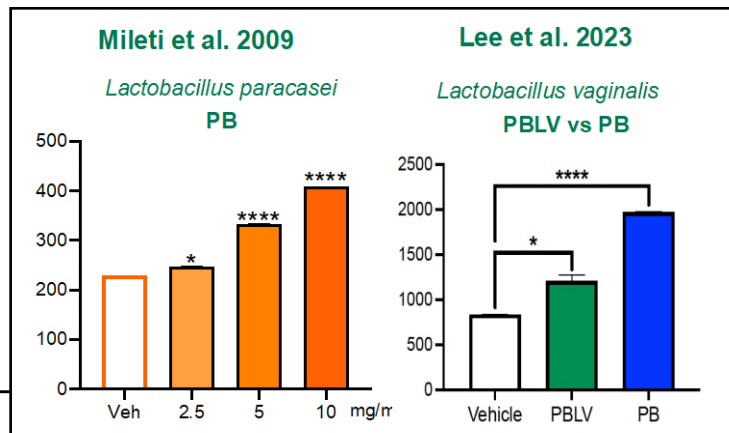
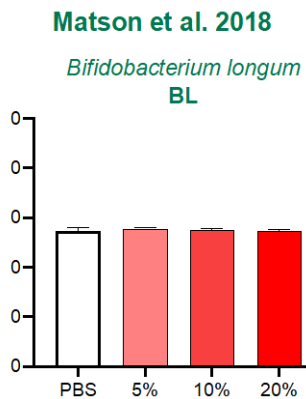
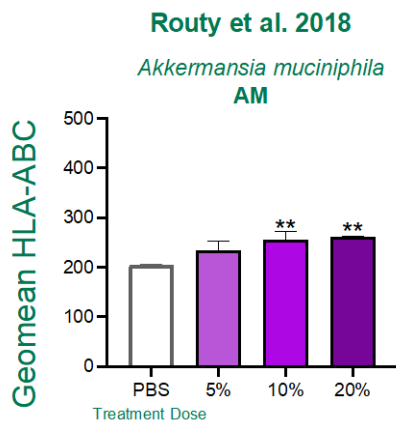
Effetti diversi sull'espressione di HLA di classe I con l'uso di postbiotici provenienti da differenti ceppi batterici

SK-BR-3 breast cancer cell line

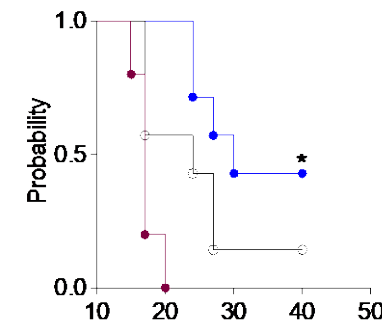
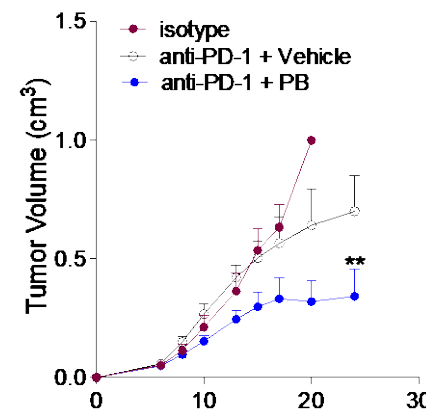
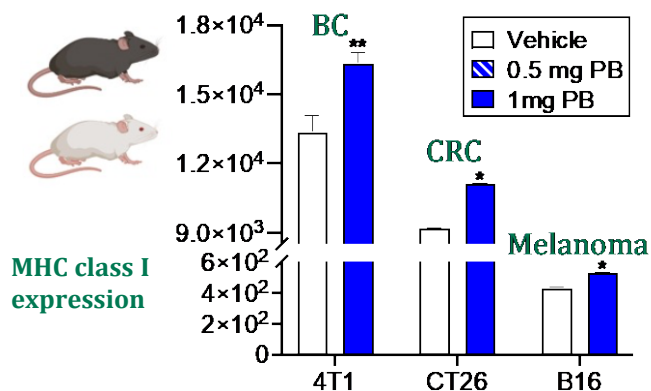
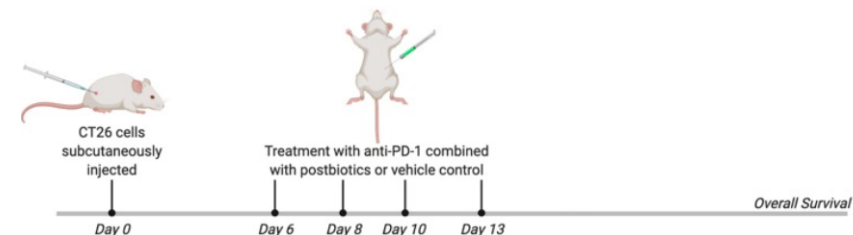


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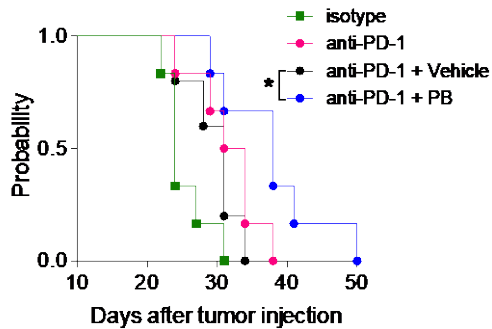
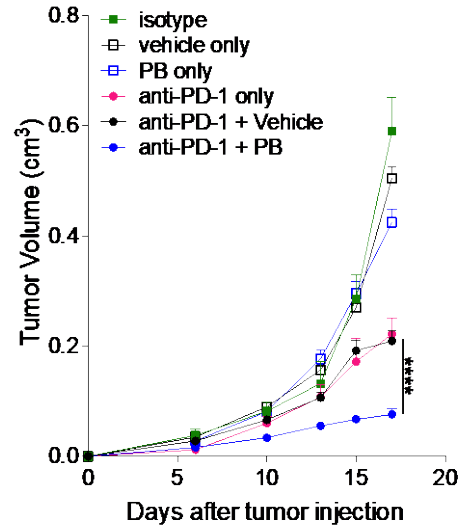


Modello di CRC CT26: Il trattamento con anti-PD-1 combinato con postbiotici controlla la crescita tumorale e prolunga la sopravvivenza

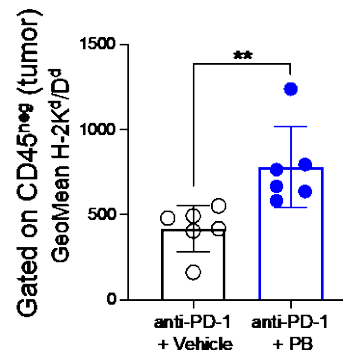
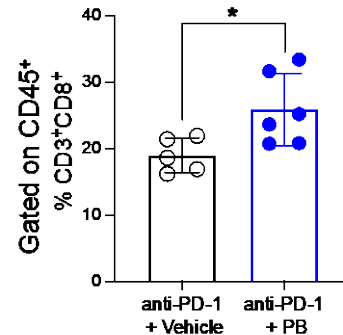


Modello 4T1 TNBC: L'assunzione orale di postbiotici incrementa l'efficacia del trattamento anti PD-1

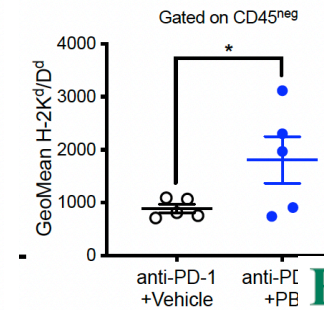
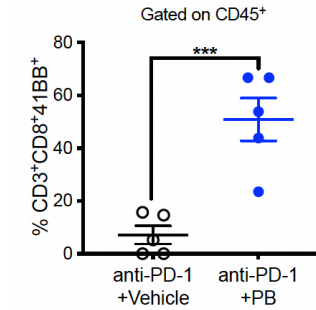
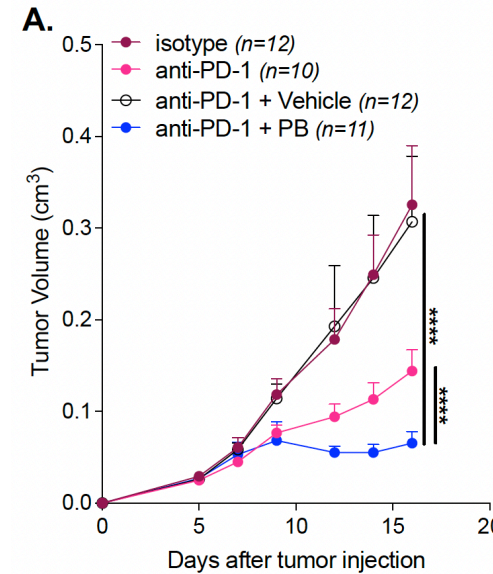
Anti-PD-1 combined with postbiotics controls tumor growth and upregulates MHC class I



