



ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ

Εθνικόν και Καποδιστριακόν  
Πανεπιστήμιον Αθηνών

— ΙΔΡΥΘΕΝ ΤΟ 1837 —

ΙΑΤΡΙΚΗ ΣΧΟΛΗ

# «Νεότερα δεδομένα στο ρόλο του μικροβιώματος στον καρκίνο»

*Μ. Γαζούλη, Καθηγήτρια, Ιατρική Σχολή, ΕΚΠΑ*

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## ❖ **What is the microbiome?**

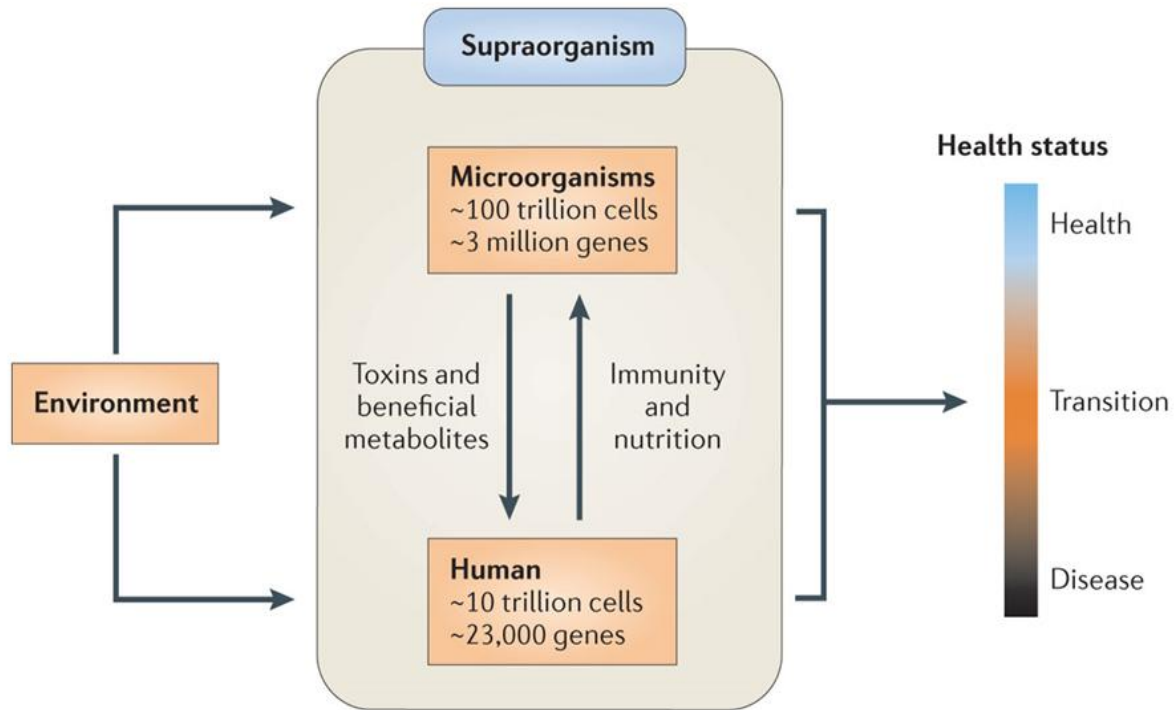
A microbiome is the collection of genomes from all the microorganisms found in a particular environment.

## ❖ **What is the microbiota?**

Microbiota, refers to specific microorganisms that are found within a specific environment. Microbiota can refer to all the microorganisms found in an environment, including bacteria, viruses, and fungi.



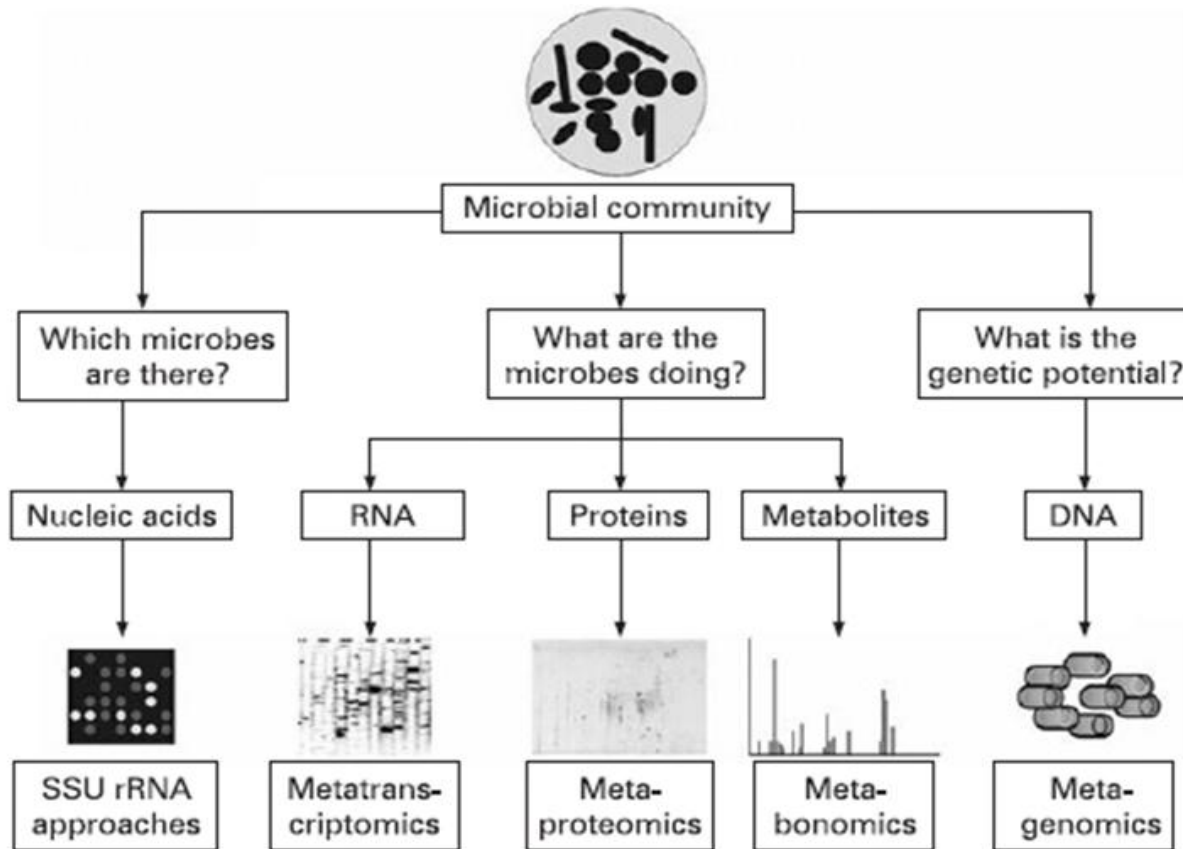
# Human-Microbiota Supraorganism



Nature Reviews | **Microbiology**

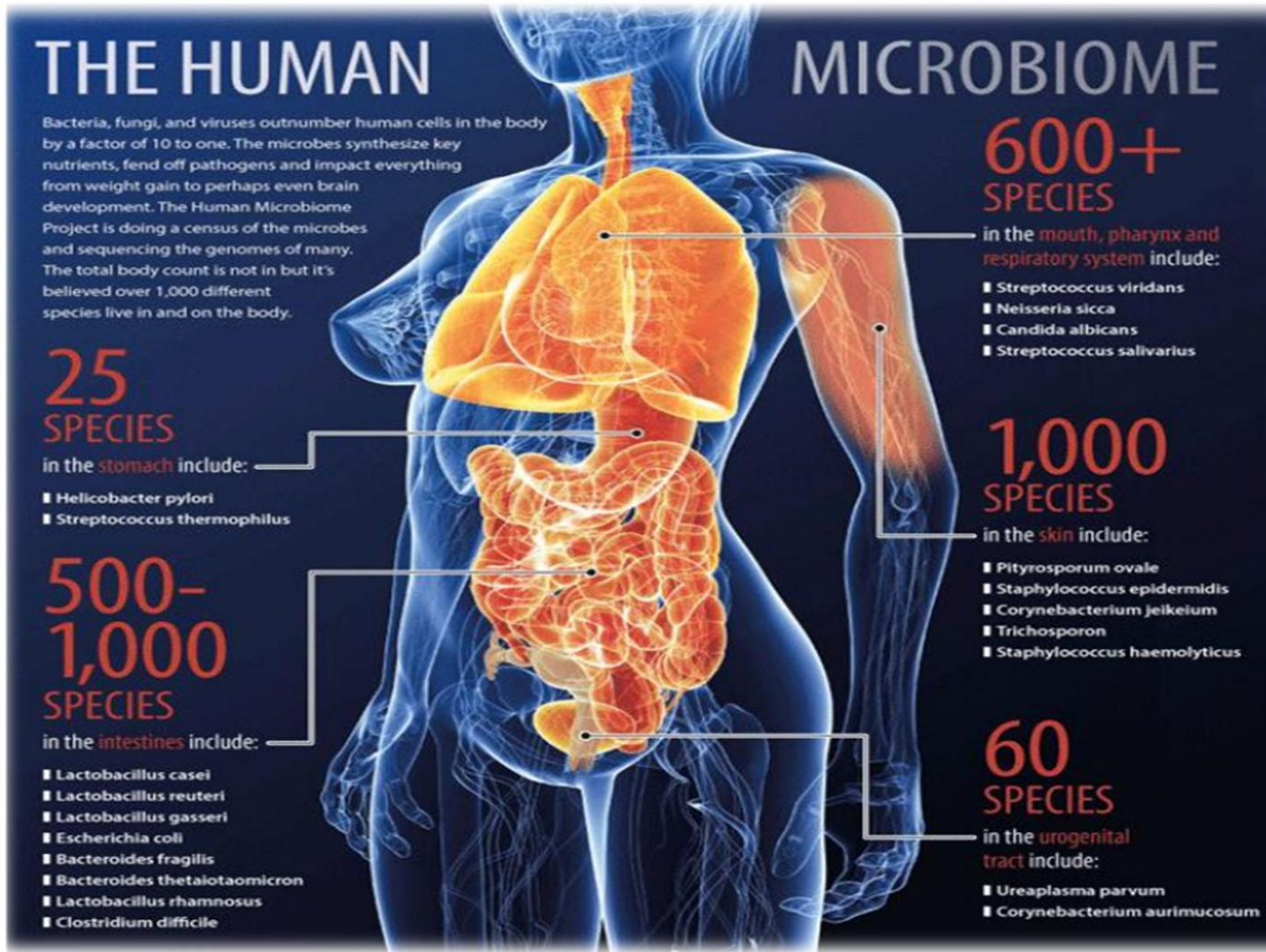
Nature Reviews Microbiology 11, 639–647 2013

