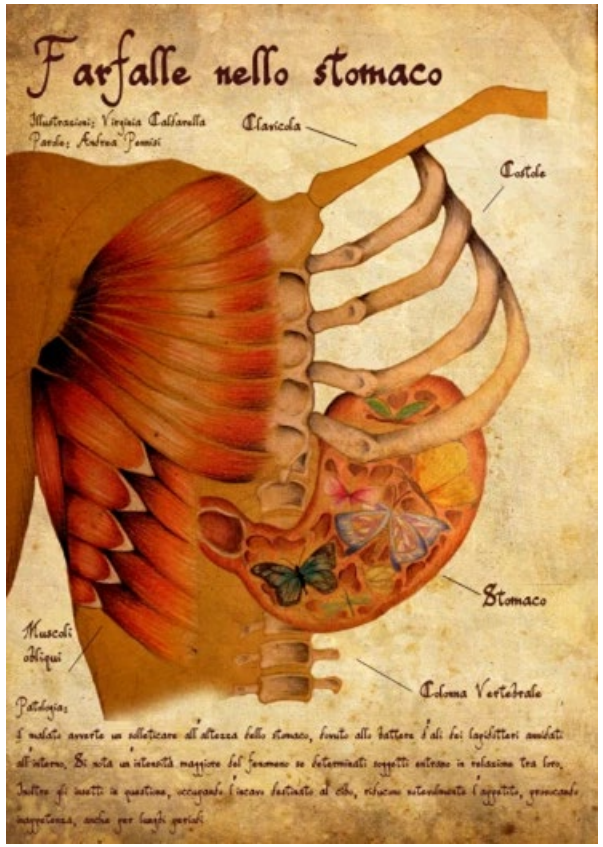
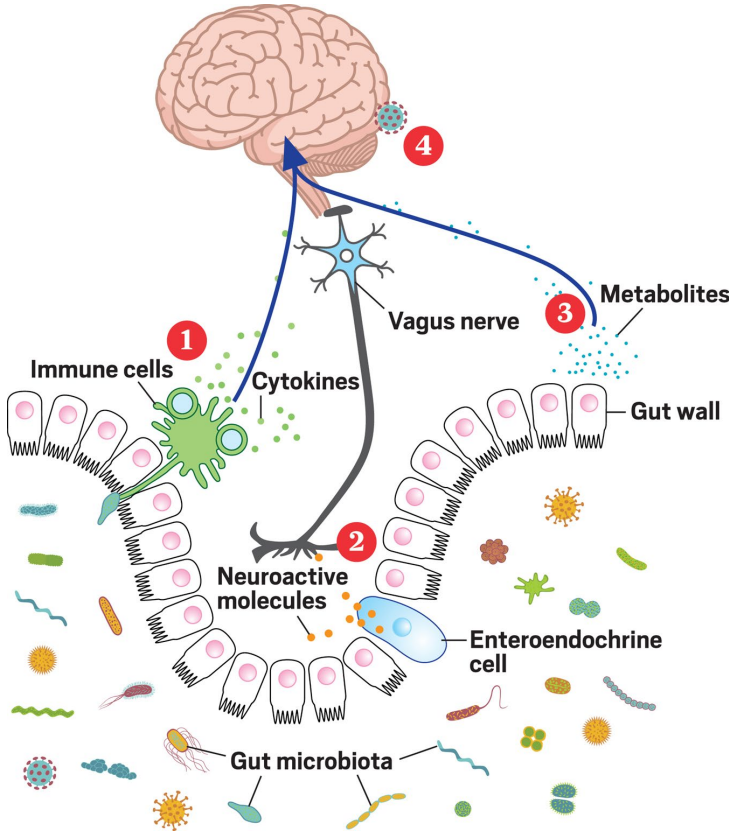
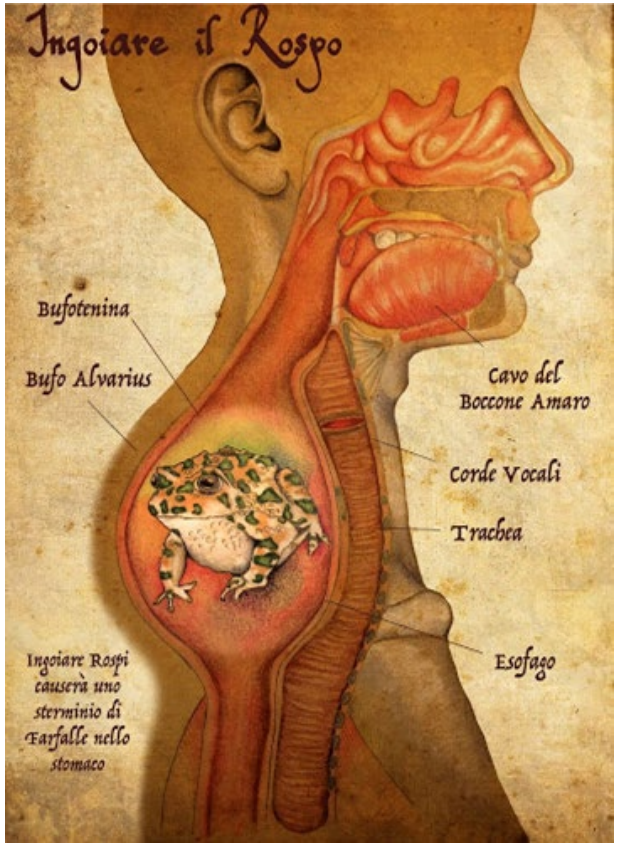






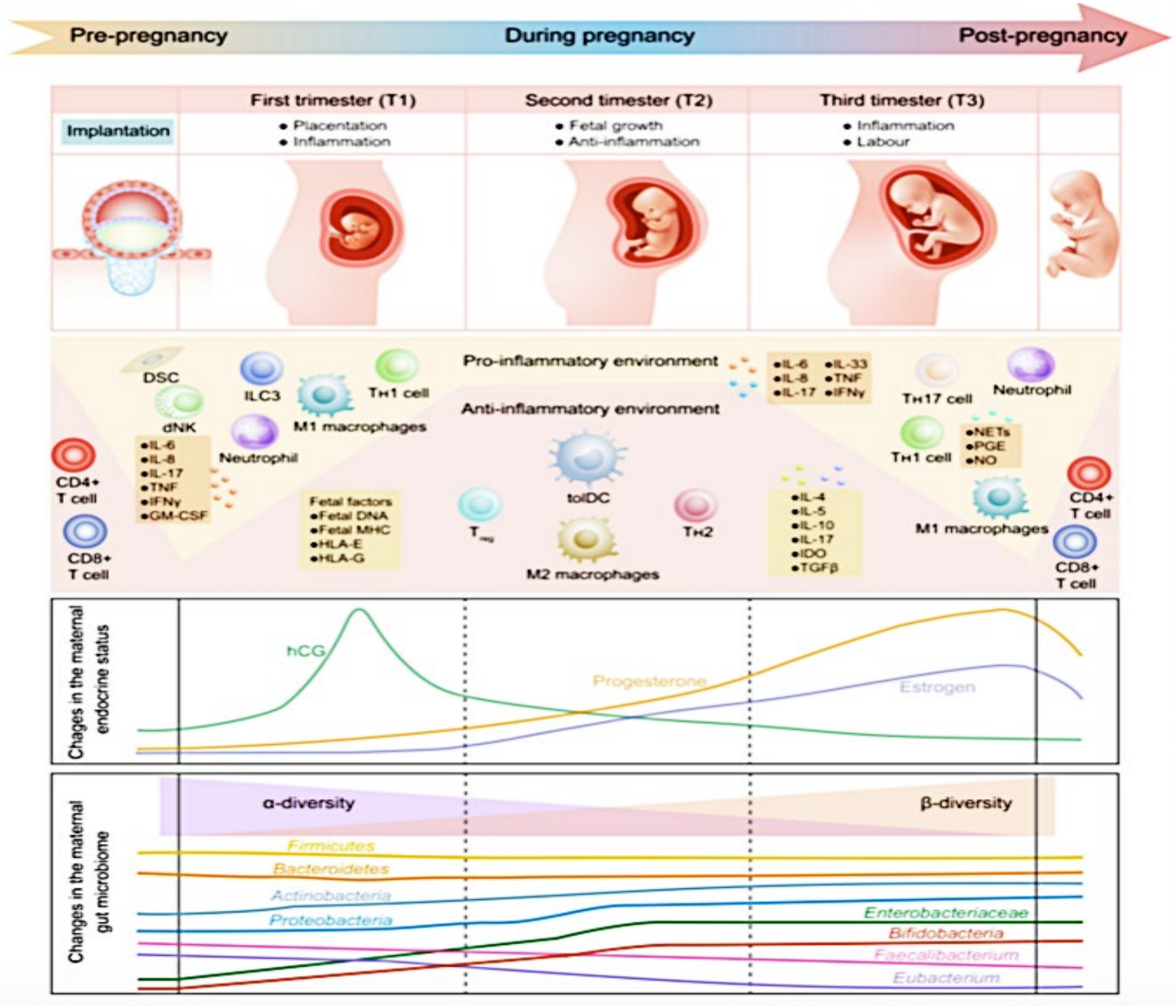
Microbiota e disturbi dello spettro autistico