Tumors processed *ex-vivo*



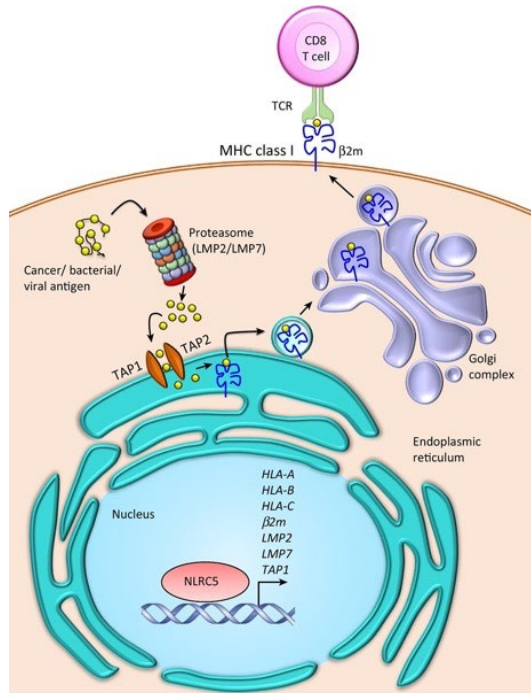
Anti-PD-1 combined with with ORAL postbiotics controlled tumor growth and induced HLA I upregulation



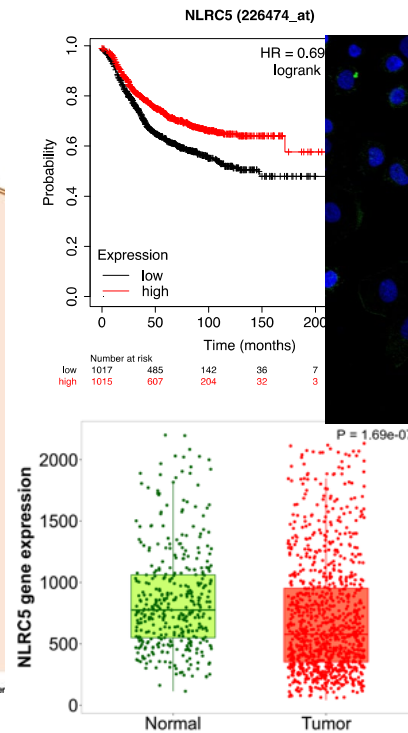
Il trattamento con postbiotici upregola l'espressione di NLRC5 ed NFkB