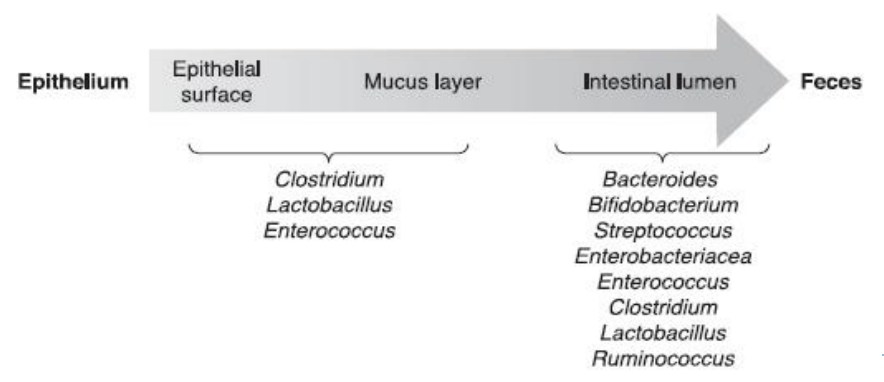
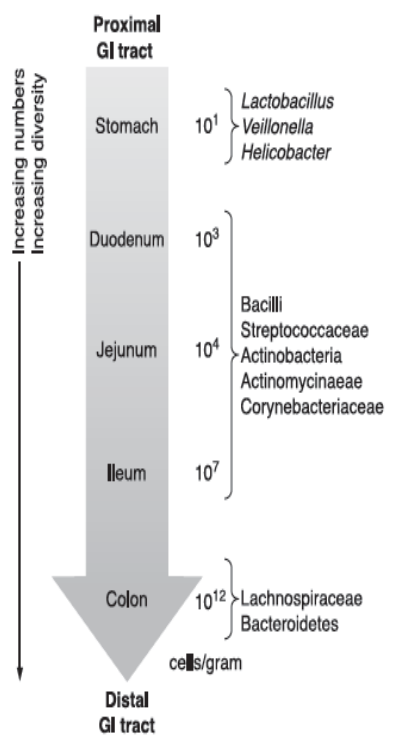
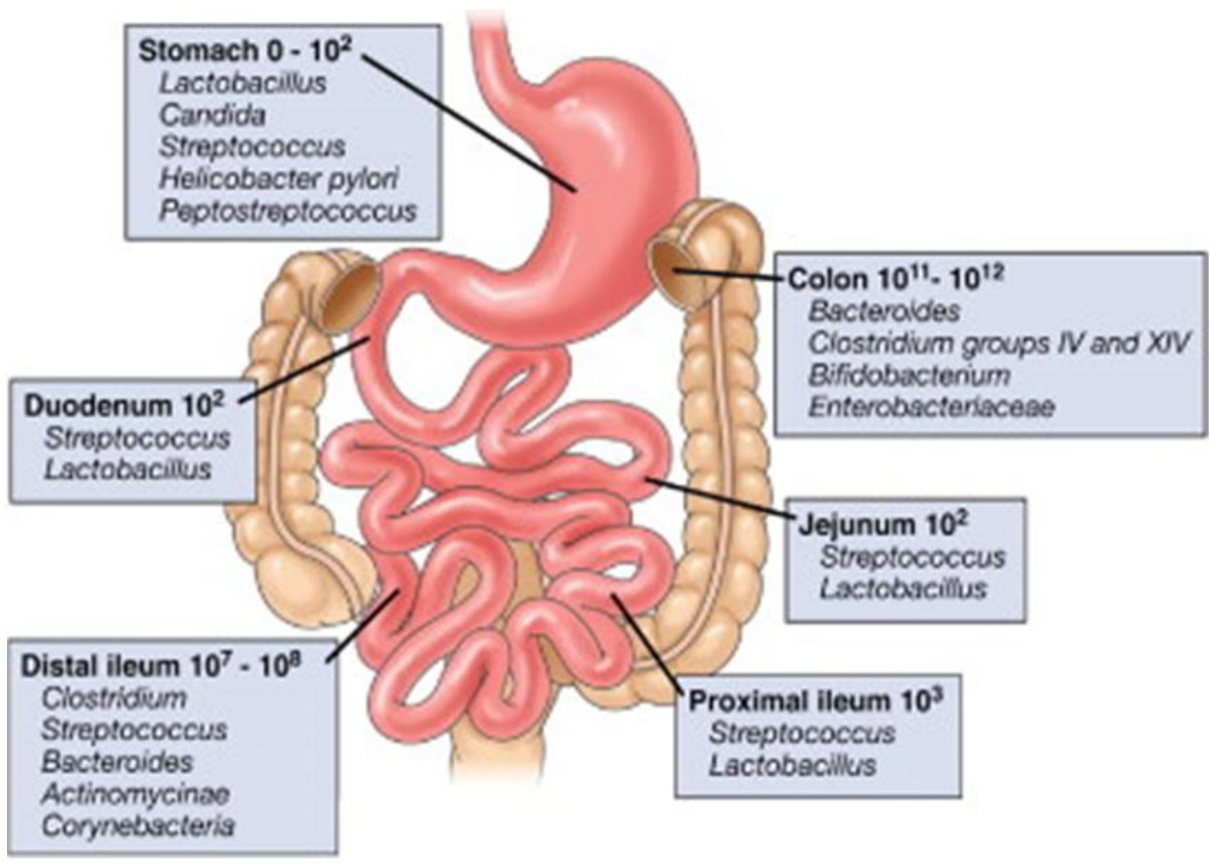
# Methods to study