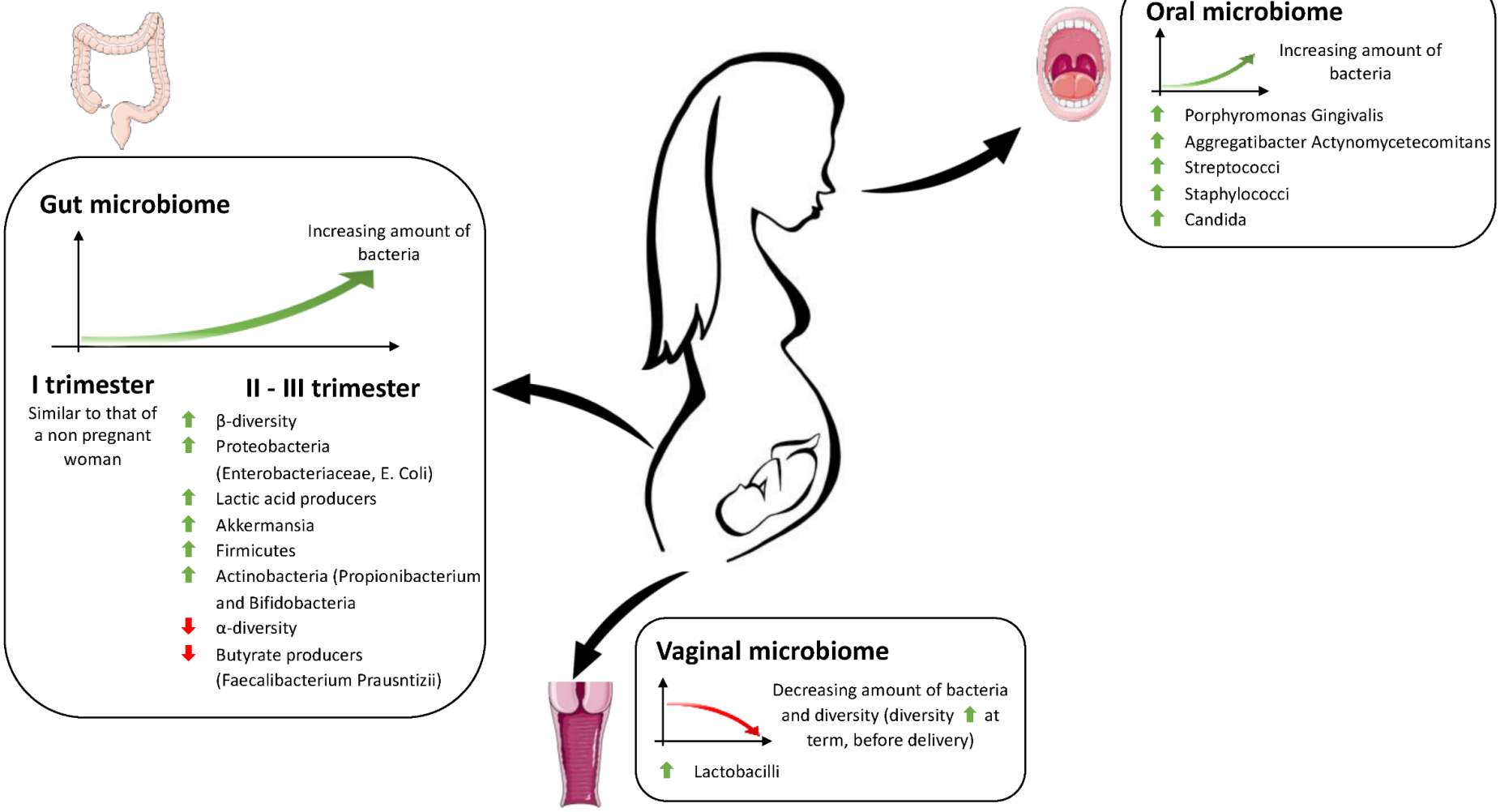
Prof.ssa Natascia Brondino
Dipartimento di Scienze del Sistema Nervoso e del Comportamento, Università di Pavia

Il nostro progetto

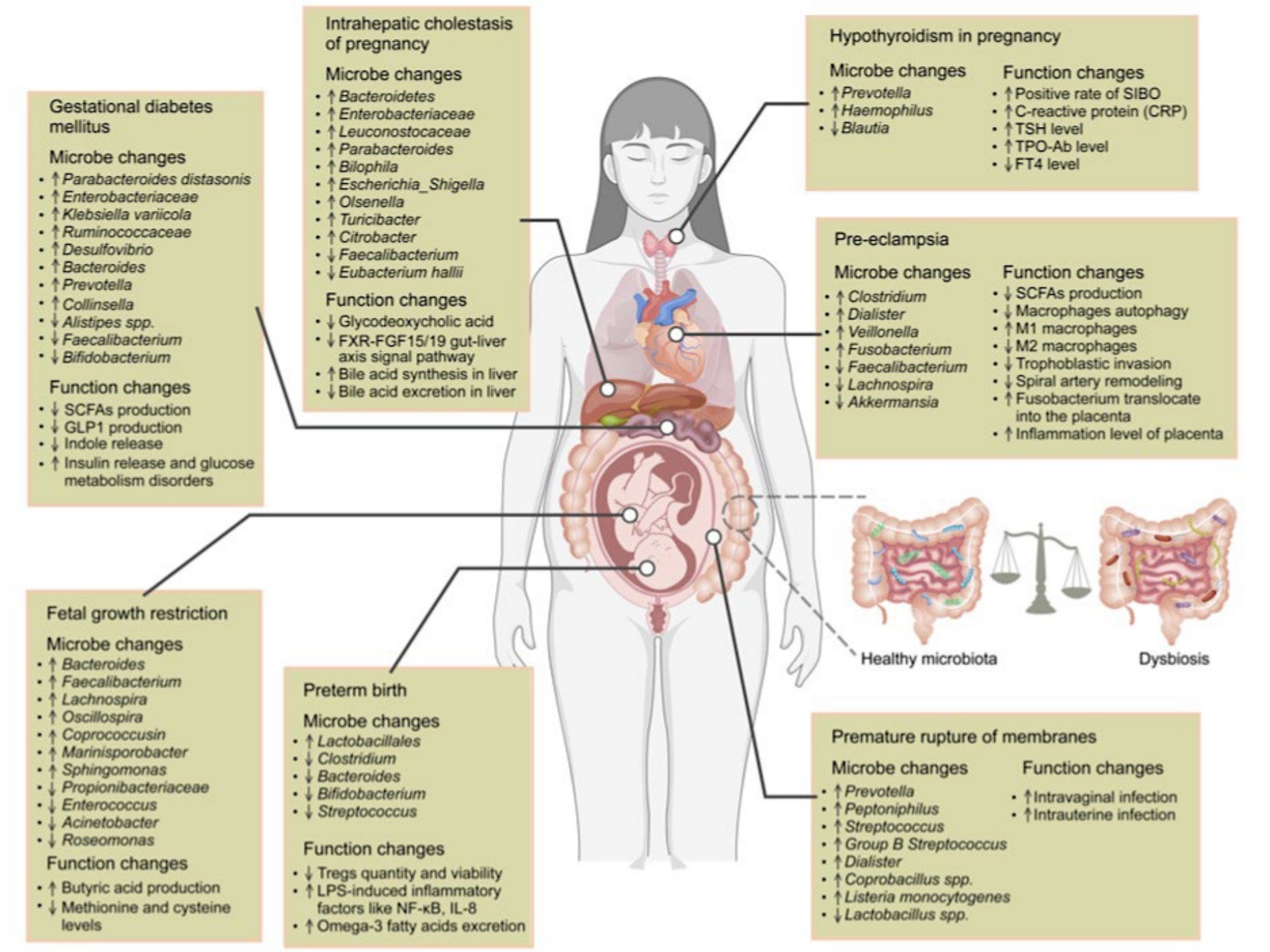
Recently, several studies have highlighted a role of microbiome composition in determining aggression both in animal models (Uzan-Yulzari et al, 2024) as well as in humans (Gulledge et al., 2023; Langmajerová et al, 2023): a potential pathophysiological mechanism linking microbiome composition and aggressiveness in ASD is the unbalance between butyrate and propionate production by the microbiome which could lead to aggressiveness in ASD patients (Taniya et al, 2022).

We will evaluate 100 patients with severe autism with or without severe aggressiveness (towards others or self) with several clinical variables. Additionally, microbiome will be assessed in order to define potential correlations with aggressiveness as well as several symptoms (sensoriality, severity of autistic symptoms, cognitive functioning…).
This will allow a better phenotypic characterization of a complex condition.