La risposta dei pazienti oncologici dipende dall'espressione di HLA

Breast Cancer



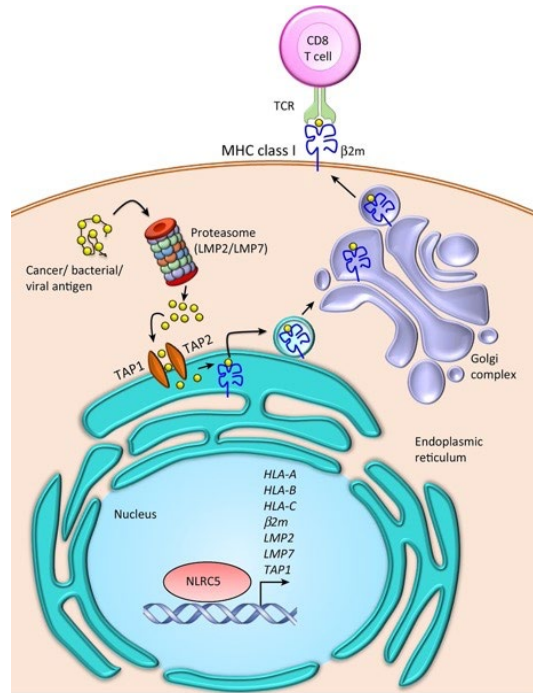
Yoshihama et al. 2013 Trends in Cancer



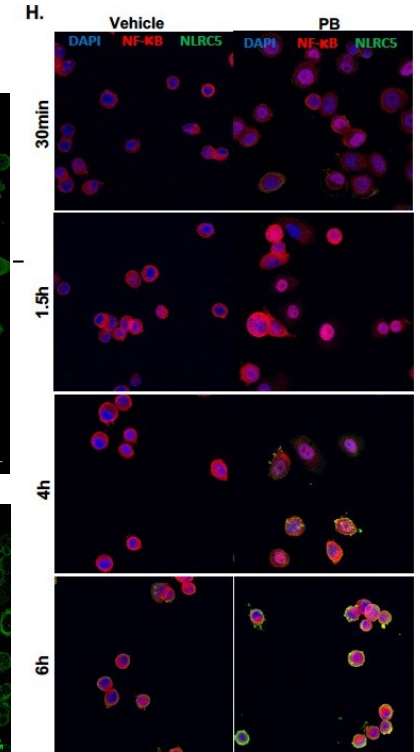
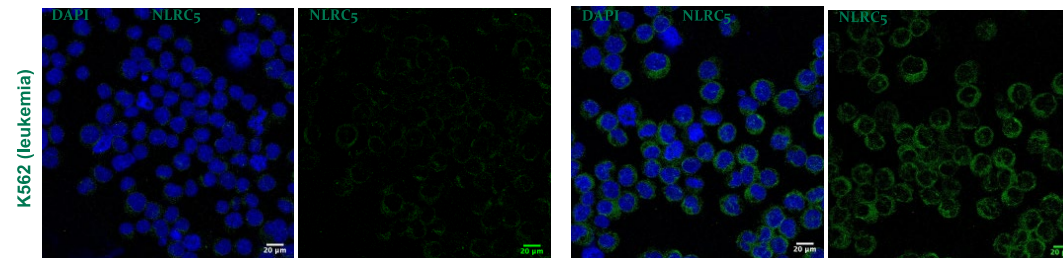
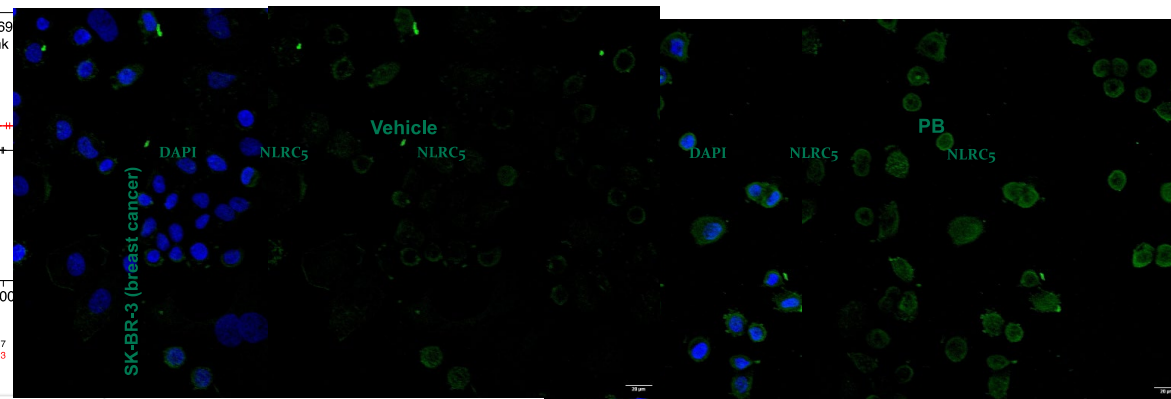
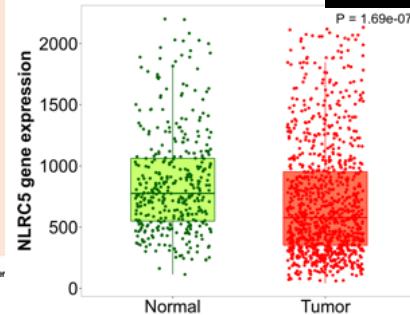
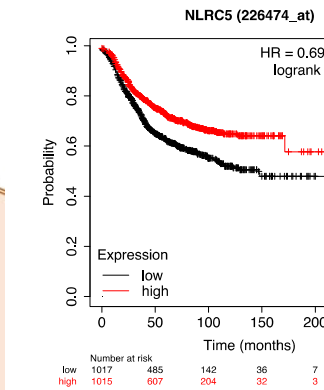
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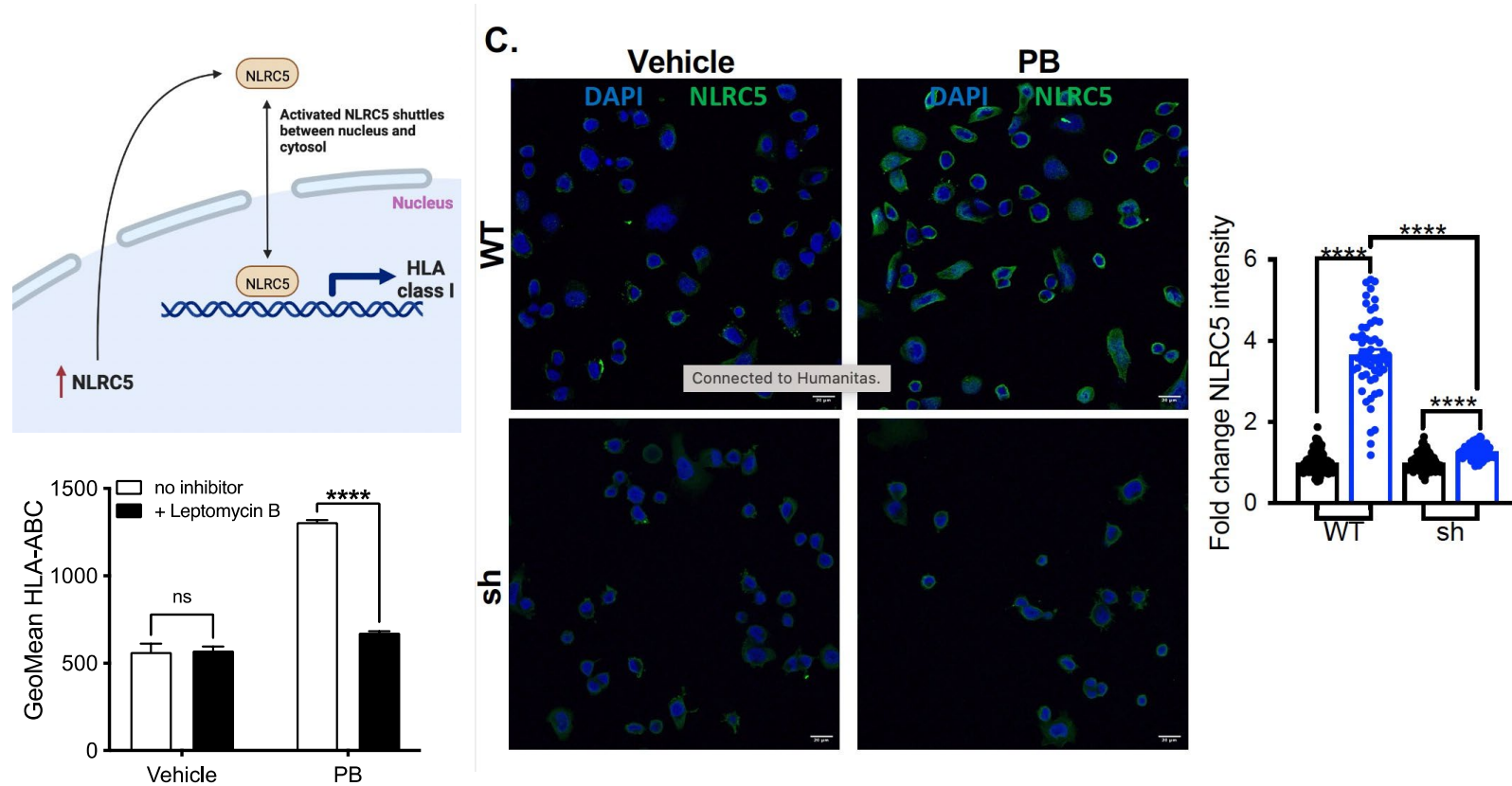
Breast Cancer



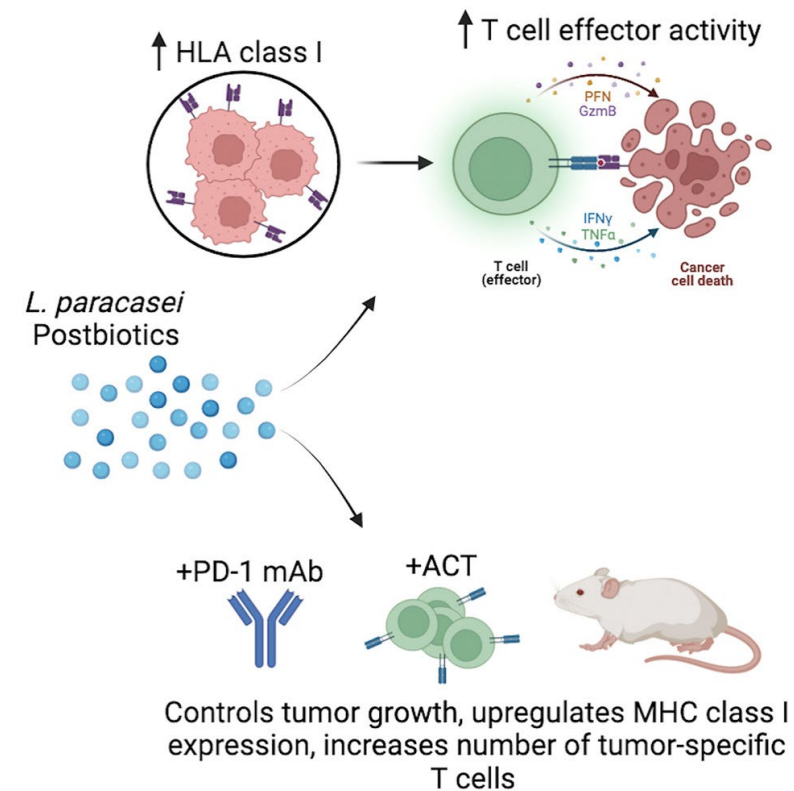
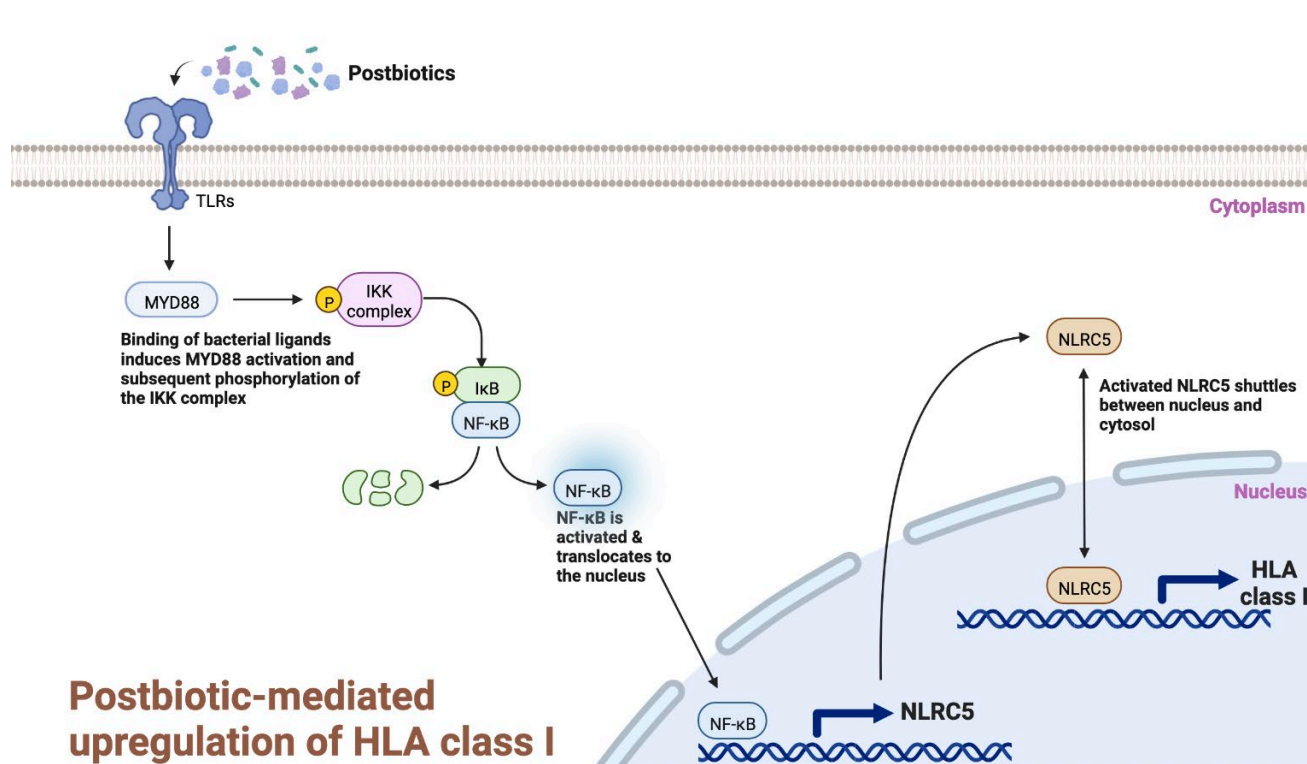
Yoshihama et al. 2013 Trends in Cancer