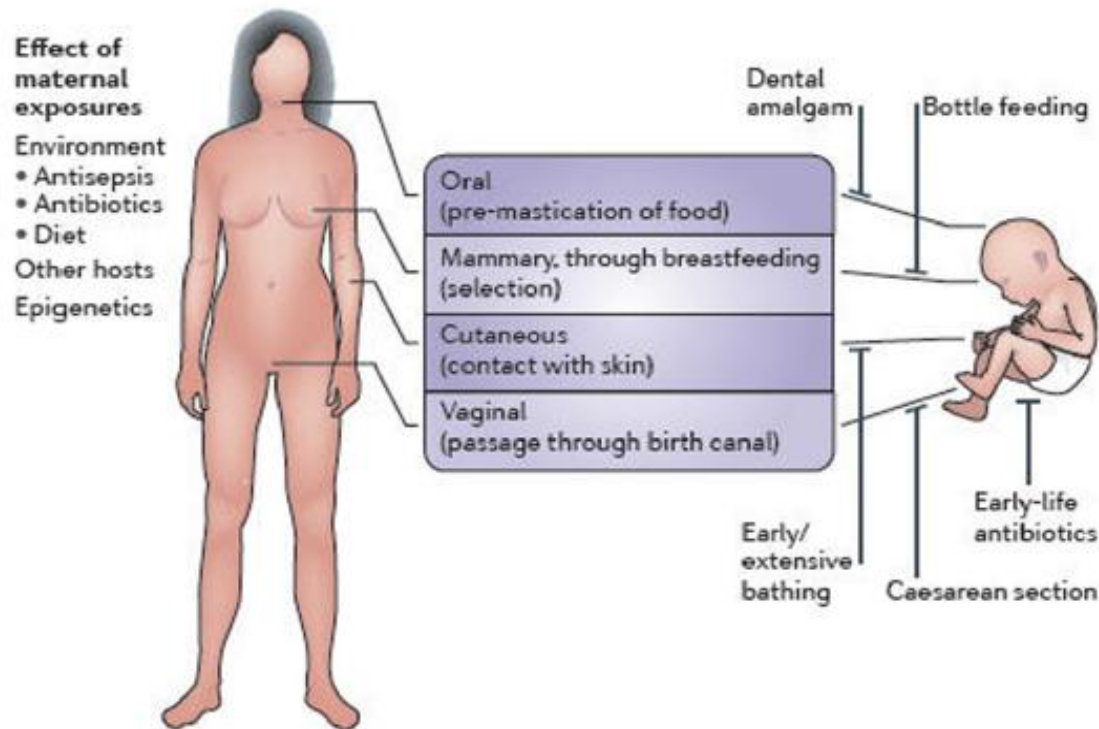
Zoetendal, Gut 2008

# Το ανθρώπινο μικροβίωμα

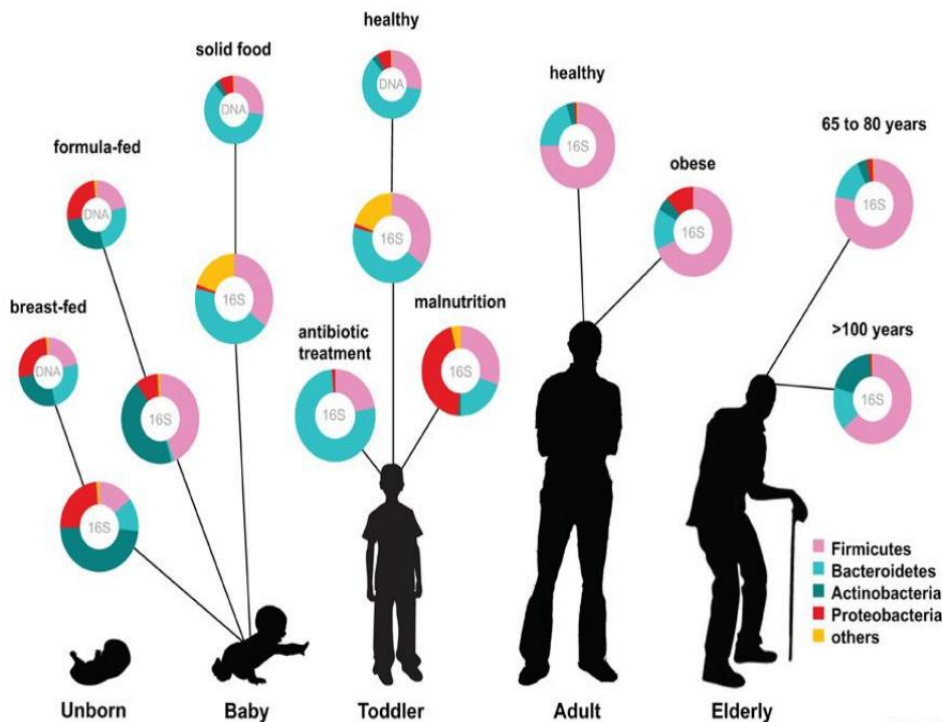




- ▶ Η αρχική έκθεση συμβαίνει κατά τον τοκετό
- ▶ Κατά τα πρώτα χρόνια ζωής επηρεάζεται από τη μητέρα και το περιβάλλον

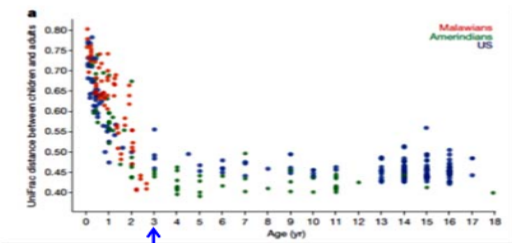


- ▶ Το μικροβίωμα σταθεροποιείται μετά τον 3 χρόνο
- ▶ Η σύνθεση συνεχίζει να επηρεάζεται από το περιβάλλον, αντιβιοτικά, διαίτα, γενετικό υπόβαθρο, φλεγμονή, υγιεινή, τρόπος ζωής



UC

### First 3 years of life – Microbiota is highly variable “The sensitive period”



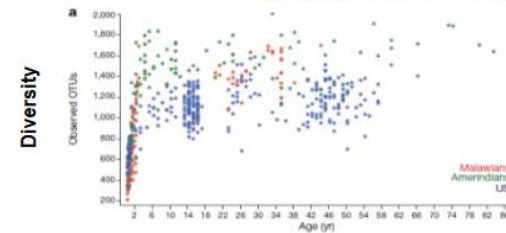
Phylogenetic composition of bacterial communities evolves toward adult composition over the first **three years of life** in all populations

Nature 486: 222, 2012

Science 331: 337, 20

### Microbiota diversity increase with age

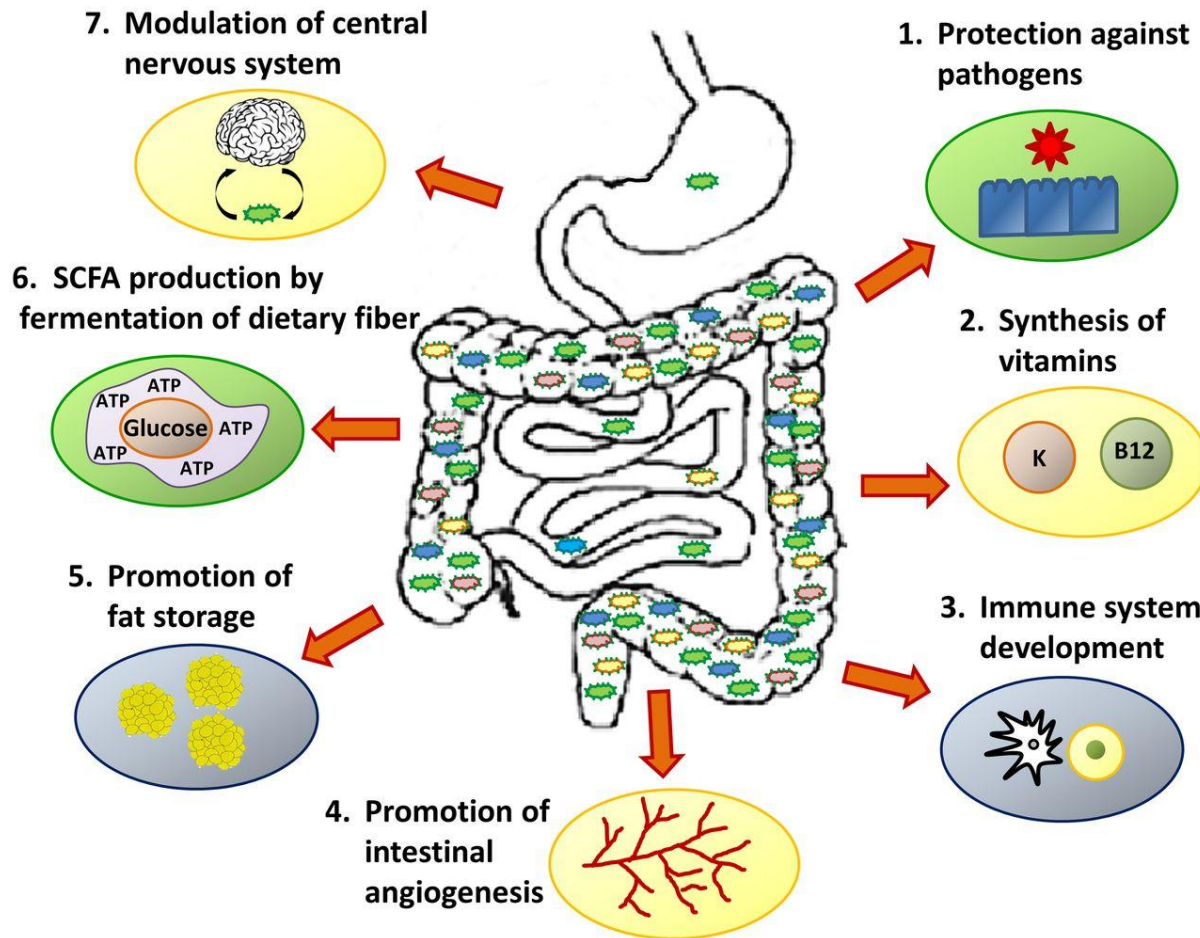
Least diverse in > 50 yr old men



Bacterial diversity increases with age in all populations.