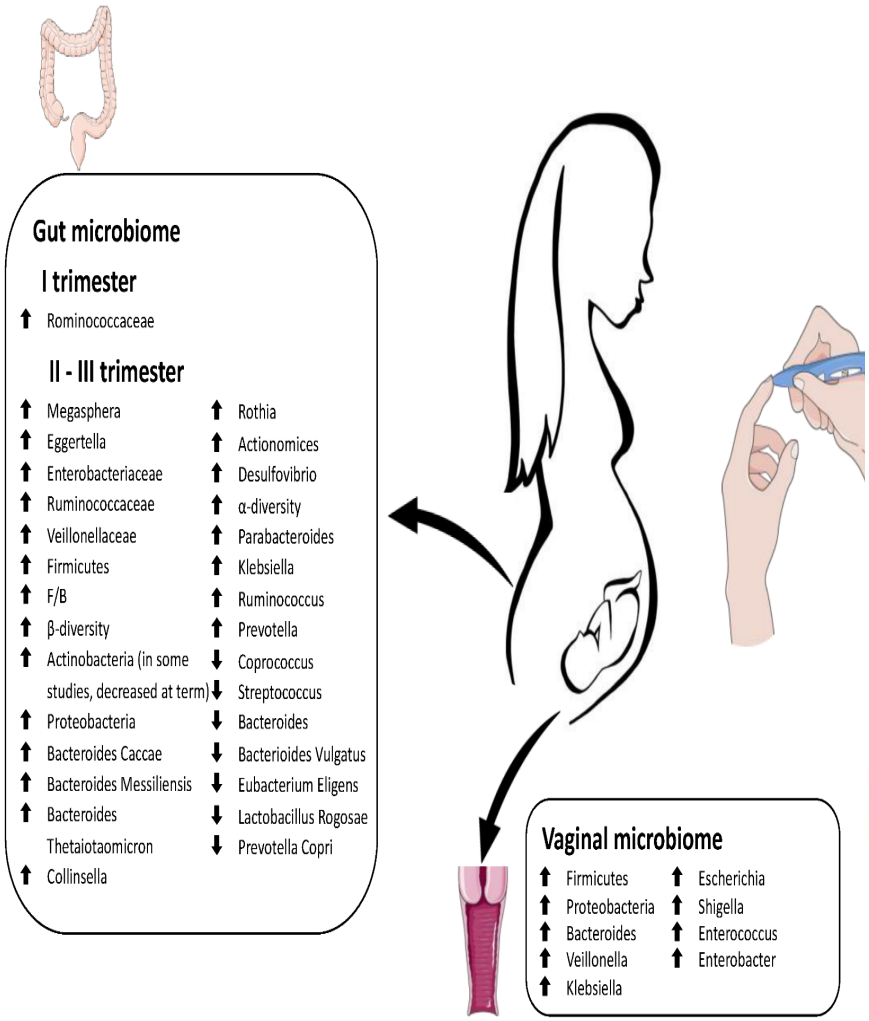

Pre-pregnancy
During pregnancy
Post-pregnancy
First trimester (T1)
Second timester (T2)
Third timester (T3)
Implantation
• Placentation
• Inflammation
• Fetal growth
• Anti-inflammation
• Inflammation
• Labour
DSC
dNK
ILC3
TH1 cell
M1 macrophages
Neutrophil
CD4+ T cell
CD8+ T cell
•IL-6
•IL-8
•IL-17
•TNF
•IFNγ
•GM-CSF
Fetal factors
•Fetal DNA
•Fetal MHC
•HLA-E
•HLA-G
Pro-inflammatory environment
Anti-inflammatory environment
•IL-6 •IL-33
•IL-8 •TNF
•IL-17 •IFNγ
TH17 cell
Neutrophil
TH1 cell
•NETs
•PGE
•NO
M1 macrophages
CD4+ T cell
CD8+ T cell
tolDC
M2 macrophages
TH2
•IL-4
•IL-5
•IL-10
•IL-17
•IDO
•TGFβ
Changes in the maternal endocrine status
hCG
Progesterone
Estrogen
Changes in the maternal gut microbiome
α-diversity
β-diversity
Firmicutes
Bacteroidetes
Actinobacteria
Proteobacteria
Enterobacteriaceae
Bifidobacteria
Faecalibacterium
Eubacterium

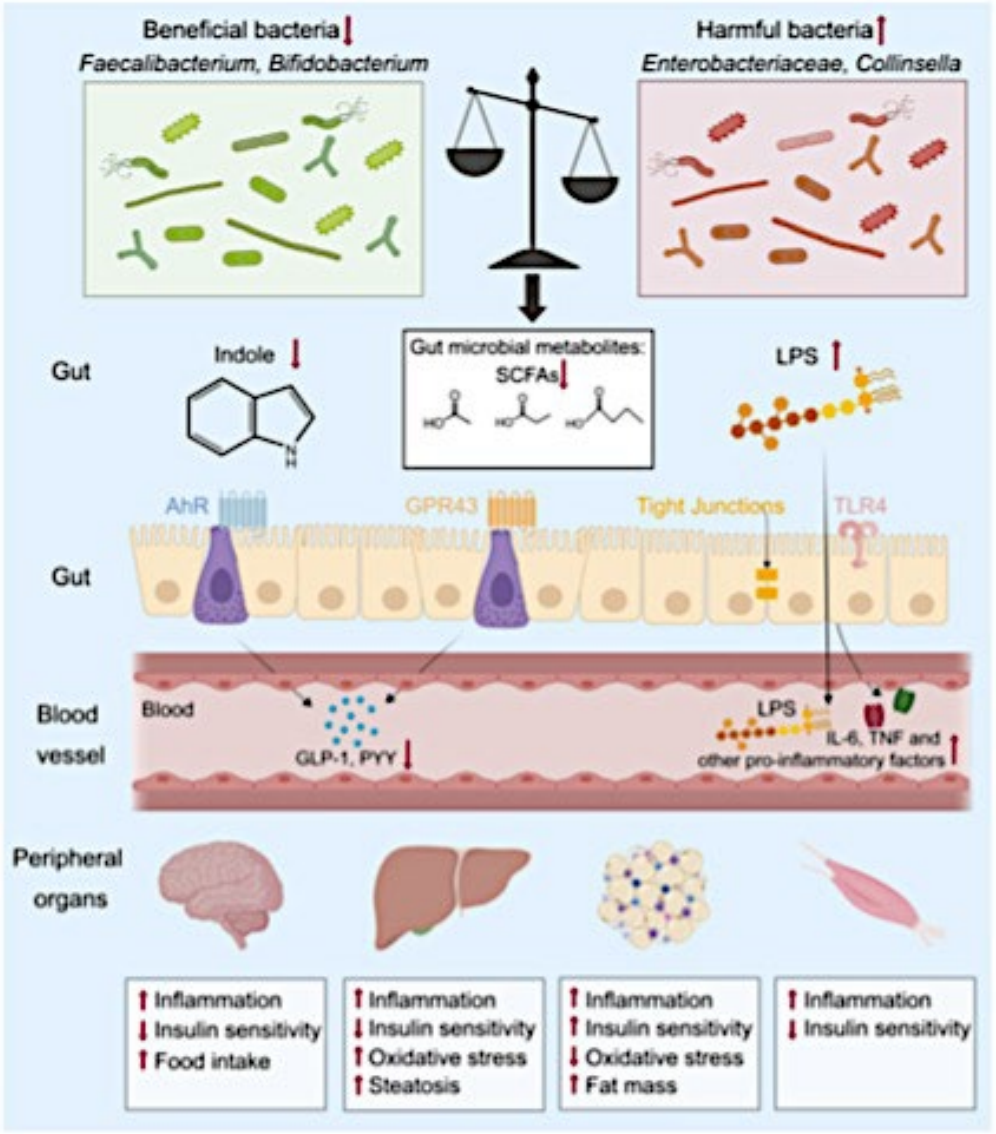


Unfavorable microbiota changes in the later stages of pregnancy may be the onset of pregnancy complications. Coincidentally, complications such as GDM, PE, and intrahepatic cholestasis of pregnancy (ICP) often occur in the later stages of pregnancy

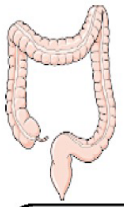

Intrahepatic cholestasis of pregnancy
Microbe changes
↑ Bacteroidetes
↑ Enterobacteriaceae
↑ Leuconostocaceae
↑ Parabacteroides
↑ Bilophila
↑ Escherichia_Shigella
↑ Olsenella
↑ Turicibacter
↑ Citrobacter
↓ Faecalibacterium
↓ Eubacterium hallii
Function changes
↓ Glycodeoxycholic acid
↓ FXR-FGF15/19 gut-liver axis signal pathway
↑ Bile acid synthesis in liver
↓ Bile acid excretion in liver
Hypothyroidism in pregnancy
Microbe changes
↑ Prevotella
↑ Haemophilus
↓ Blautia
Function changes
↑ Positive rate of SIBO
↑ C-reactive protein (CRP)
↑ TSH level
↑ TPO-Ab level
↓ FT4 level
Gestational diabetes mellitus
Microbe changes
↑ Parabacteroides distasonis
↑ Enterobacteriaceae
↑ Klebsiella variicola
↑ Ruminococcaceae
↑ Desulfovibrio
↑ Bacteroides
↑ Prevotella
↑ Collinsella
↓ Alistipes spp.
↓ Faecalibacterium
↓ Bifidobacterium
Function changes
↓ SCFAs production
↓ GLP1 production
↓ Indole release
↑ Insulin release and glucose metabolism disorders
Pre-eclampsia
Microbe changes
↑ Clostridium
↑ Dialister
↑ Veillonella
↑ Fusobacterium
↓ Faecalibacterium
↓ Lachnospira
↓ Akkermansia
Function changes
↓ SCFAs production
↓ Macrophages autophagy
↑ M1 macrophages
↓ M2 macrophages
↓ Trophoblastic invasion
↓ Spiral artery remodeling
↑ Fusobacterium translocate into the placenta
↑ Inflammation level of placenta
Healthy microbiota
Dysbiosis
Fetal growth restriction
Microbe changes
↑ Bacteroides
↑ Faecalibacterium
↑ Lachnospira
↑ Oscillospira
↑ Coprococcusin
↑ Marinisporobacter
↑ Sphingomonas
↓ Propionibacteriaceae
↓ Enterococcus
↓ Acinetobacter
↓ Roseomonas
Function changes
↑ Butyric acid production
↓ Methionine and cysteine levels
Preterm birth
Microbe changes
↑ Lactobacillales
↓ Clostridium
↓ Bacteroides
↓ Bifidobacterium
↓ Streptococcus
Function changes
↓ Tregs quantity and viability
↑ LPS-induced inflammatory factors like NF-κB, IL-8
↑ Omega-3 fatty acids excretion
Premature rupture of membranes
Microbe changes
↑ Prevotella
↑ Peptoniphilus
↑ Streptococcus
↑ Group B Streptococcus
↑ Dialister
↑ Coprobacillus spp.
↑ Listeria monocytogenes
↓ Lactobacillus spp.
Function changes
↑ Intravaginal infection
↑ Intrauterine infection

Microbiota and gestational diabetes



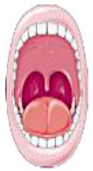


Microbiota and preterm birth



Gut microbiome

- ↑ Porphyromonas
- ↑ Streptococcus
- ↑ Fusobacterium
- ↑ Veillonella
- ↓ Coprococcus
- ↓ Gemmiger



Oral microbiome

- ↑ Porphyromonas G.
- ↑ Aggregatibacter A.
- ↑ Tannerella F.
- ↑ Treponema D.
- ↑ Fusobacterium N.
- ↑ Prevotella I.