Leptomycina B/shNLRC5 annulla l'upregolazione mediata dai postbiotici di HLA classe I



I postbiotici sensibilizzano le cellule tumorali agli inibitori del checkpoint immunitario mediante l'upregolazione della classe I di HLA



Ringraziamenti

Prof. Maria Rescigno

Giuseppe Penna

Erika Mileti

Francesca Algieri

Valentina Ferrari

Alessia Melacarne

Alessandra Silvestri

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top
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in gastroenterologia

14[^] EDIZIONE

24-25 NOVEMBRE 2023

BERGAMO

HOTEL EXCELSIOR SAN MARCO
Piazza della Repubblica, 6

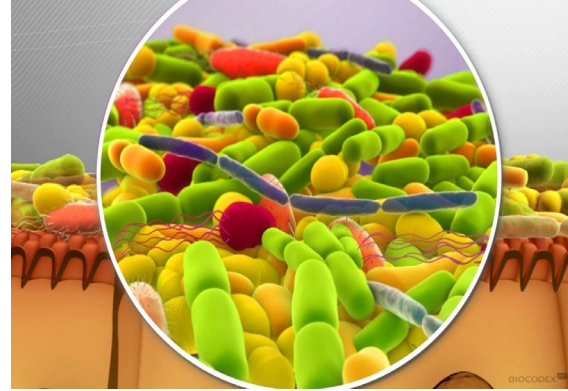
TOP TEN Slides

Strategie per modulare il microbiota



PREBIOTIC

Prebiotics are substances (non-digestible fiber) that induce the growth or activity of microorganisms that contribute to the well-being of their host.



PROBIOTIC

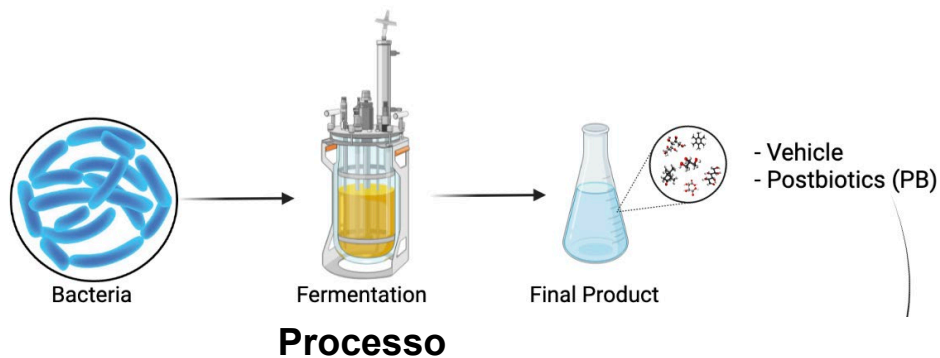
Probiotics are "live" microorganisms which, when administered in adequate amounts, confer a health benefit on the host"
FAO/WHO



POSTBIOTIC

Postbiotics are substances generated by probiotics metabolism, key factors in maintaining long-term health benefit

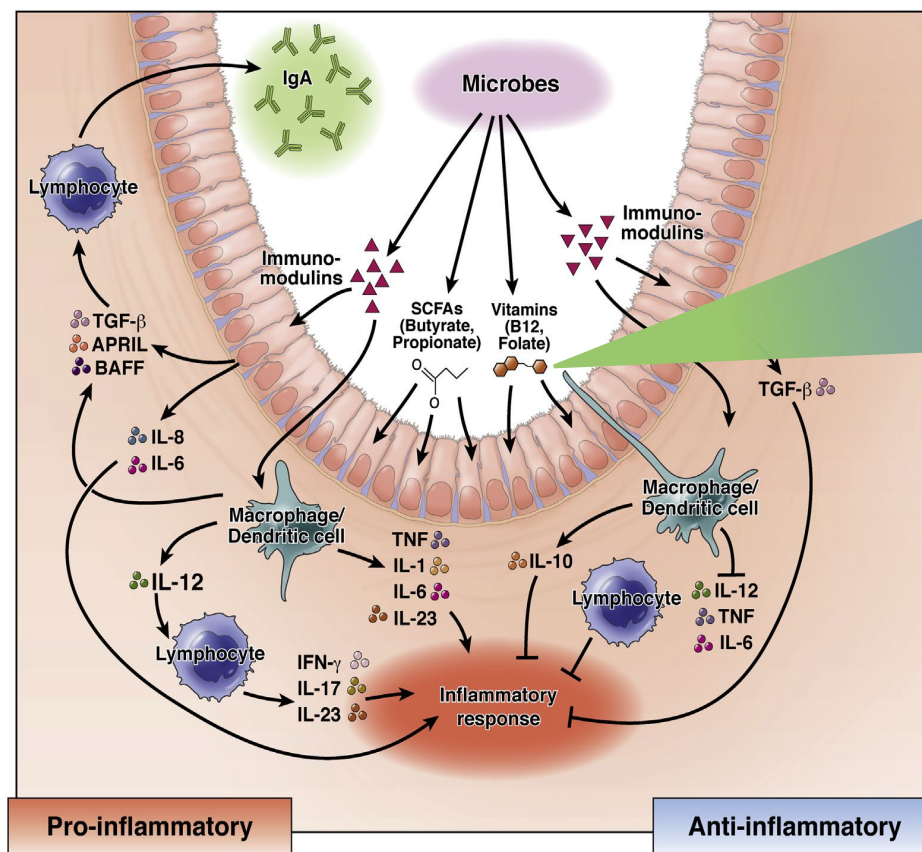
Postbiotici: Componenti chiave dell'interazione tra ospite e microbi



Effetto specifico e differente su:

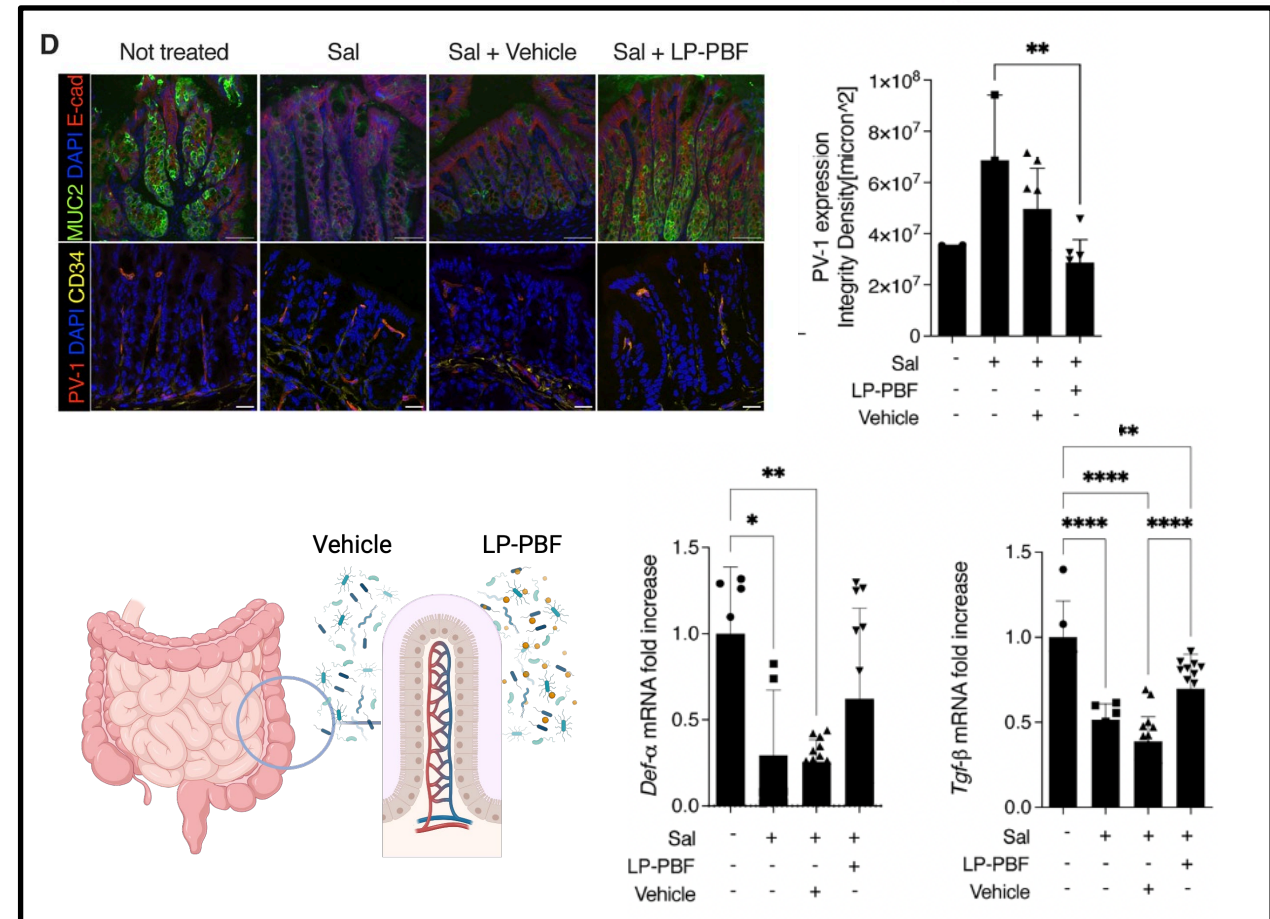
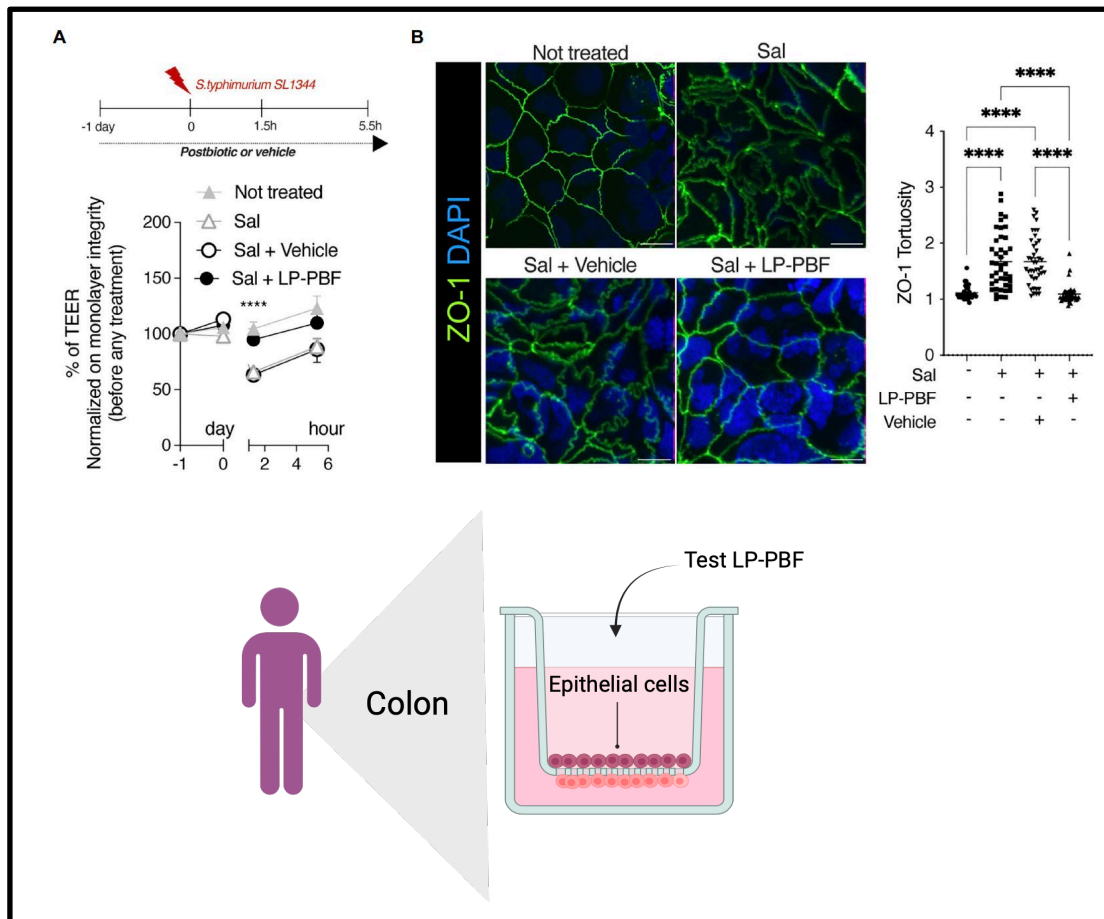
1-Pathways anti-infiammatori

2-Protezione della barriera epiteliale intestinale



Il postbiotico derivato da *Lactobacillus paracasei* CNCM I-5220 protegge dall'insorgenza della permeabilità intestinale

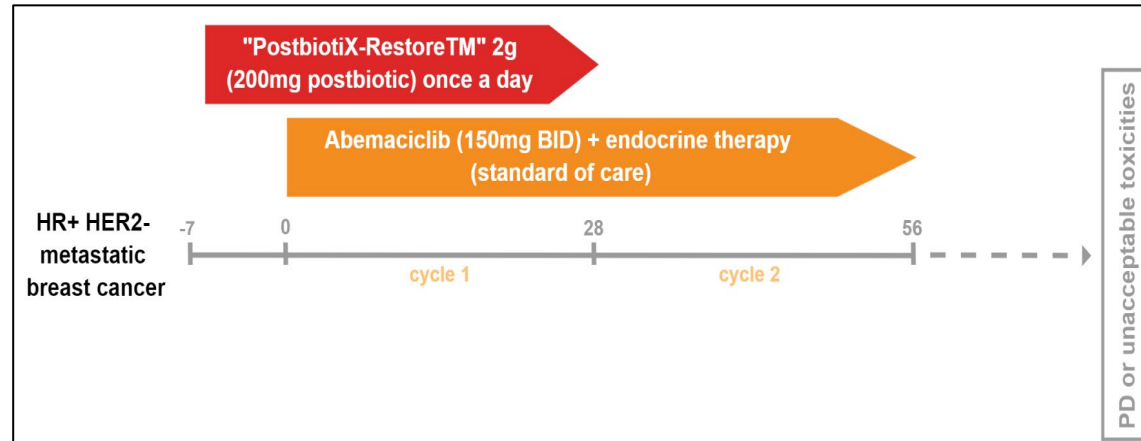
Algieri, Tanaskovic et al. *Frontiers Microbiology* 2023



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La terapia postbiotica in profilassi stabilizza la diarrea indotta da ademaciclin: dati preliminari

- Abemaciclib è un **CDK 4/6 inhibitor** for the treatment of HR+/HER2- advanced breast cancer;
- **Abemaciclib-induced diarrhea** can affect patients' quality of life and cause treatment discontinuation and/or dose modifications
- Diarrhea could be induced by **microbiota** alterations



Clinical Study:

- A prospective, observational, open-label study planned to enroll 30 HR+/HER2- advanced breast cancer patients at IRCCS Humanitas Research Hospital, Italy;
 - The **primary endpoint** was the **median time to diarrhea onset**;
 - The **secondary objectives** were **incidence, severity, and duration** of diarrhea.