# Λειτουργίες μικροβιώματος



# Δυσβίωση



**Balanced gut microbiota**

↓ Gut permeability;  
↓ Toxemia/Sepsis;  
↓ Proinflammation;  
↑ Insulin sensitivity;  
↑ gut/metabolic/cardiovascular health

High-fat/ high-sugar diets,  
over-nutrition, sedentary  
lifestyle, antibiotic abuse



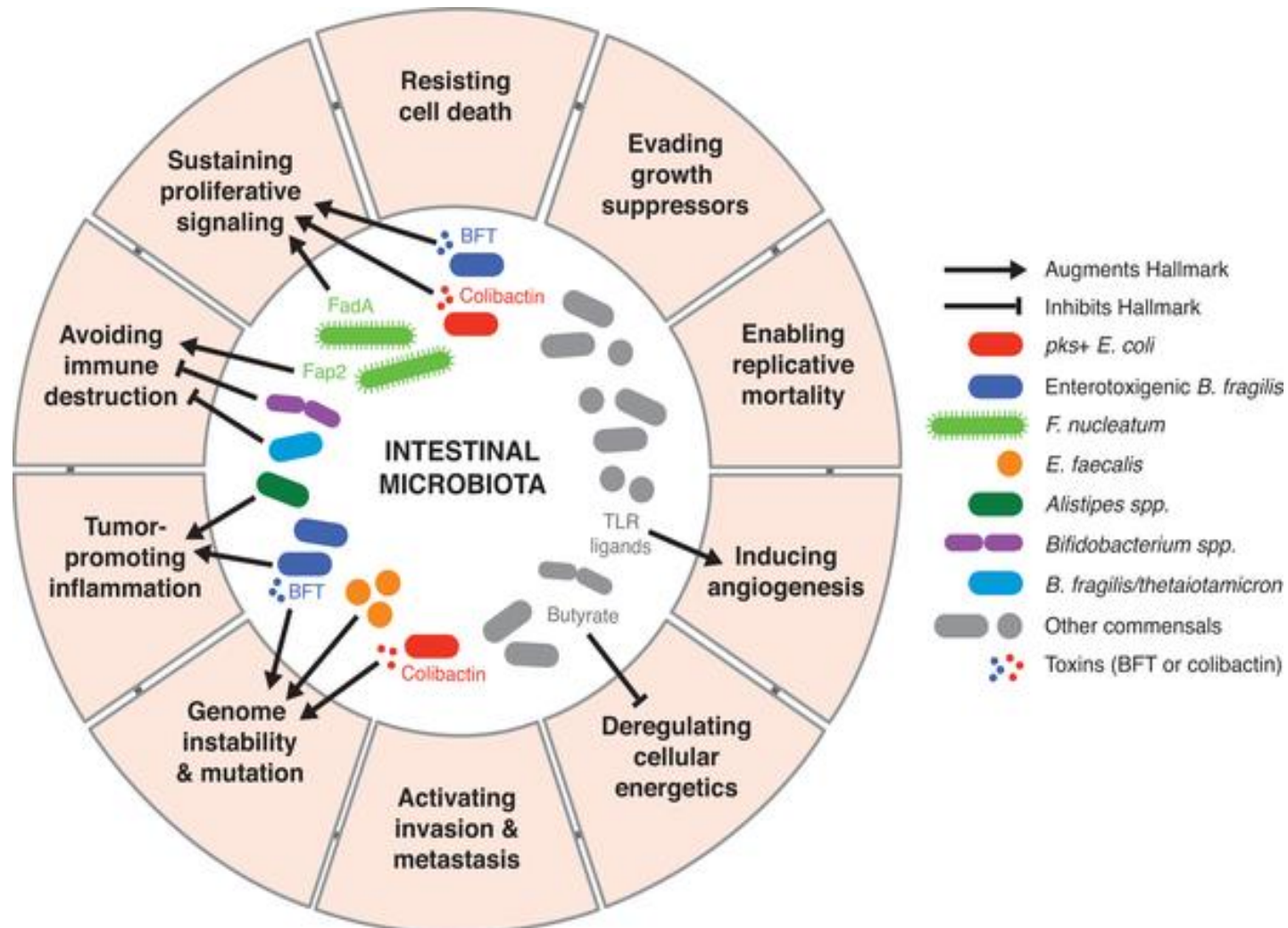
Prudent diet & lifestyle,  
probiotics/ prebiotics,  
Anti-inflammatory/  
immune-potentiating  
therapeutics, nutraceuticals



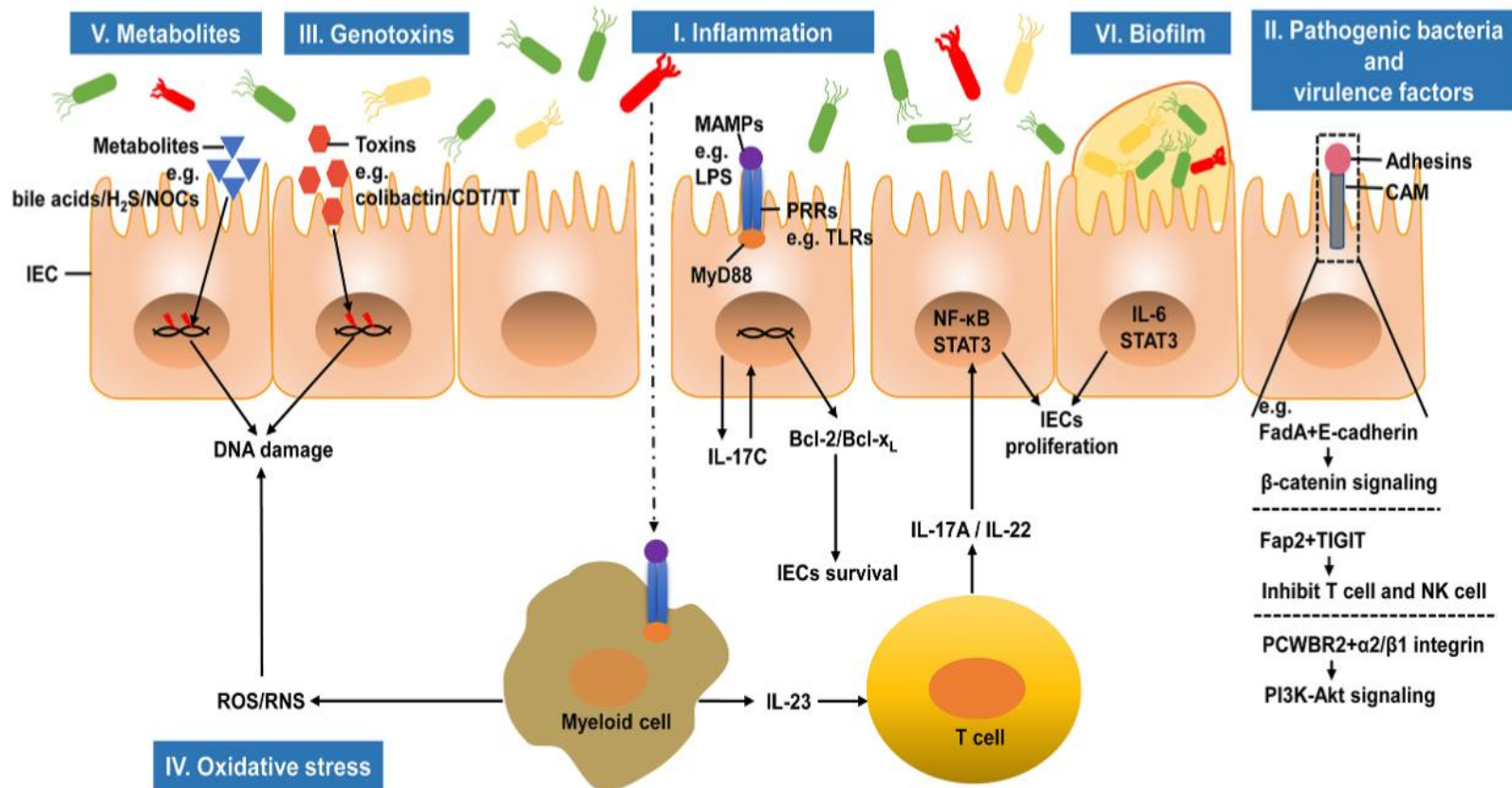
**Gut microbial dysbiosis**

↑ Gut permeability;  
↑ Endotoxemia; septicemia;  
↑ Systemic inflammation;  
↑ Insulin resistance;  
↑ Adiposity, diabetes, MetS,  
CVD, NAFLD, NASH, IBD, IBS etc.