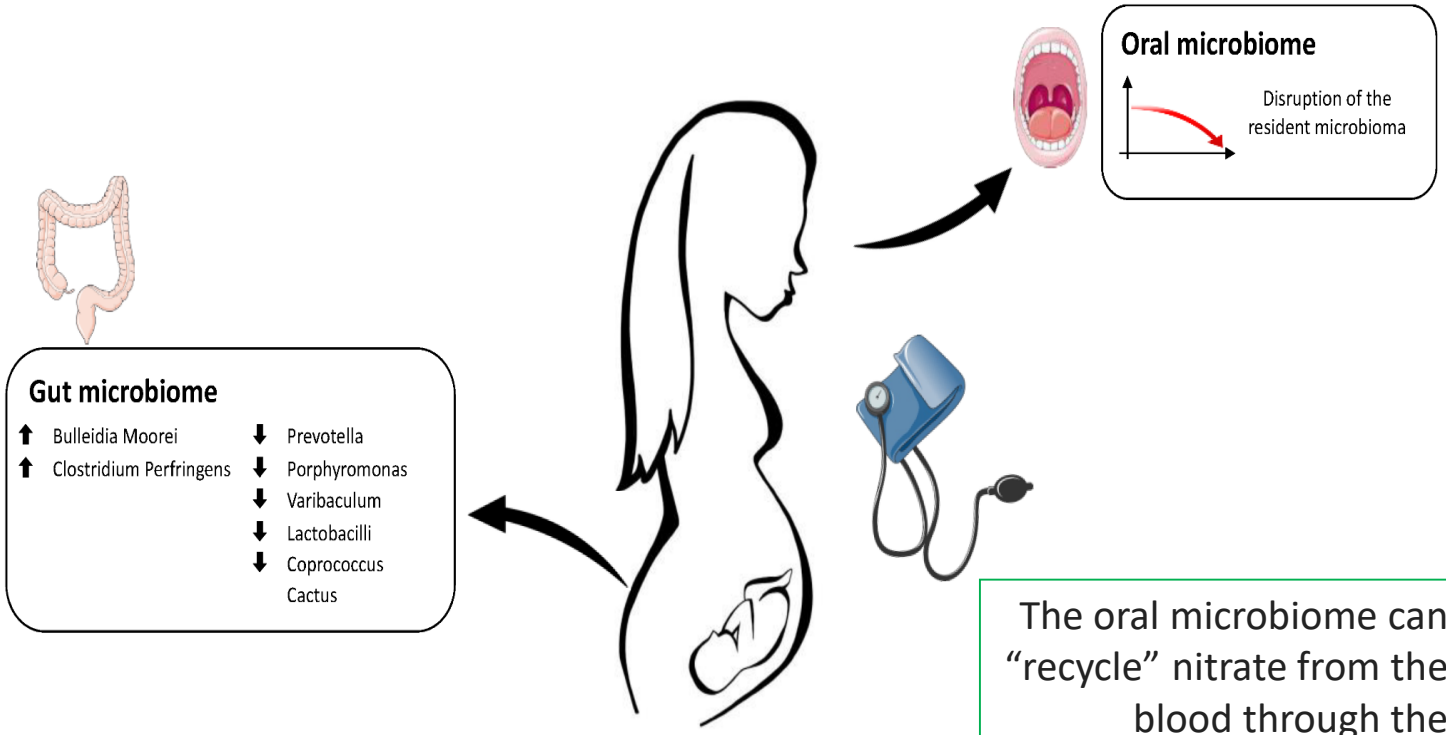
Periodontal pathogens and their products can reach the placenta and affect the fetal unit through blood circulation. Moreover, they might be involved in the development and progression of systemic inflammation. High periodontal pathogens during pregnancy have been associated with an increased risk for preterm delivery.

Vaginal microbiome

- ↑ Lactobacillus Iners
- ↑ Gardnerella
- ↑ Ureaplasma
- ↑ Mycoplasma
- ↑ Prevotella
- ↑ Klebsiella
- ↑ Escherichia
- ↑ Enterococci
- ↑ Staphylococci
- ↑ Streptococci group B
- ↑ Atopibum
- ↑ Veillonellaceae
- ↓ Lactobacilli

Lactobacillus crispatus dominance characterizes full-term pregnancies, while the prevalence of Lactobacillus iners in the second trimester increases the risk of early spontaneous PTB.
Indeed, Lactobacillus iners growth in ongoing pregnancy is a marker of vaginal microbiota instability.

Microbiota and preeclampsia



The oral microbiome can "recycle" nitrate from the blood through the enterosalivary pathway to extend NO bioavailability.

Prevotella is implicated in producing short-chain fatty acids (SCFAs), such as butyrate, which lower maternal blood pressure during pregnancy.

Butyrate is the primary energy source for cells that constitute the intestinal epithelium and is involved in T lymphocyte differentiation.

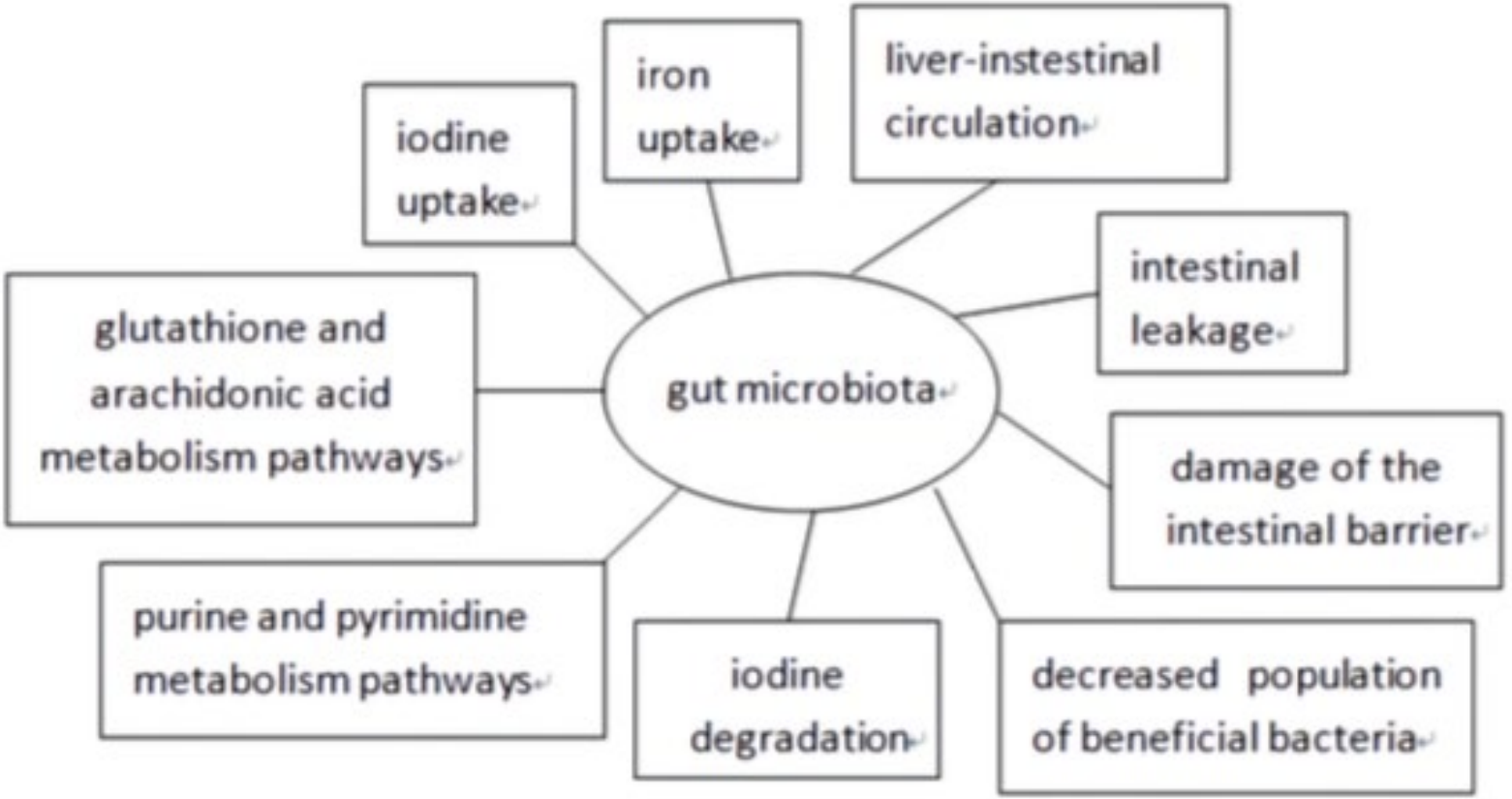
Protective effect of butyrate on the occurrence of preeclampsia by inhibiting the synthesis of the plasminogen activator-1 inhibitor (PAI-1), which causes a reduction in vasoconstriction and a decreased secretion of nitric oxide (NO), damaging the vascular endothelium

Microbiota and obesity

obesity is intimately tied to an imbalance of gut microbiota, metabolic disorders, and systemic inflammation in pregnant women

Effect	Microbiota characteristics	Mechanism
Increased energy absorption	Expansion of *Desulfovibrio* and loss of Clostridia	Elevated the expression of genes that control lipid absorption such as CD36
Extra energy for the host	The inverse association between fecal SCFAs and gut microbiota diversity; Faecalibacterium prausnitzii, Roseburia faecis, and other Clostridiales increased; Akkermansia muciniphila, Alistipes finegoldii, Bacteroides, Christensenellaceae, Methanobrevibacter, and Oscillospira decreased	Excessive SCFAs
Increased appetite	A community dominated by members of the Clostridial clusters XIVa and IV	The levels of peptide YY and GLP-1 in obese patients decrease significantly
Decreased Fat storage	Germ free mice colonized with *Lactobacillus paracasei*	Increase the expression of ANGPTL4, and inhibit LPL, leading to decreased fat storage
Increased fat storage	Transplanting gut microbes from conventionally raised mice into germ-free mice	Increasing the expression of ChREBP and SREBP-1, Fiaf is inhibited, activate LPL, help triglycerides enter the circulatory system from the liver
Decreased chronic inflammation	Increase levels in the butyrate-producing bacteria such as Ruminococcaceae and Lachnospiraceae	Inhibit pathways leading to the production of pro-inflammatory cytokines; Stimulate adipolioIysis and mitochondrial oxidative phosphorylation, thereby achieving greater energy consumption; Reduce LPS, thereby reducing chronic low-grade inflammation
Interruption of circadian rhythm	Bile salts biotransformation bacteria such as Lachnospiraceae, Clostridiaceae, Ruminococcaceae, Lactobacillus, Bacteroides, and Bifidobacterium	Regulate transcription of key genes involved in circadian rhythm (*Dbp, Per1/2*) and lipid metabolism (*Pparγ, Angptl4*)

Microbiota and autoimmune thyroiditis



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Trapianto di microbiota in un paziente con Graft-*versus*-Host-Disease dopo trapianto di cellule staminali emopoietiche in Onco-Ematologia Pediatrica