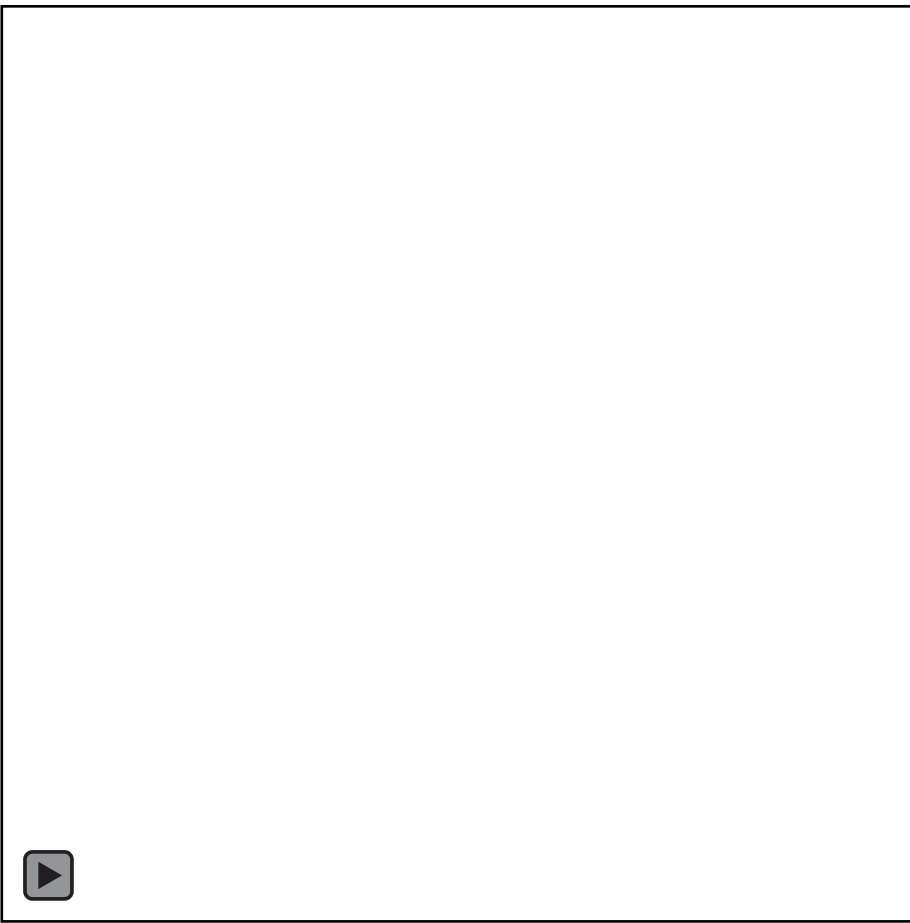
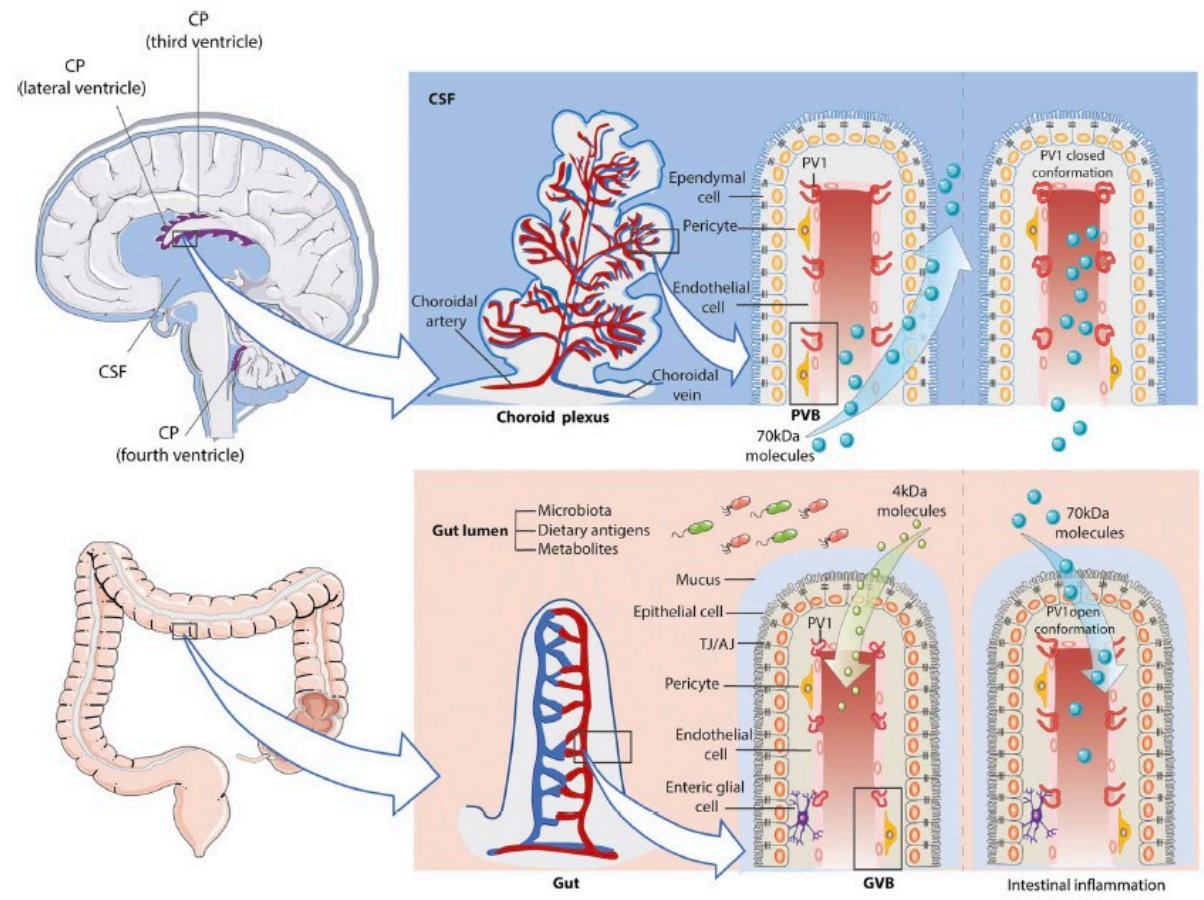
Regularization of bowel movements (frequency and consistency) in the first week of PostbioticX-RestoreTM alone;

Compared to the Monarch1 trial³, we observed a **lower degree of toxicity**, no cases of severe diarrhea (**G3/G4** 0 vs 20%), **G1** (90% vs 42%) and **G2** (10% vs 30%), and a **shorter duration of diarrhea (median time 6 days)**.

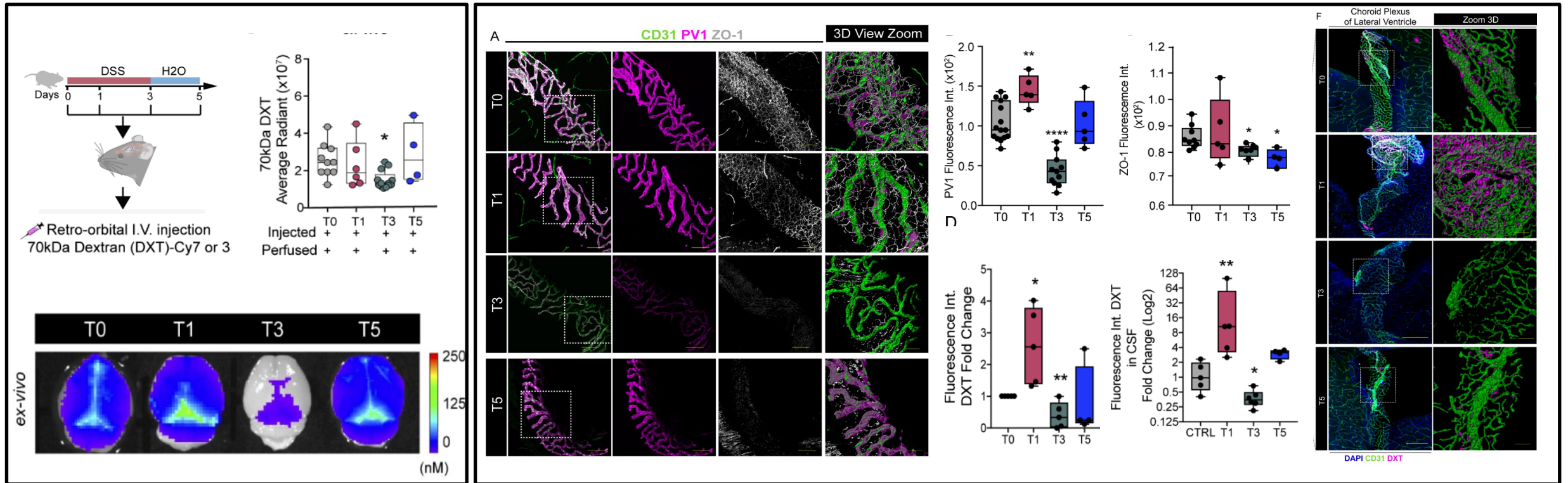
No case of **treatment discontinuation** due to diarrhea.