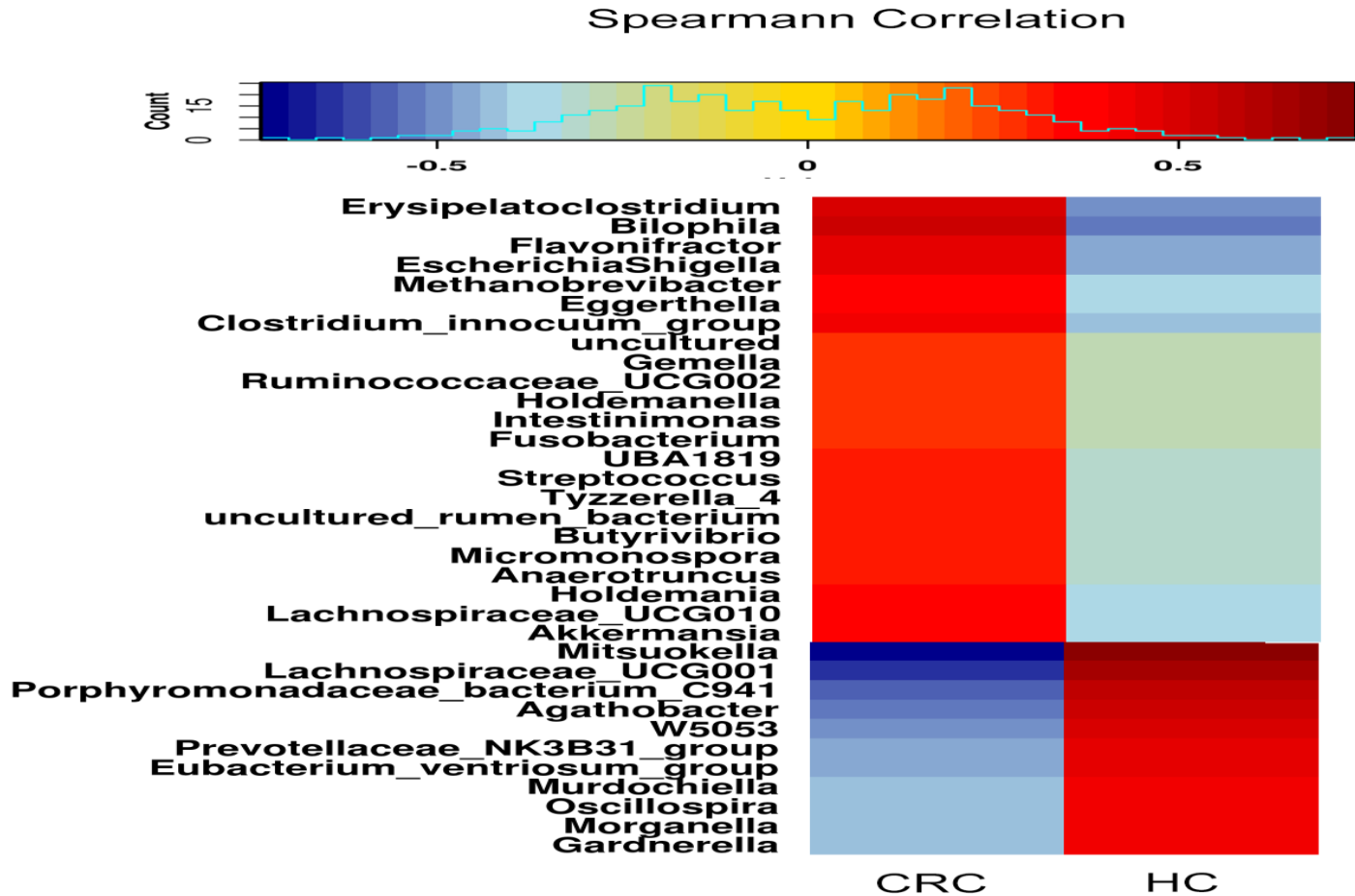
# Microbial-derived signals modulate numerous hallmarks of cancer through diverse mechanisms.



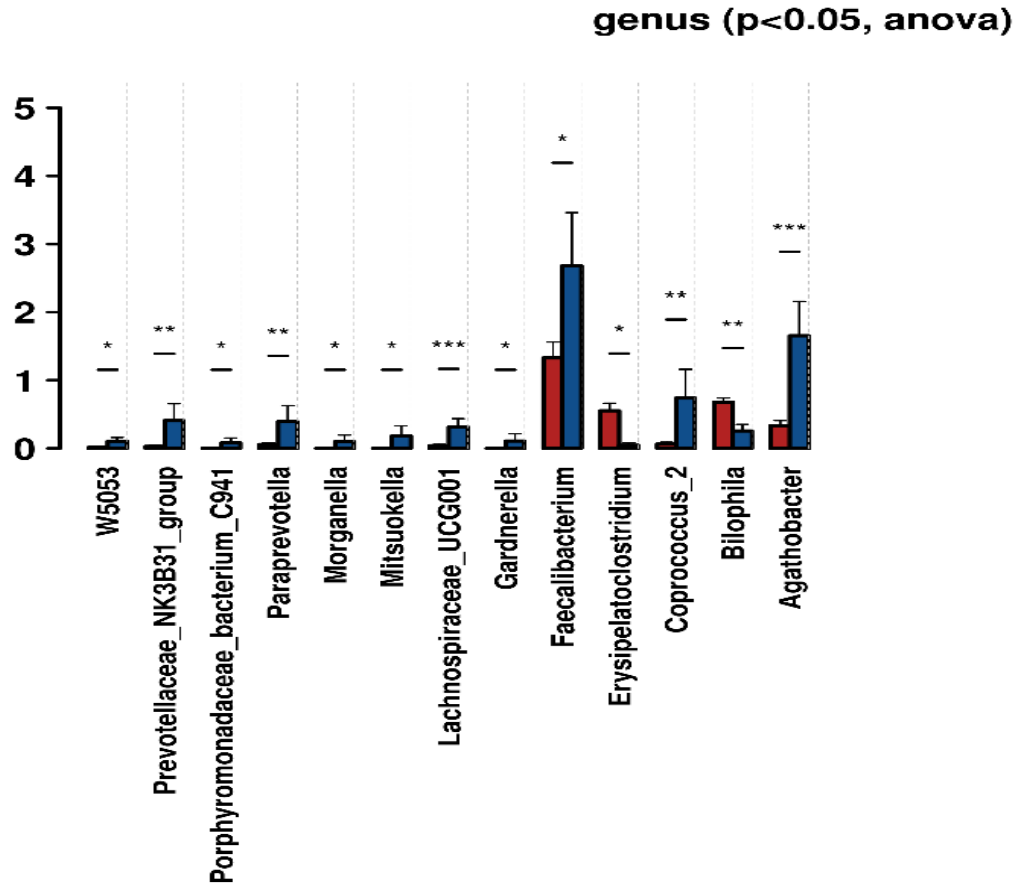
# Μηχανισμοί που σχετίζονται με το μικροβίωμα και εμπλέκονται στην παθογένεση του καρκίνου του παχέος εντέρου.



# CRC vs Healthy Theodoropoulos / Gazouli et al

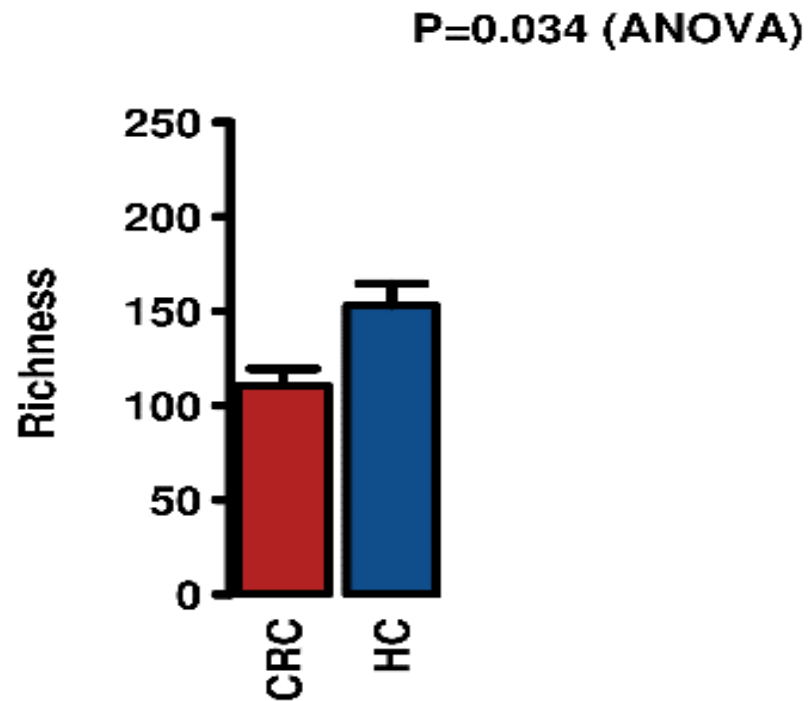


Abundance sqrt(TSS)