Francesca Compagno
Marco Zecca
SC Ematologia 2 Oncoematologia Pediatrica

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Trapianto di cellule staminali emopoietiche (TCSE) e ruolo del microbiota

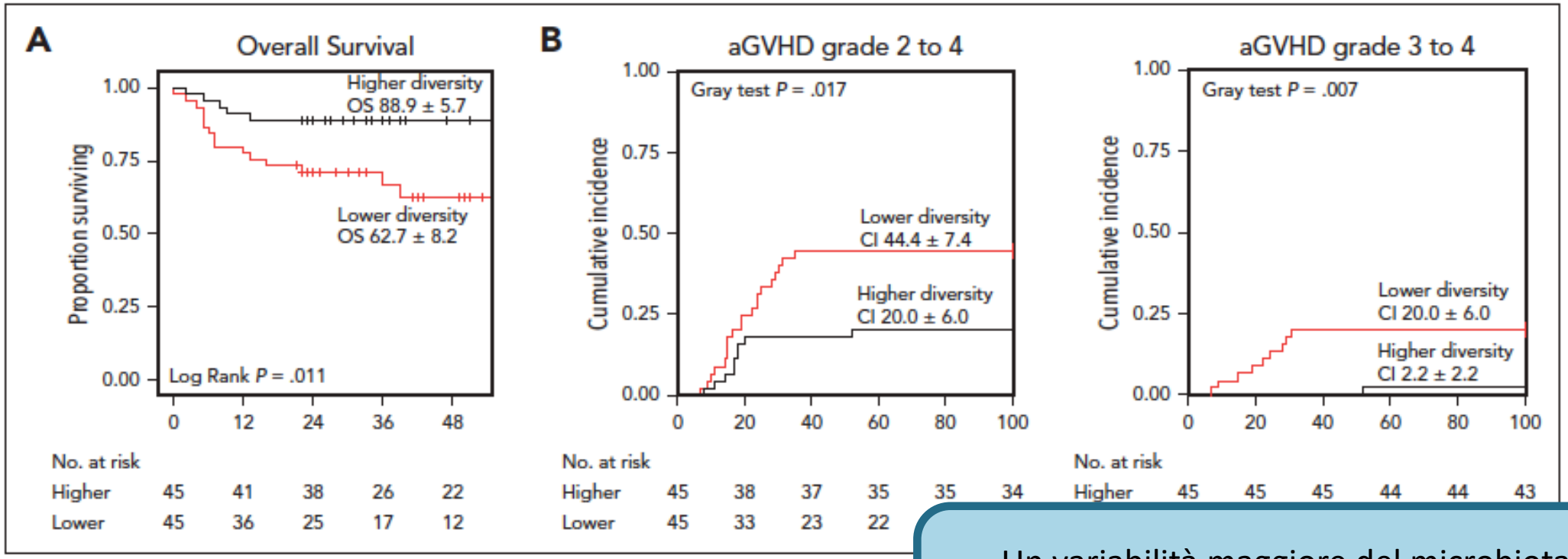

Figure 2. Overall survival and aGVHD incidence in respect to pre-allo-HSCT GM diversity. Kapl
and 3 to 4 aGVHD (B) for the higher- and lower-diversity groups before allo-HSCT. CI, confidence i

Un variabilità maggiore del microbiota intestinale prima del TCSE correla con una miglior OS e una minor incidenza di GvHD

blood

Masetti R, Zecca M et al. *Blood*2023;142(16): 1387–1398.

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Trapianto di microbiota in Italia

Indicazioni ministeriali

- Possono essere candidate al trapianto di microbiota fecale (FMT) le persone adulte, con infezione ripetuta e accertata da *Clostridioides Difficile (CD)*, trascorse 8 settimane dall'ultima terapia antibiotica effettuata senza successo con vancomicina o fidaxomicina per 10 giorni.
- Per infezione ripetuta si intende quella che causa episodi di diarrea con 3 o più scariche in 24 ore per almeno 2 giorni.
- Le persone, inoltre, devono risultare positive ad alcune indagini di laboratorio come l'*immunoassay* enzimatico positivo per la tossina di CD (EIA) o il test molecolare per la ricerca del gene (gene locus) della tossina di CD nelle feci.

Istituto Superiore di Sanità

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Trapianto di microbiota nella GvHD intestinale: Future altre indicazioni?

Fecal microbiota transplantation for patients with steroid-resistant acute graft-versus-host disease of the gut.
Kakihana et al. Blood 2016:128(16);2083-2088.

Fecal microbiota transplantation for the treatment of steroid-refractory, intestinal, graft-versus-host disease in a pediatric patient
Merli at al. BMT 2022

Pooled allogeneic faecal microbiota MaaT013 for steroid-resistant gastrointestinal acute graft-versus-host disease: a single-arm, multicentre phase 2 trial
Malard F et al. EClinicalMedicine.2023 Jul 26:62:102111

Fecal Microbiota Transplantation for Acute Graft-versus-Host Disease after Allogeneic Hematopoietic Cell Transplantation: Expanding the Horizon into Pediatrics
Gray A and DeFilipp Z. Transplant Cell Ther.2023 Aug;29(8):484-491

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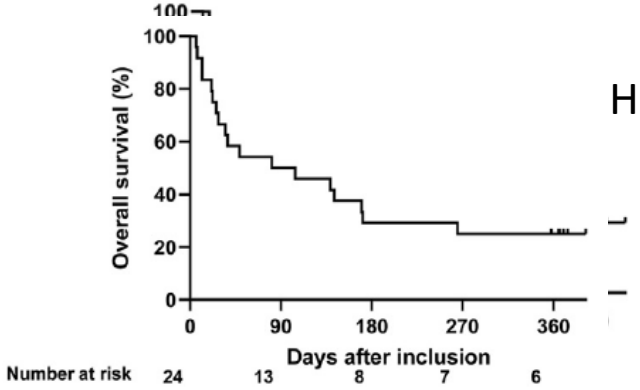
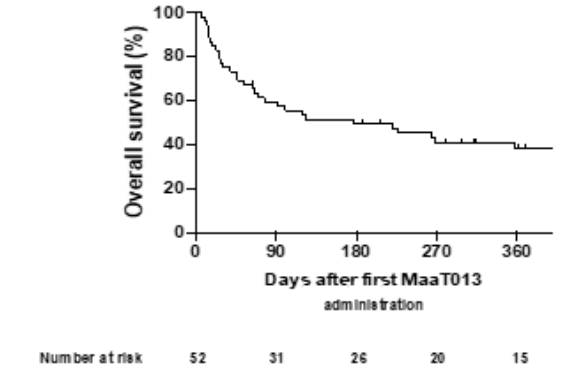
Il prodotto farmacologico MaaT013

L'azienda MaaT Pharma ha sviluppato, MaaT013, un microbiota intestinale bioterapeutico allogenico, costituito da un intero ecosistema derivato da donatori sani, rigorosamente controllati e selezionati e reso disponibile ai pazienti con aGVHD in Francia attraverso uno specifico programma di accesso anticipato (Early Access Program)

01	Characteristics	**Pooled microbiota:** high-richness, high-diversity, full ecosystem Microbiome Therapy containing Butycore® **Non immunosuppressive treatment**
02	Current indication	**Acute Graft-vs-Host Disease with Gastrointestinal Involvement** ~ 3k patients per year
03	Efficacy evaluation in EAP	**28-Days GI-ORR:** 52% **12-months OS:** 47% **18-months OS:** 42% **Data in all patients (n=140)**
04	Available Clinical Data	**HERACLES Phase 2** Clinical Trial, N=24, 2L **ARES Phase 3 – Ongoing -** Positive **DSMB** review (n= 30) – 3L **Ongoing Early Access Program (EAP),** N > 140, prior treatment median 2 (range 1-6) **> 250** patients treated to date
05	Administration	**3 doses** (enema bag) – within 10 days



Heracles



EAP

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Caso clinico

Età 13 anni - Sesso M
Diagnosi di Anemia di Blackfan-Diamond in regime trasfusionale cronico
2024: **Trapianto allogenico di cellule staminali emopoietiche da donatore volontario non consanguineo HLA-identico**.

GvHD acuta persistente di grado IV complessivo (intestinale stadio 4) steroido-refrattaria, non resposiva a:

→ Terapia di prima linea
STEROIDE
→ Terapia di seconda linea
RUXOLITINIB
→ Terapia di terza linea
AFERESI TERAPEUTICA (FEC)

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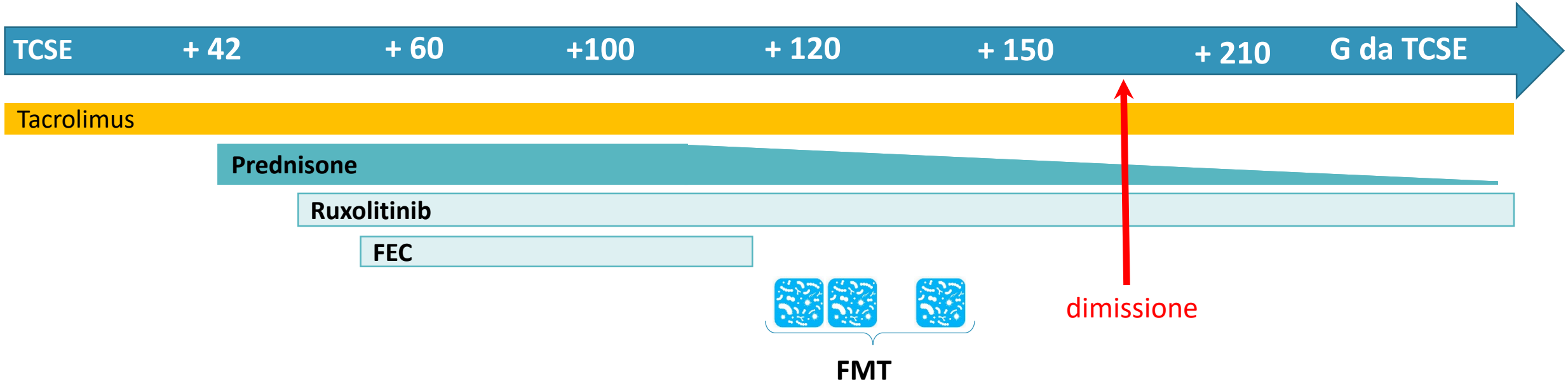
Trapianto di microbiota con il prodotto farmacologico MaaT013

MaaT013

MaaT013 è utilizzabile solo per uso rettale
MaaT013 150 ml è stato somministrato una volta alla settimana per un massimo di 3 settimane (con 7 giorni di intervallo tra le somministrazioni).
Ad ogni somministrazione devono essere somministrati 150 ml di sospensione tutti in una volta.
Gli antibiotici sono stati sospesi circa 12 ore prima dall'infusione.