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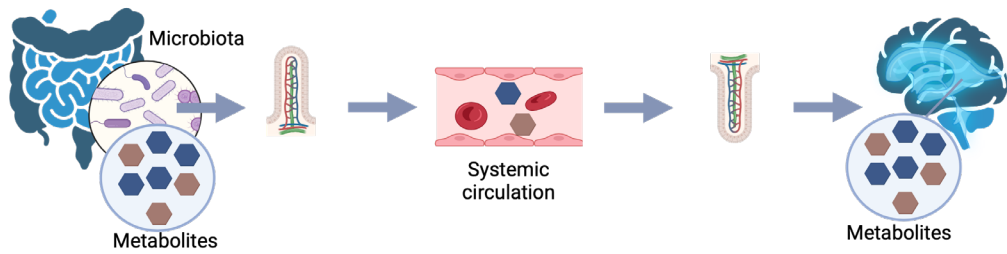
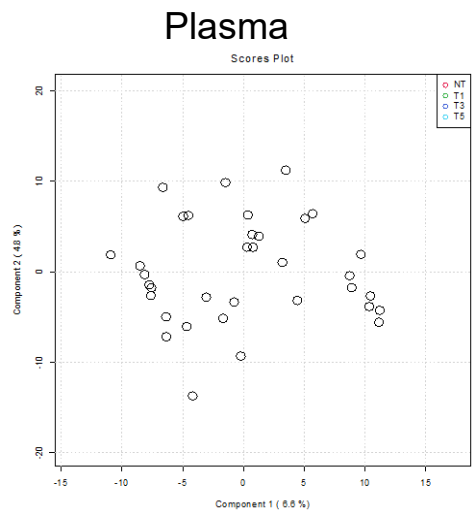
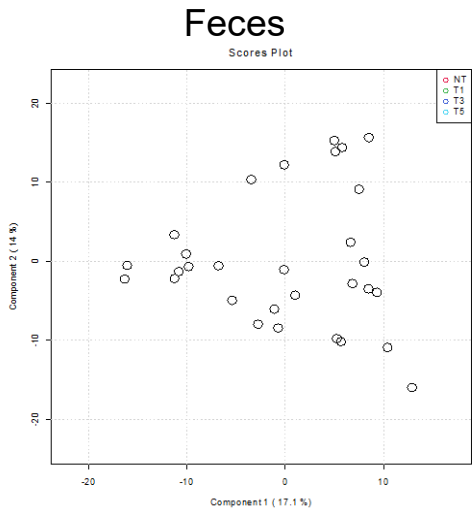
Una nuova barriera collega l'asse intestinale-circolatorio-cerebrale: la barriera vascolare del plesso corioideo (PVB)



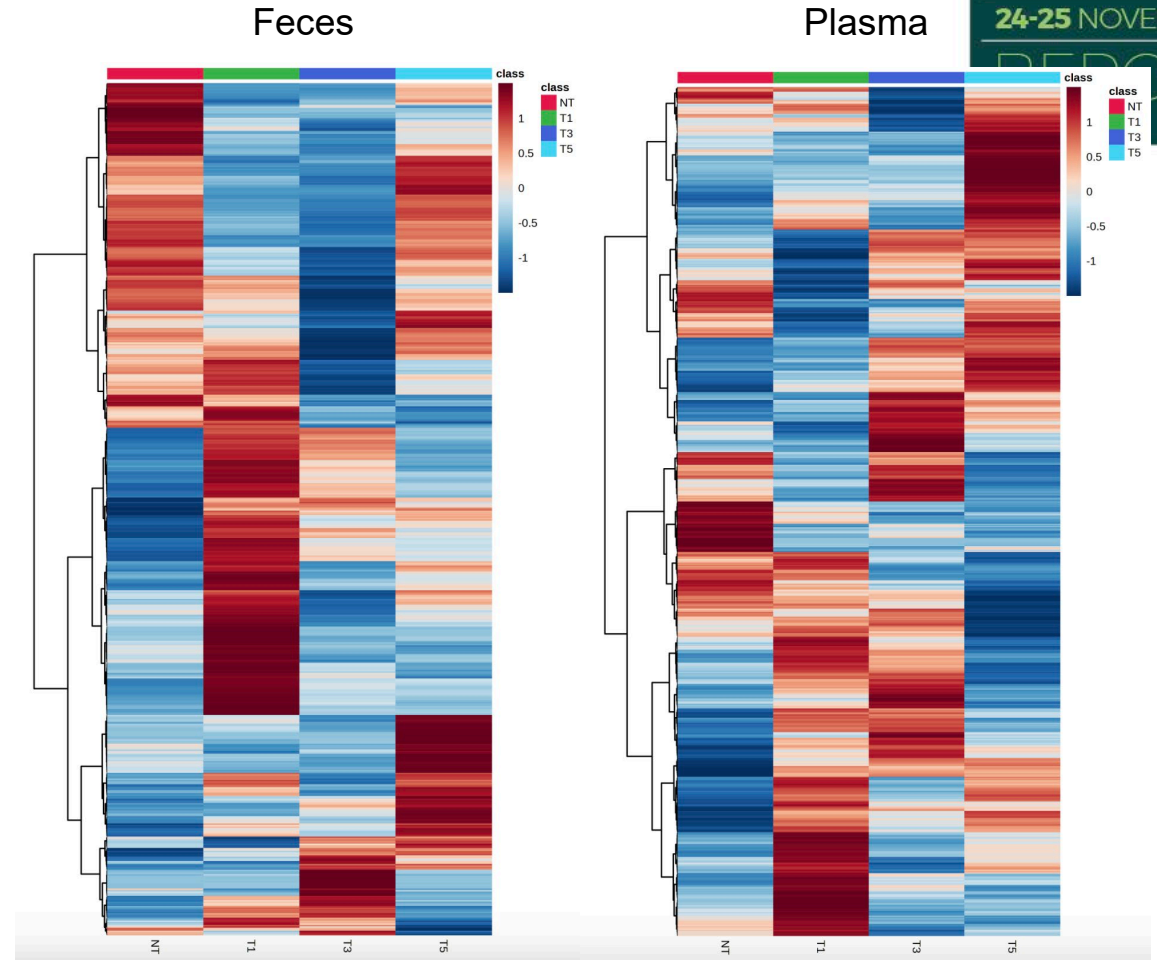
La PVB nel modello di UC risulta chiusa



Nel modello di UC si ha una signature metabolica intestinale e circolatoria

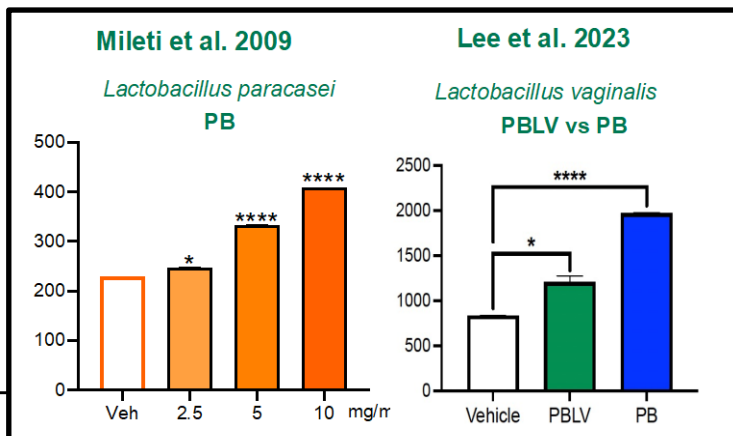
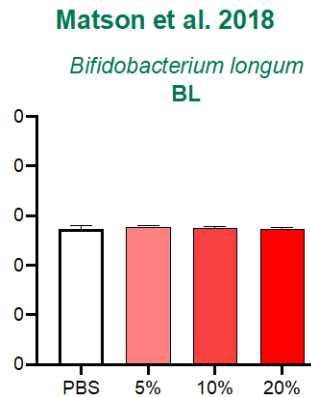
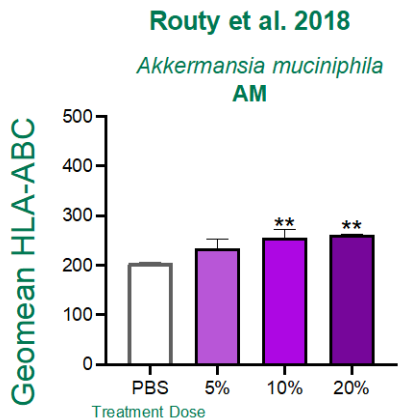