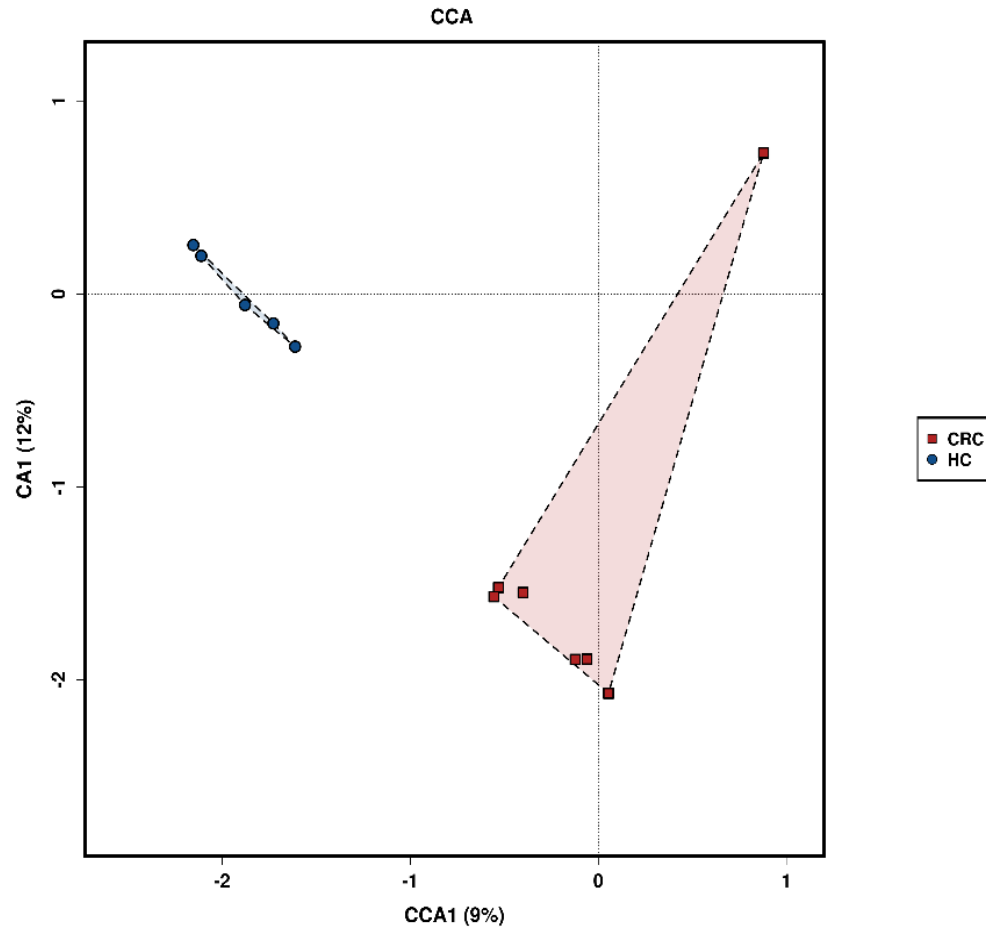
Richness is higher in HC which means that we have a loss of bacterial populations in CRC

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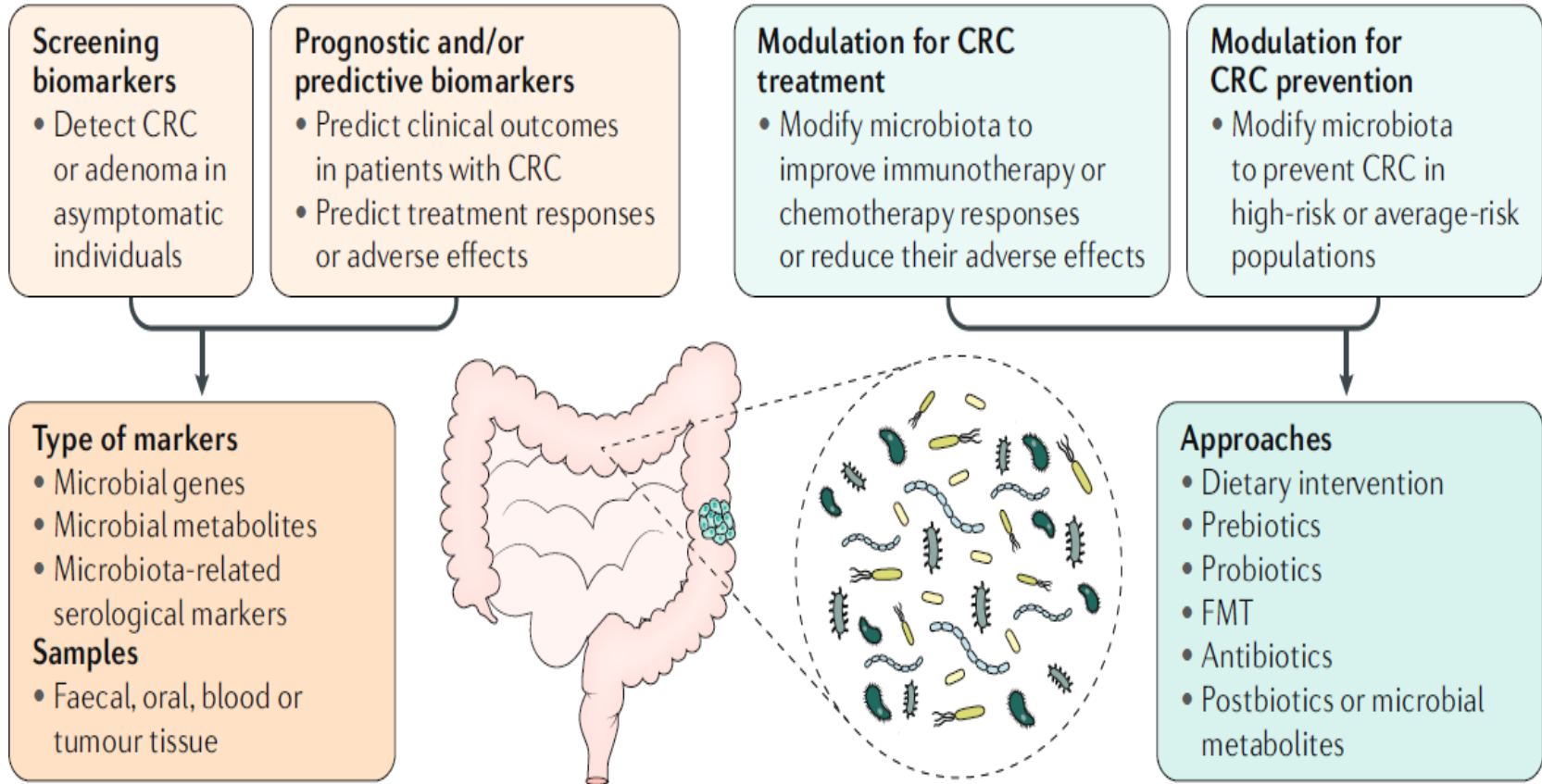
B-diversity is a qualitative measure which basically tells us how different one microbiota is from another

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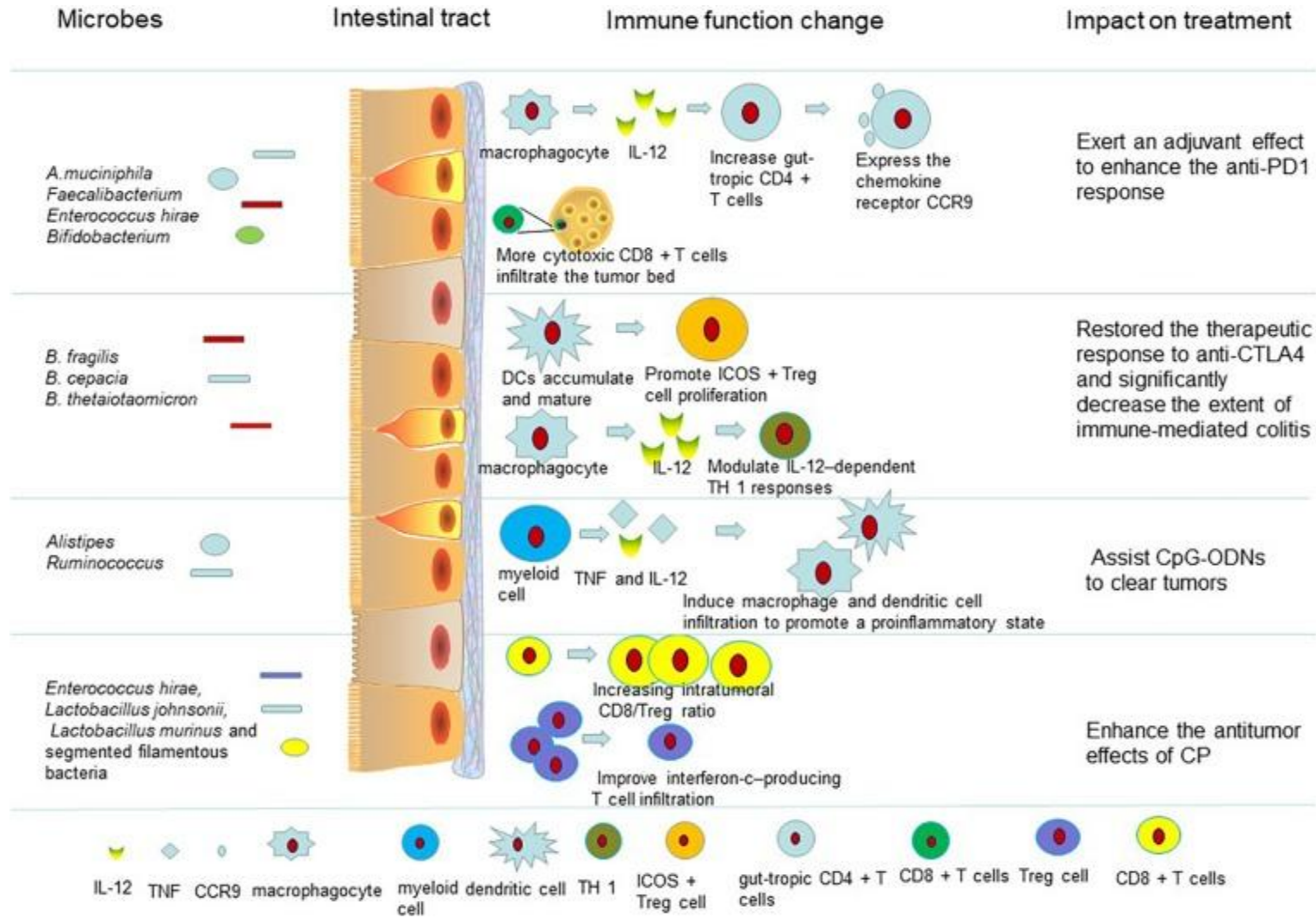