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Grazie per l’attenzione

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Gruppo multidisciplinare di ricerca sul microbiota umano

Ruolo della S.C. Dietetica e Nutrizione Clinica

Dr.ssa Valentina Da Prat

Direttore: Dott. Riccardo Caccialanza

1. POTENZIALE RUOLO DELLA S.C. DIETETICA E NUTRIZIONE CLINICA NEGLI STUDI CHE PREVEDONO L'ANALISI DEL MICROBIOTA FECALE

A. **QUANTIFICAZIONE DELLE VARIABILI LEGATE ALLA DIETA**
   - Aderenza alla dieta mediterranea (score validati)
   - Consumo di nutrienti specifici (fibre solubili, fibre insolubili, glutine, ecc.)

B. **ELABORAZIONE DI PIANI DIETETICI** FINALIZZATI A RIDURRE LE DIFFERENZE DI MAGGIORE IMPATTO SULL'ALIMENTAZIONE (ES. COUNSELING PER DIETA MEDITERRANEA/A CONTENUTO CONTROLLATO DI FIBRA)

C. **VALUTAZIONE DELLO STATO NUTRIZIONALE** (BASELINE/VARIAZIONI)

D. **VALUTAZIONE DELLA COMPOSIZIONE CORPOREA** (BASELINE/VARIAZIONI) MEDIANTE BIOIMPEDENZIOMETRIA E/O ANALISI IMMAGINI TC + **DIAGNOSI DI SARCOPENIA** (DINAMOMETRIA)

2. STUDI PROMOSSI DALLA S.C. DIETETICA E NUTRIZIONE CLINICA COMPRENDENTI L'ANALISI DEL MICROBIOTA FECALE

A. **IN PASSATO →** LIMITI LOGISTICI/METODOLOGICI

B. **IN FUTURO →** POTENZIALE ENDPOINT IN:

- **STUDI SU ALIMENTI A FINI MEDICI SPECIALI/INTEGRATORI** (es. immunonutrizione in pazienti in trattamento immunoterapico, supplementi nutrizionali orali in trapianto di cellule staminali emopoietiche, ecc)

- **STUDI SU TRATTAMENTO DIETETICO** (es. fibromialgia)

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ATS Pavia

GRAND ROUNDS CLINICI DEL MERCOLEDÌ

con il Policlinico San Matteo

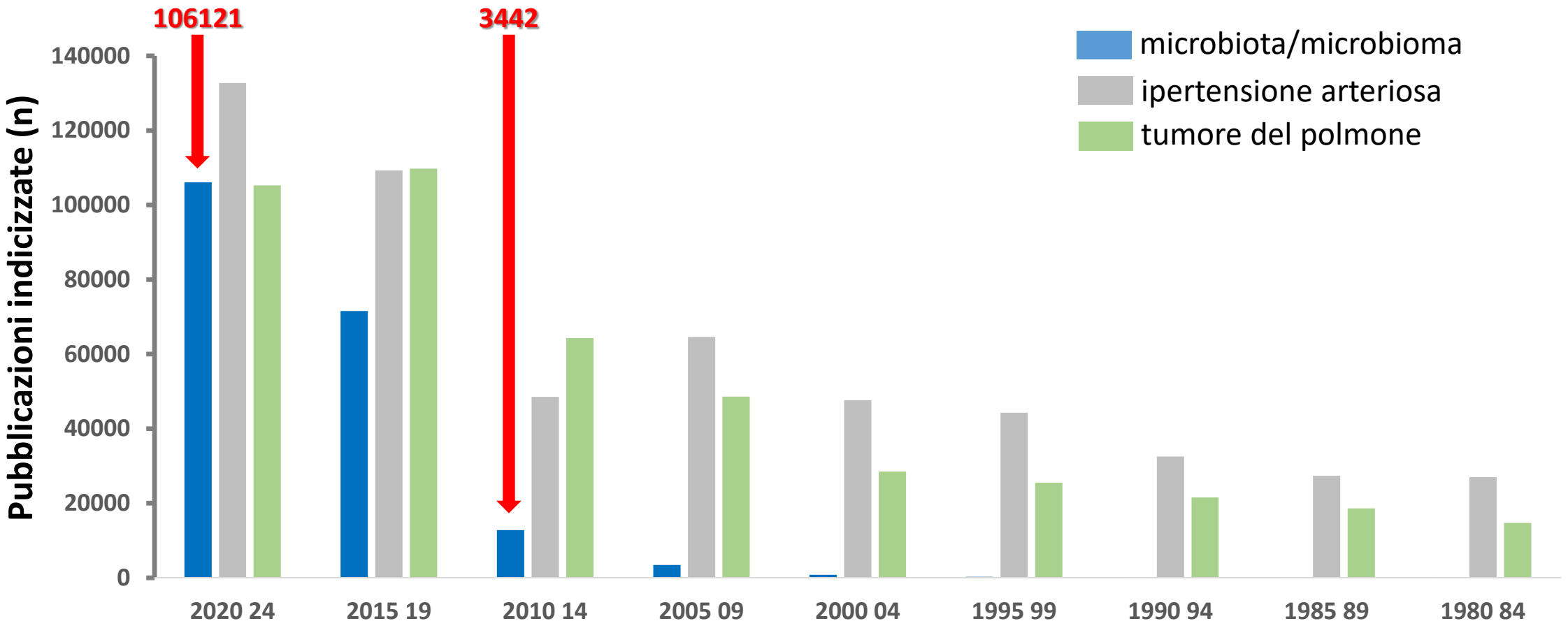
Aula Magna "C. Golgi" & WEBINAR

Il ruolo del microbiota in fisiopatologia e terapia: un modello per un approccio clinico e scientifico multidisciplinare

Michele Di Stefano

30.10.2024

NUMERO DI PUBBLICAZIONI REPERIBILI SU PUBMED NEL PERIODO 1980-2024



IL MICROBIOTA UMANO: UN TOPIC MULTIDISCIPLINARE COME POCHI ALTRI

- **MICROBIOTA UMANO**

MICROBIOTA, IBS, IBD, STEATOSI, OBESITA' IN PUBMED

Microbiota and IBS	1636 papers
Microbiota and IBD	4190 papers
Microbiota and Steatosis	4547 papers
Microbiota and Obesity	10200 papers

20573 papers

AGGIORNAMENTO E PLETORA DI INFORMAZIONI

Difficoltà oggettiva nell'aggiornamento continuo su un tema trasversale

↓

Necessità di focalizzarsi su alcuni aspetti di interesse specifico

↓

Integrazione delle conoscenze tra diversi specialisti

UN BRAIN STORMING PROGRESSIVAMENTE PIU ALLARGATO…

Idea in forma embrionale condivisa con un piccolo gruppo di colleghi internisti

→

Condivisione con colleghi di altre discipline già coinvolti nella ricerca sul microbiota

→

Valutazione della fattibilità e dell'interesse teoricamente evocabile in colleghi di altre discipline

Coinvolgimento della Direzione Scientifica Aziendale

→

Definizione di uno spazio di confronto in occasione di un "Grand Round"

→

Condivisione del progetto con i colleghi di altre discipline

LE CARATTERISTICHE DEL GRUPPO

Il gruppo è:

- aperto
- indipendente
- multidisciplinare

Il gruppo:

- si finanzia con application a bandi interni ed esterni
- non intende dettare alcuna linea di indirizzo della ricerca in Fondazione

LA SCELTA DI PROPORRE UN PROTOCOLLO DI RICERCA AL GRUPPO E' FACOLTATIVA

LE 15 UNITA' OPERATIVE ADERENTI AL PROGETTO AD OGGI

-Dr. Riccardo Albertini, *UOC Laboratorio Analisi Chimico-Cliniche*
-Prof. Andrea Anderloni, *UOC Gastroenterologia*
-Prof. Luca Arcaini, *UOC Ematologia*
-Prof. Fausto Baldanti, *UOC Microbiologia e Virologia*
-Prof.ssa Natascia Brondino, *UOC Psichiatria ASST Pavia*
-Prof. Raffaele Bruno, *UOC Malattie Infettive*
-Prof. Riccardo Caccialanza, *UOC Dietetica e Nutrizione Clinica*
-Prof. Angelo Corsico, *UOC Pneumologia*
-Prof. Antonio Di Sabatino, *UOC Medicina Interna*
-Dr. Stefano Ghirardello, *UOC Neonatologia e Terapia Intensiva Neonatale*
-Prof. Gian Luigi Marseglia, *UOC Pediatria*
-Prof. Paolo Pedrazzoli, *UOC Oncologia*
-Prof. Giovanni Sarnelli, *UOC Gastroenterologia, Università Federico II, Napoli*
-Prof. Arsenio Spinillo, *UOC Ginecologia ed Ostetricia*
-Prof. Marco Zecca, *UOC Onco-Ematologia Pediatrica*

- ……..
- ……..
- ……..