Post biotici

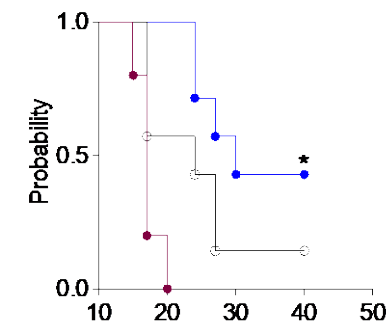
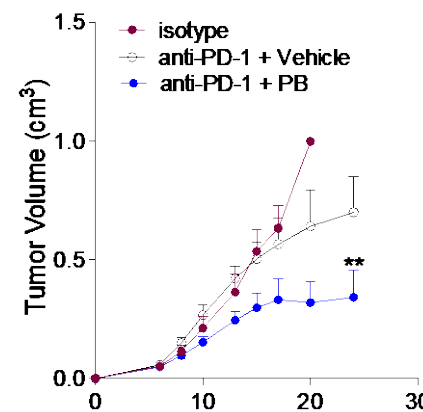
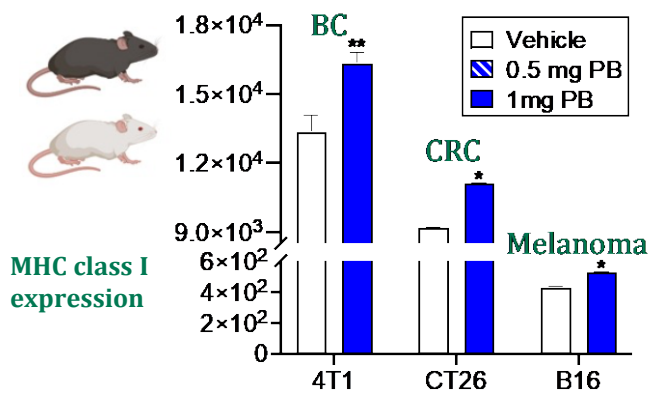
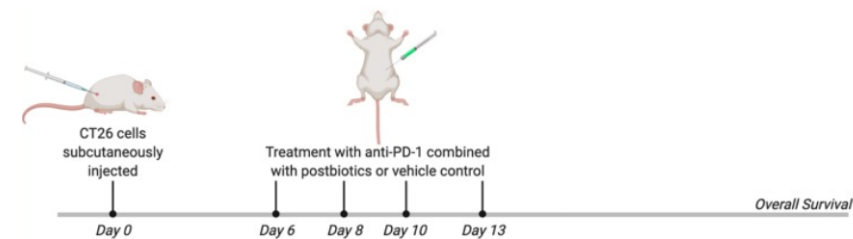


Effetti diversi sull'espressione di HLA di classe I con l'uso di postbiotici provenienti da differenti ceppi batterici

SK-BR-3 breast cancer cell line

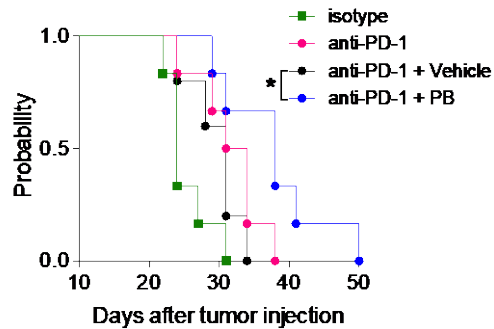
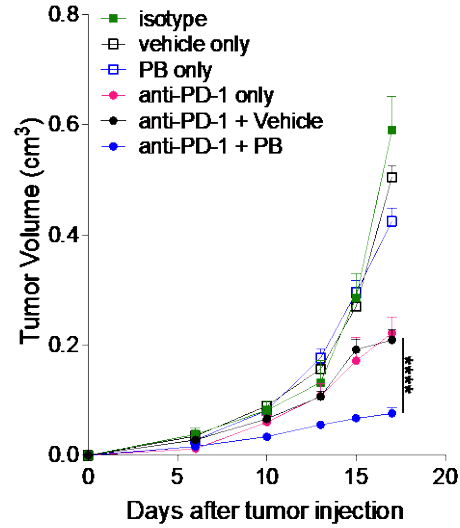


Modello di CRC CT26: Il trattamento con anti-PD-1 combinato con postbiotici controlla la crescita tumorale e prolunga la sopravvivenza

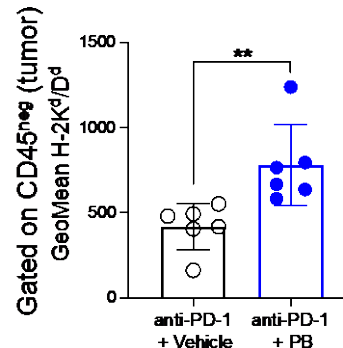
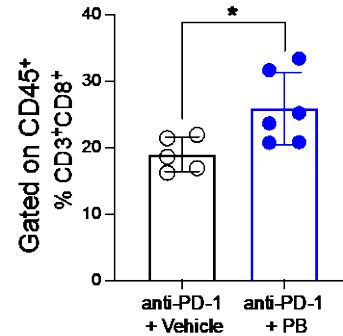


Modello 4T1 TNBC: L'assunzione orale di postbiotici incrementa l'efficacia del trattamento anti PD-1

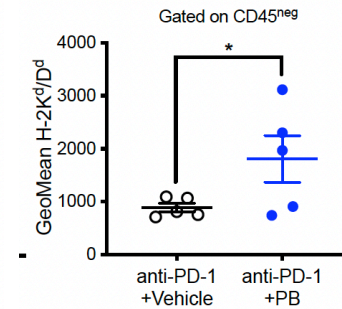
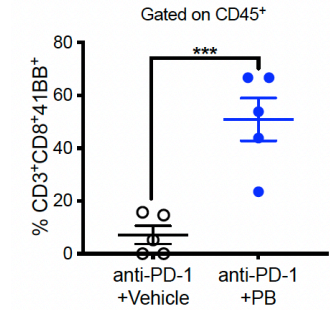
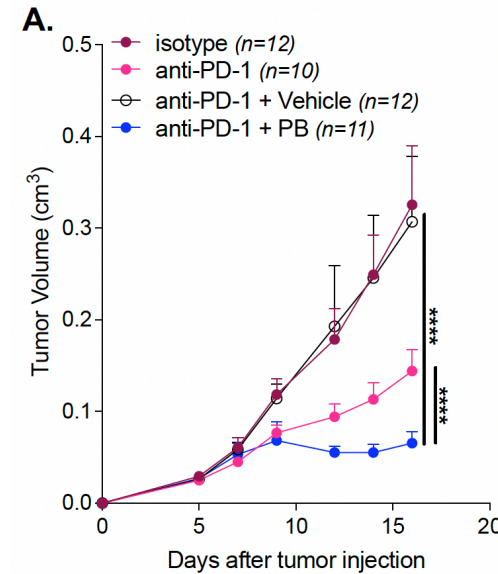
Anti-PD-1 combined with postbiotics controls tumor growth and upregulates MHC class I



Tumors processed ex-vivo



Anti-PD-1 combined with with ORAL postbiotics controlled tumor growth and induced HLA I upregulation



I postbiotici sensibilizzano le cellule tumorali agli inibitori del checkpoint immunitario mediante l'upregolazione della classe I di HLA