# Πιθανές κλινικές εφαρμογές



# Gut Microbiota Shapes the Efficiency of Cancer Therapy



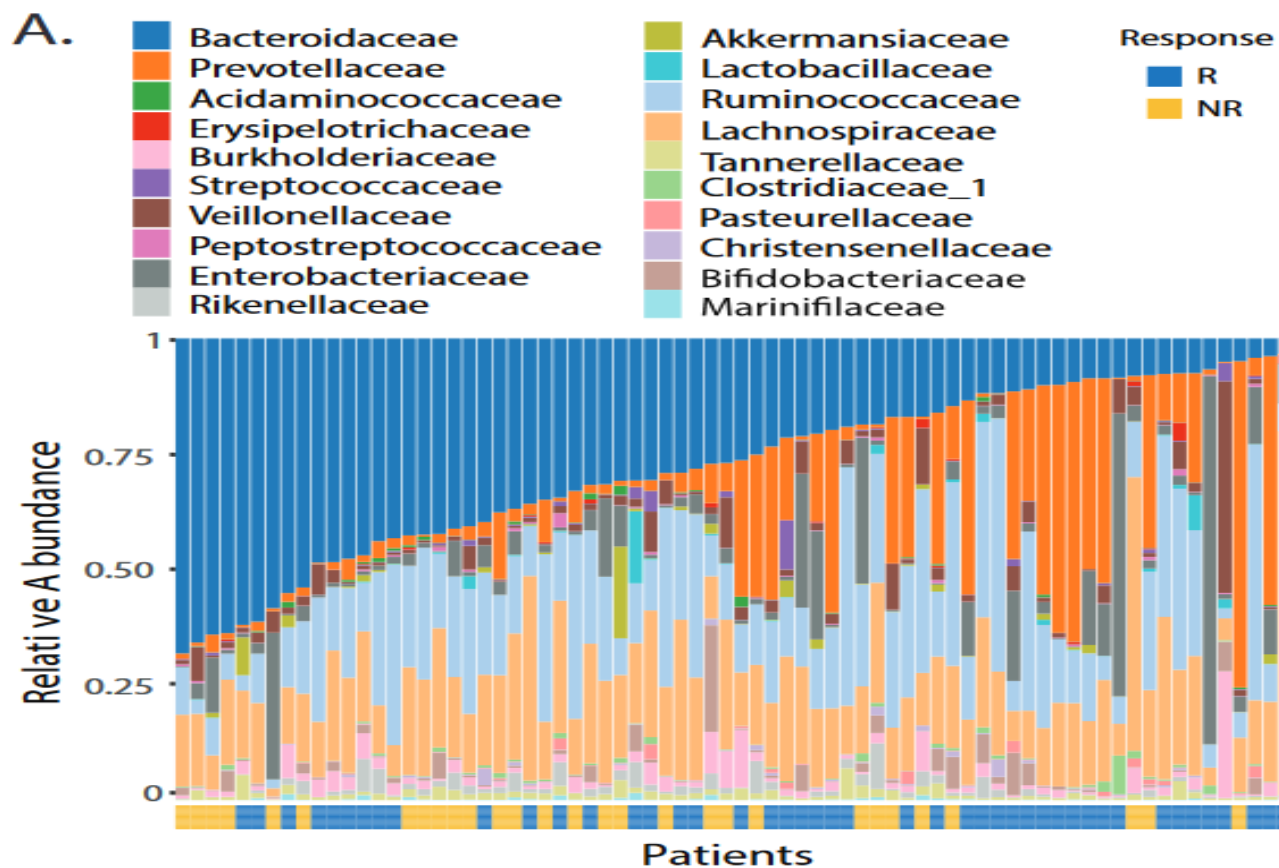
Research Articles

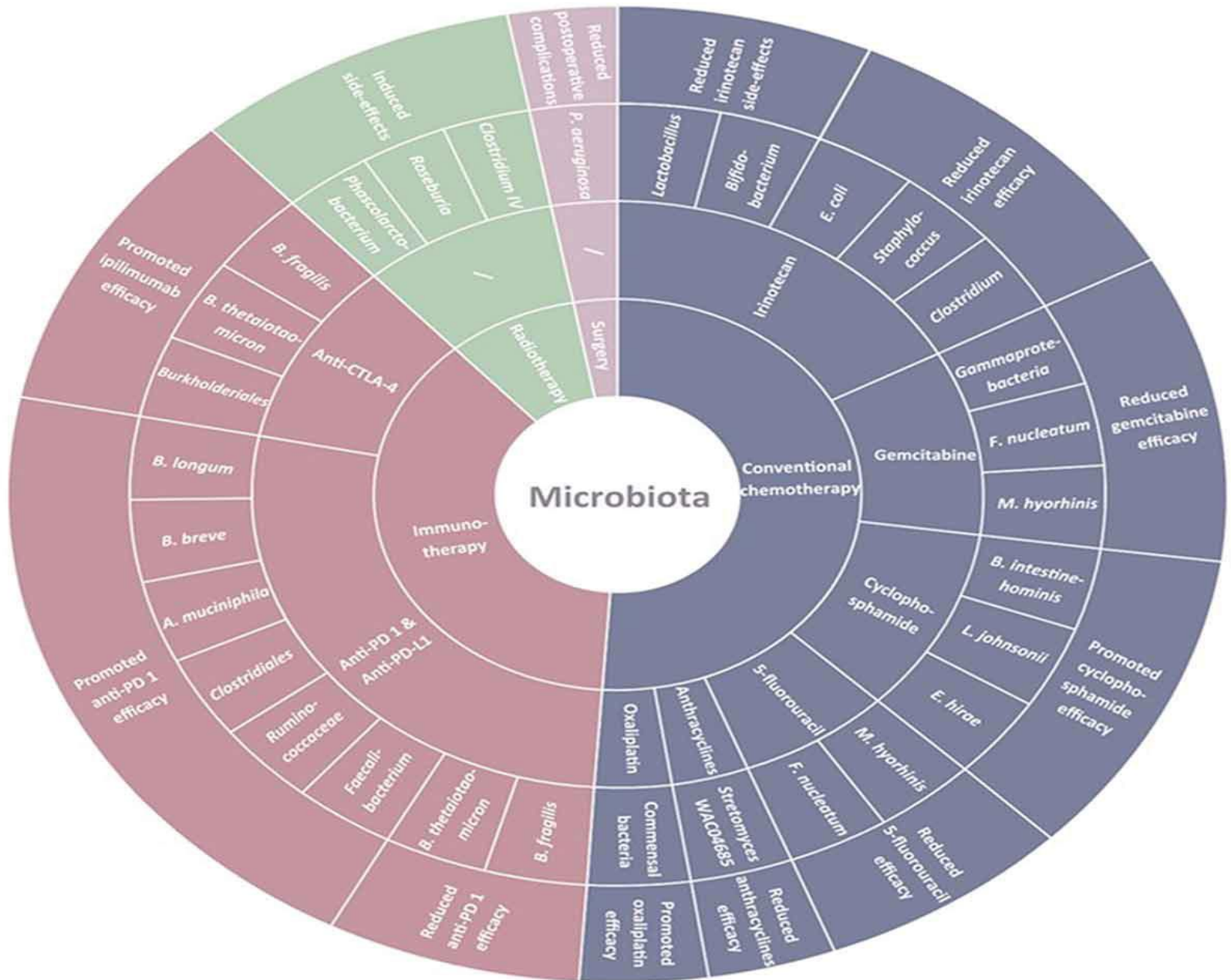
## The Gut Microbiome Is Associated with Clinical Response to Anti-PD-1/PD-L1 Immunotherapy in Gastrointestinal Cancer

Zhi Peng, Siyuan Cheng, Yan Kou, Ziqi Wang, Rong Jin, Han Hu, Xiaotian Zhang, Ji-fang Gong, Jian Li, Ming Lu, Xicheng Wang, Jun Zhou, ZhiHao Lu, Quan Zhang, David T.W. Tzeng, Dongtao Bi, Yan Tan, and Lin Shen

Purchase Access (\$35)

DOI: [10.1158/2326-6066.CIR-19-1014](https://doi.org/10.1158/2326-6066.CIR-19-1014) Published October 2020 [Check for updates](#)