ALCUNI INTERVENTI PROGRAMMATI

-Prof.ssa Natascia Brondino, *UOC Psichiatria ASST Pavia*

-Dr.ssa Chiara Cavagnoli, *UOC Ginecologia e Ostetricia*

-Dr.ssa Francesca Compagno, *UOC Onco-Ematologia Pediatrica*

-Dr.ssa Valentina Da Prat, *UOC Dietetica e Nutrizione Clinica*

-Dr.ssa Angioletta Lasagna, *UOC Oncologia*

-Dr.ssa Emanuela Miceli, *UOC Medicina Interna*

-Dr.ssa Valentina Zuccaro, *UOC Malattie Infettive*

GRAZIE PER

LA VOSTRA

ATTENZIONE

Fondazione IRCCS Policlinico San Matteo

Sistema Socio Sanitario

Regione Lombardia

Ground Rounds Clinici del Mercoledì

Il Ruolo del Microbiota in Oncologia

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Fondazione IRCCS Policlinico San Matteo

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Gut microbiota (GM) and Breast Cancer (BC)

pathogens MDPI

Article

The Bio-Diversity and the Role of Gut Microbiota in Postmenopausal Women with Luminal Breast Cancer Treated with Aromatase Inhibitors: An Observational Cohort Study

Angioletta Lasagna [1,*], Mara De Amici [2], Chiara Rossi [3], Valentina Zuccaro [4], Marta Corbella [5], Greta Petazzoni [5], Francesco Comandatore [6], Lucia Sacchi [7], Giorgia Testa [8], Elisa Ferraris [1], Gianpiero Rizzo [1], Richard Tancredi [1], Alessandra Ferrari [1], Marco Lucioni [3], Paolo Sacchi [4], Raffaele Bruno [4,9] and Paolo Pedrazzoli [1,10]

The interactions between aromatase inhibitors (AI) in BC and GM have not been completely established yet. The aim of the study is to evaluate the bio-diversity of GM and the relationship between GM, inflammation and tumor-infiltrating lymphocytes (TILs) in postmenopausal women with BC during adjuvant AI treatment compared to women with disease relapse during or after one year of AI therapy (“endocrine-resistant”). We conducted a monocenter observational case-control study

84 women with BC (8 cases, 76 controls) were enrolled from 2019 to 2021. We observed a significant difference in the mean microbial abundance between the two groups for the taxonomic rank of order (p 0.035) and family (p 0.029).

The *Veillonella* family was the most abundant in our case group (p 0.022): it is able of producing the genus-producing GUS enzymes leading to increasing levels of free estrogens.

We obtained a statistically significant difference (p 0.045) in IL-17 levels among the groups, with patients with low TILs levels showing a higher median value for IL-17 (0.15 vs. 0.08 pg/mL)

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RC 2023: Gut microbiota (GM) biodiversity in patients with solid tumors treated with immune checkpoint inhibitors (ICIs): a monocenter prospective study to identify the interactions between GM and ICIs

The compositional and functional alterations in GM lead to the intestinal barrier breakage with an increased translocation of toxins and inflammatory factors that may be able to alter dynamically the immunological profile in a pro-inflammatory direction. Most of the studies focused on the baseline GM composition as a predictive marker of response to ICIs and of the occurrence of ICI-induced immune-related adverse events (irAEs). Few studies have tried to evaluate the relationship between GM and ICIs in patients with cancer via the dynamic analysis of the GM

Our project aims to investigate **the dynamic modification of the biodiversity** in the same subject and its relationship with ICIs

The **samples (stool and blood) and the clinical data, including nutritional variables, will be obtained from the patients at these time-points**:

T0 = at the start of ICIs

T1 = after 3/4 weeks

T2 = after 12 weeks

T3 = after 24 weeks

T4 = in the case of progression disease/onset of irAEs

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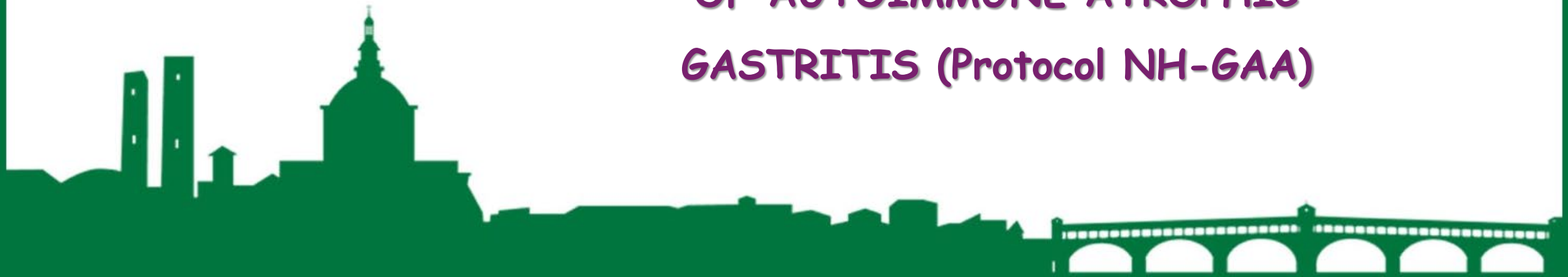
con il Policlinico San Matteo

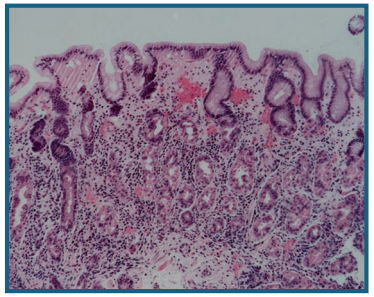
Aula Magna "C. Golgi" & WEBINAR

NATURAL HISTORY, EVOLUTION, AND CLINICAL FEATURES OF AUTOIMMUNE ATROPHIC GASTRITIS (Protocol NH-GAA)



AUTOIMMUNE ATROPHIC GASTRITIS (AAG)

- organ-specific immunomediate disease
- slowly progressive
- stomach corpus/fundus atrophy



Hypo-achlorhydria
IF deficiency

→ micronutrients deficiency → Vitamin B12, Iron, Calcium

→ ↑ Gastrin & Chromogranin A

Modification of intestinal microbiota composition according to the severity of gastric acid secretion impairment and the different clinical patterns

Total DNA from stool samples will be processed with:

- ✓ **QIAamp PowerFecal Pro DNA Kit**
- ✓ **Shotgun Sequencing**

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30 ottobre 2024
ore 13.00 - 14.00

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Il ruolo del microbiota in fisiopatologia e terapia: un modello per un approccio clinico e scientifico multidisciplinare

Completed Activities and Future Goals

Infectious Diseases Departement, IRCCS Fondazione San Matteo di Pavia
Dipartimento di Scienze Clinico-Chirurgiche, Diagnostiche e Pediatriche, Università di Pavia

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Overview of Completed Activities GM & CDI

BACKGROUND

Antibiotic therapy is recognized as a risk factor and exacerbates dysbiosis of the intestinal microbiota, whose role in CDI is increasingly acknowledged.

Disruption in microbiota composition is profound in patients with rCDI who have received multiple antibiotic courses

To characterize the fecal microbiota of CDI and rCDI patients (sampled at initial and recurrent episode) and of non-infected controls

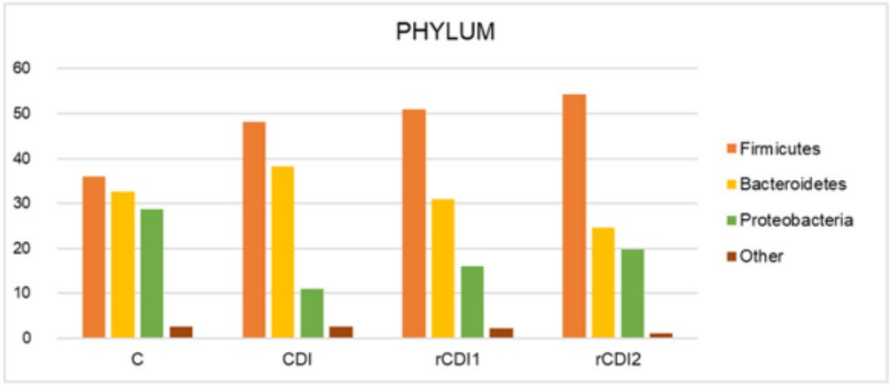
to establish if differential microbiota signatures may be associated with the severity of the infection.

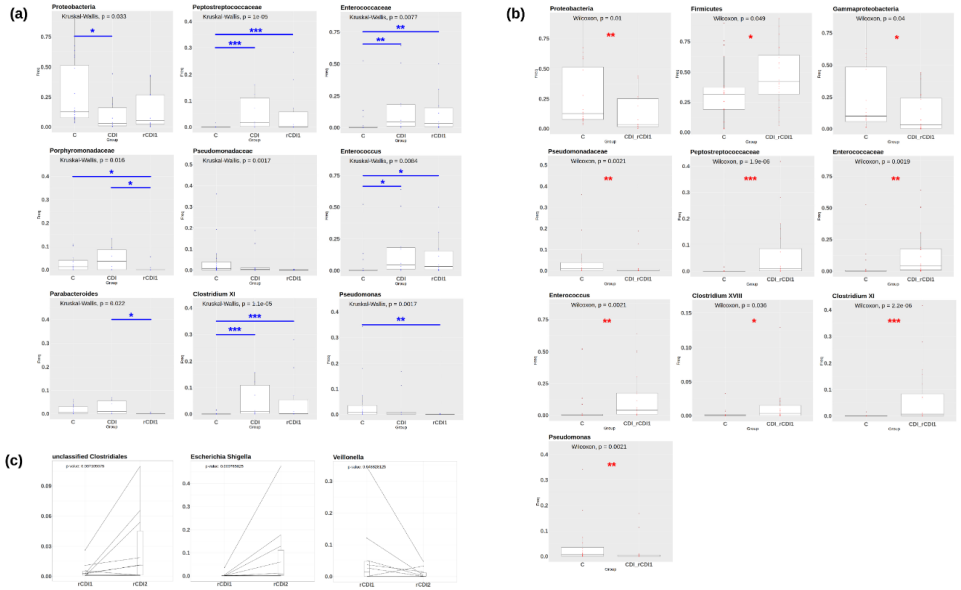
biomedicines
MDPI

Article

Microbiota in *Clostridioides difficile*-Associated Diarrhea: Comparison in Recurrent and Non-Recurrent Infections

Alessandra Gazzola [1,2], Simona Panelli [3,*], Marta Corbella [4], Cristina Merla [4], Francesco Comandatore [3], Annalisa De Silvestri [5], Antonio Piralla [4], Valentina Zuccaro [1], Claudio Bandi [6], Piero Marone [4] and Patrizia Cambieri [4]





total of 40 subjects : 10 cases of single CID, 10 of recurrent infection (rCDI), for which samples collected at both first (rCDI1) and second (rCDI2) episode of diarrhea were available; 20 subjects, tested for being non-infected by CDI, age- and sex-matched, served as controls (C)