## Σχέση αιτιολογική ή προσεταιριστική;

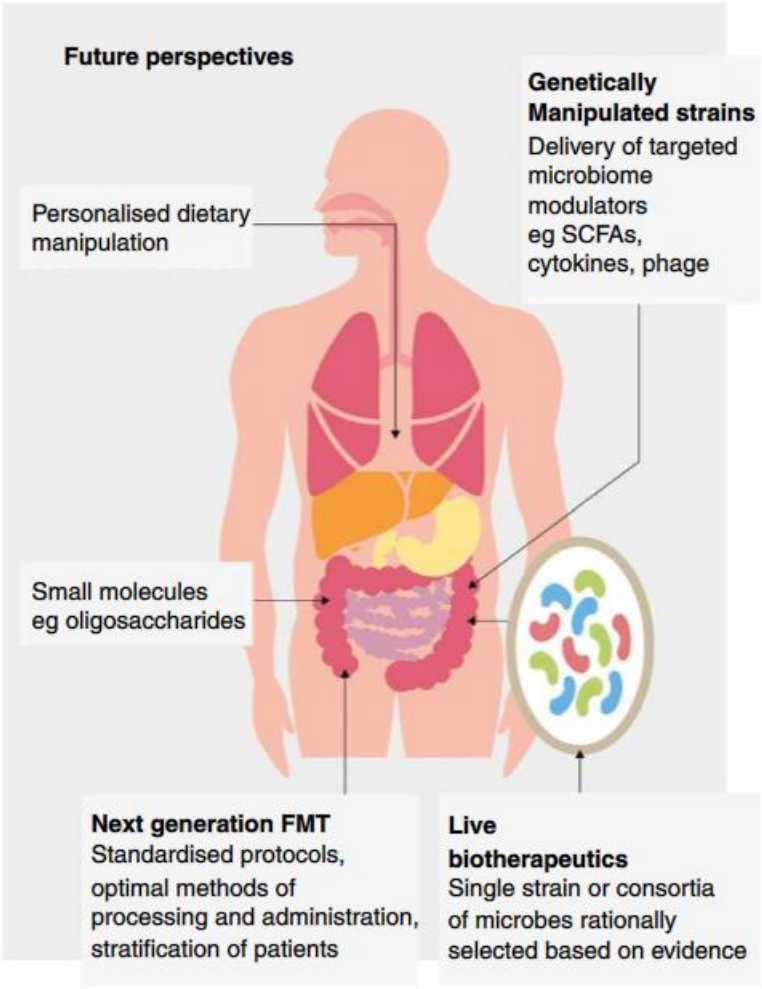
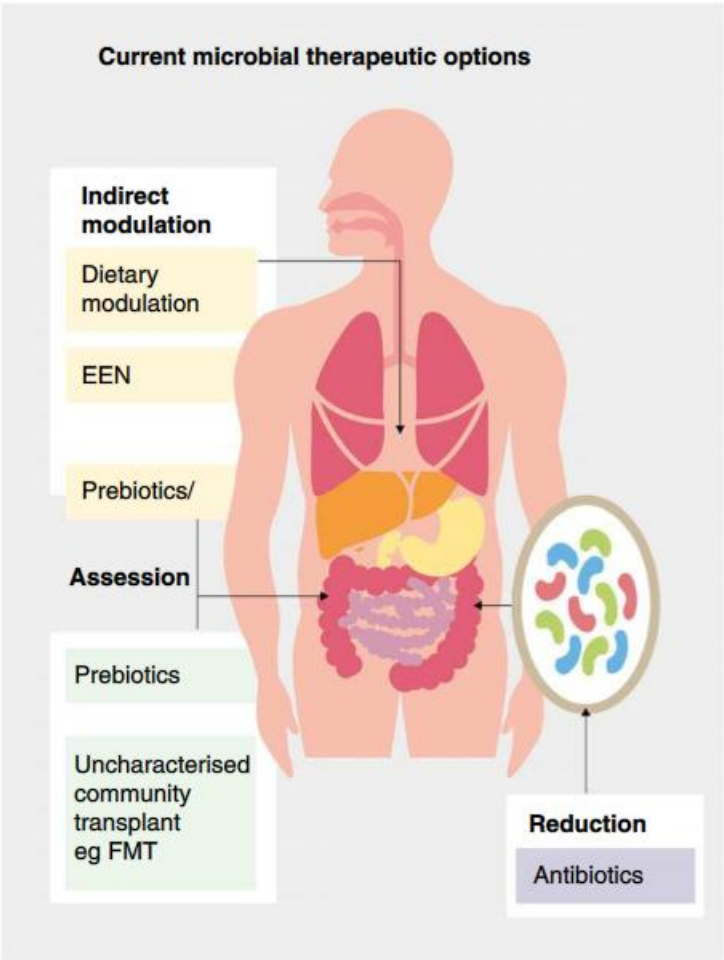
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- At the single organism level, the role of microorganisms as aetiological agents (or risk factors) in carcinogenesis is well established.
- A causal relationship between the human symbiotic microbiome and the development of cancer is not firmly established.



# Ερευνητικές προσεγγίσεις

| Setting  | Challenge  | Possible solutions and directions for research  |
|--|--|---|
| <i>Biomarker discovery</i>                                       |  |   |
| Faecal microbial markers for CRC screening                       | Imperfect sensitivity and specificity  | Combination panel of different microbial markers, molecular markers and occult blood tests  |
|  | Uncertain test performance across ethnic groups  | Validation cohorts using different populations <sup>22,26</sup><br>Identification of core biomarkers robust across populations <sup>30,31,47-49</sup> |
|  | Uncertain test performance with dietary changes, drug use, or with other comorbid diseases | Standardized methods of sample collection and quantification for the microbial markers  |
|  | Inconvenient sampling logistics  | Use of residual buffer from occult blood test cartridges <sup>265</sup><br>Development of a point-of-care test  |
| Prognostic biomarkers for CRC                                    | Mostly markers from tumour tissues   | Identification of faecal or oral markers as surrogates for easier sample accessibility  |
| <i>Microbiota manipulation to prevent CRC or improve therapy</i> |  |   |
| Dietary intervention   | Optimal dietary components and their amounts undefined                                     | Need for nutritional and clinical studies   |
| Probiotics to prevent CRC or improve therapy                     | Optimal strains, dosage and formulation of bacteria undefined                              | Need for bacteriological viability and clinical studies   |
|  | Lack of standardization and regulatory framework   | Formalization of IND application or other regulatory frameworks   |
| Antibiotics to remove deleterious bacteria                       | Lack of specific antimicrobial activity for many standard antibiotics                      | Use of narrow-spectrum antibiotics<br>Development of highly selective bacterial-targeting strategies  |
| Faecal microbiota transplantation                                | Risk of transforming pathogens and other microbiota-related diseases                       | Rigorous donor screening<br>Development of defined microbial communities as alternatives to whole-faeces transplantation                              |
|  | Optimal transplantation regimen undefined  | Consensus guidelines and clinical trials to define the optimal regimen <sup>266</sup>   |
|  | Lack of regulatory framework   | Formalization of IND application or other regulatory frameworks   |




# Key points

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- ▶ Ο καρκίνος του παχέος εντέρου (CRC) είναι ένας από τους πιο συχνούς καρκίνους παγκοσμίως, κατατάσσεται τρίτος όσον αφορά την επίπτωση και δεύτερος στη θνησιμότητα μεταξύ όλων των καρκίνων.
- ▶ Το μικροβίωμα του εντέρου περιλαμβάνει έναν μεγάλο πληθυσμό μικροοργανισμών που αλληλεπιδρούν στενά με τα εντερικά κύτταρα του ξενιστή και μπορεί να επηρεάσει την ανοσία και το μεταβολισμό στο γαστρεντερικό σωλήνα.
- ▶ Σύμφωνα με πειραματικά στοιχεία, το μικροβίωμα του εντέρου εμπλέκεται στη δημιουργία, την εξέλιξη του CRC και την ανταπόκρισή του στη θεραπεία.
- ▶ Ουσιαστικές αλλαγές στην αφθονία συγκεκριμένων βακτηρίων μπορούν να ανιχνευθούν σε ασθενείς με CRC και μπορεί να χρησιμεύσουν ως βιοδείκτες για τον έλεγχο της νόσου, την πρόγνωση και την πρόβλεψη της ανταπόκρισης στη θεραπεία.
- ▶ Η διαμόρφωση του μικροβιώματος του εντέρου είναι μια πολλά υποσχόμενη στρατηγική για την ενίσχυση της αποτελεσματικότητας της θεραπείας και τη μείωση των δυσμενών επιπτώσεων των θεραπειών CRC.
- ▶ Η μελλοντική έρευνα θα πρέπει να εξετάσει τους καλύτερους τρόπους ρύθμισης του εντερικού μικροβιώματος και να διερευνήσει τα βραχυπρόθεσμα και μακροπρόθεσμα οφέλη του μέσω κλινικών δοκιμών.






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### Microbiome in Human Health and Diseases

The present online course in Microbiome in Human Health and Diseases has a clinical focus on understanding the microbial communities as well as their diversity, and how they impact our health and disease processes. Students have the opportunity to learn about the role of microbiome in different pathologies. Additionally, they will be exposed to the concepts and methodologies involved in the study and characterization of the microbial communities.

The course is open to suitably qualified Greek and International graduates, holding at least a Degree in Medicine, Biology, Biochemistry or related fields. It is included in the Health category of our online courses and it runs via a user-friendly educational platform. Once the participant completes all the units successfully, he/she receives a certificate of training.

🕒 Start Date: Sep 20th 2021

🕒 Duration: 10 weeks

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📄 Programme leads to Certificate of Continuing Education

👤 Education type: Personal educational support

📄 ECVET: 5

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💰 Total cost: 300 €

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