Results

- CID is accompanied by a decrease in biodiversity indexes compared to non-infected controls, with a maximum (and statistical significance) in recurrent patients
- severity of a CID, calculated based on the widely used Zar score, does not correlate either with a peculiar microbiota composition, or with a significant reduction in its diversity. I

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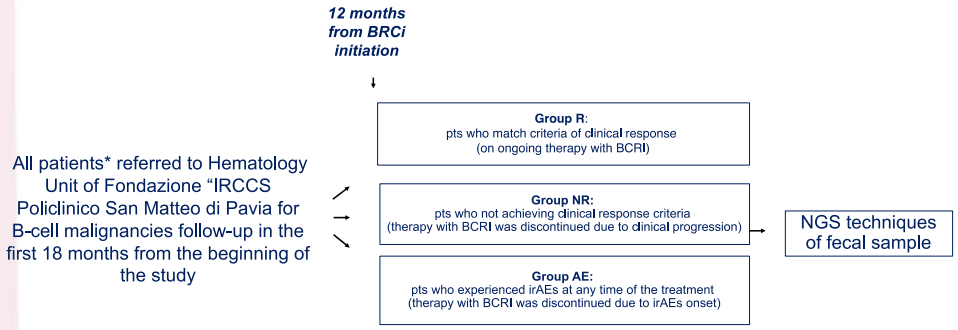
Overview of Completed Activities GM & Cancer

BACKGROUND

Targeted therapies including B-cell receptor (BCR) inhibitors (BCRi) represent the newest approach to the treatment of CLL: not all patients achieve a satisfactory response, and immune-related adverse events (irAEs) can also impact the efficacy.

We hypothesize that the BCRi could be influenced by distinct GM compositions or modifications during treatment, by microbial translocation or by the type of immunotherapy.

CROSS SECTIONAL EXPLORATORY INVESTIGATION



OBJECTIVES

- compare patients (belonging to one of the three diagnoses) with/out clinical response in terms of enterotypes
- compare patients with/out irAEs in terms of enterotypes
- explore patient-related factors associated to different enterotypes
- investigate which kind of clinical factors are able to influence enterotype composition

* Pts with chronic lymphocytic leukemia, mantle cell lymphoma and Waldenström macroglobulinemia who underwent to BCRi therapy Btk- and PI3K-inhibitors

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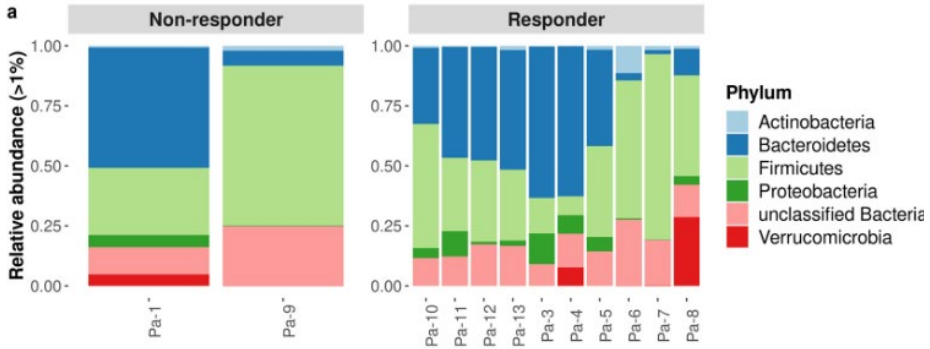
microorganisms

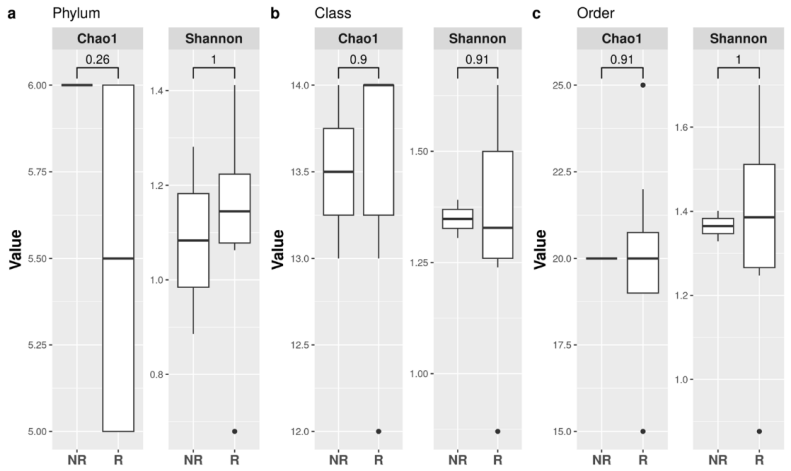
MDPI

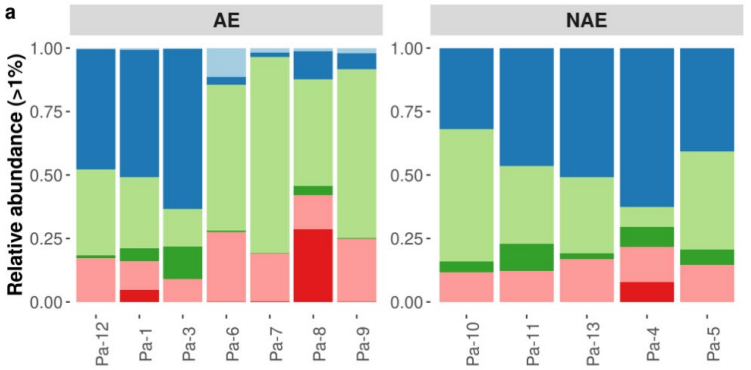
Article

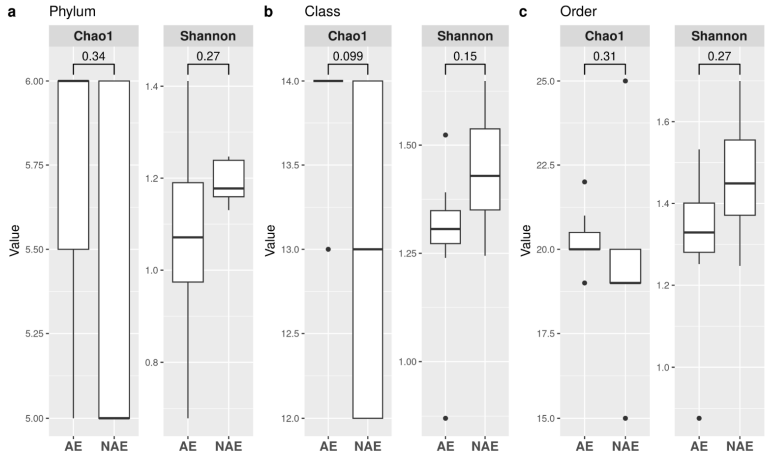
Gut Microbiota and B Cell Receptor (BCR) Inhibitors for the Treatment of Chronic Lymphocytic Leukemia: Is Biodiversity Correlated with Clinical Response or Immune-Related Adverse Event Occurrence? A Cross-Sectional Study

Valentina Zuccaro [1,*], Greta Petazzoni [2,3], Irene Mileto [2], Marta Corbella [2], Erika Asperges [1], Paolo Sacchi [1], Sara Rattotti [4], Marzia Varettoni [4], Irene Defrancesco [3,4], Patrizia Cambieri [2], Fausto Baldanti [2,3], Luca Arcaini [4,5] and Raffaele Bruno [1,3]









Results

we did not observe a significant difference across the study population in terms of relative abundance and alpha and beta diversity BUT we found a signatures across analyzed groups in terms of taxa

Overview of Completed Activities GM & Cancer

pathogens MDPI

Article

The Bio-Diversity and the Role of Gut Microbiota in Postmenopausal Women with Luminal Breast Cancer Treated with Aromatase Inhibitors: An Observational Cohort Study

Angioletta Lasagna [1,*], Mara De Amici [2], Chiara Rossi [3], Valentina Zuccaro [4], Marta Corbella [5], Greta Petazzoni [5], Francesco Comandatore [6], Lucia Sacchi [7], Giorgia Testa [8], Elisa Ferraris [1], Gianpiero Rizzo [1], Richard Tancredi [1], Alessandra Ferrari [1], Marco Lucioni [3], Paolo Sacchi [4], Raffaele Bruno [4,9] and Paolo Pedrazzoli [1,10]

CROSS SECTIONAL EXPLORATORY INVESTIGATION

All postmenopausal women with luminal breast cancer HER2-negative undergoing adjuvant hormonal treatment with AI since at least three years therapy at the Medical Oncology Unit of Fondazione IRCCS Policlinico San Matteo Pavia

- ***Cases:*** patients who documented disease relapse during AI therapy or within 12 months of completing adjuvant AI
- ***Controls:*** patients who did not experienced relapse

→ NGS techniques of fecal sample

→ CD14, PGE and IL17 concentrations on blood sample*

OBIECTIVES

to assess whether the GM biodiversity differed between *cases* and *controls*

to compare TILs' levels and serum marker of immune-activation, immune-exhaustion and bacterial translocation between *cases* and *controls*

to compare the characteristic of GM according to clinicopathological features between *cases* and *controls*

* marker of immune-activation, immune-exhaustion and bacterial translocation

Overview of Future Projects
Ongoing study

Fondazione IRCCS Policlinico San Matteo
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Prevalence of Multi-Drug Resistant bacteria in long-term care facilities (PreMDRinLTCF)

Primary objective: to assess the bacterial ecology of LTCFs in the province of Pavia in terms of prevalence of ESBL Enterobacterals and CRE

Study design
This is an observational, point prevalence study

→ The stool material was collected and analysed (more than 500 stool samples)
→ Isolates will be cultured and susceptibility testing will be performed using gradient diffusion
→ to investigate the GM characteristics in order to establish if differential microbiota signatures may be associated with intestinal carriage

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Overview of Future Projects

A world of ideas

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Hepatic encefalopathy

Graft versus host diseases

MDR colonisation

MDR infections

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