

# Translational implications of gut microbiota in cancer therapy

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## Outline

1. Introduction
2. Bacteria and cancer
3. Gut microbiota and cancer
4. Implication of gut microbiota in cancer treatments
5. Future direction and challenges
6. Conclusion

# Bacteria and cancer

- Infection of certain bacterial species promote tumors.
  - *H.pylori* in gastric cancers; *F. nucleatum* in colon cancers.
- Mechanisms include inducing chronic inflammation, DNA damage, and activation of oncogenic pathways



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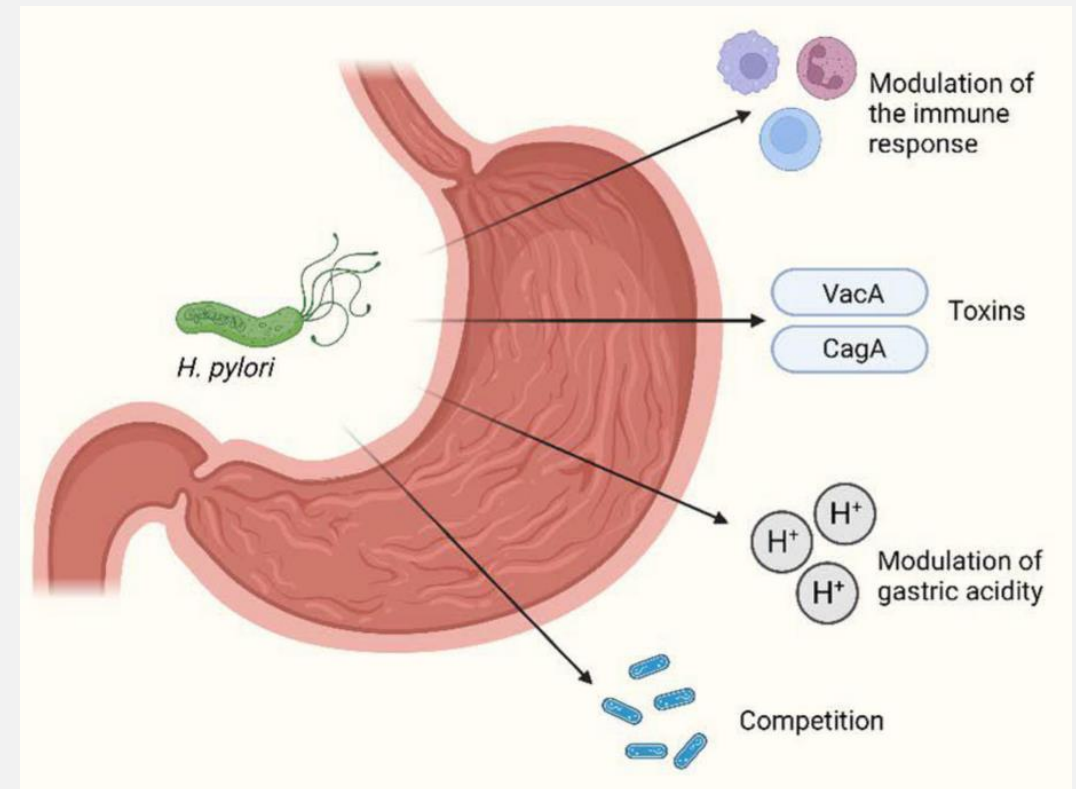


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# Mechanism of Bacteria-mediated carcinogenesis

## *H. pylori*

- Competition with other microorganisms
- DNA damage via oxidative stress in gastric mucosa
- Suppression of immune response

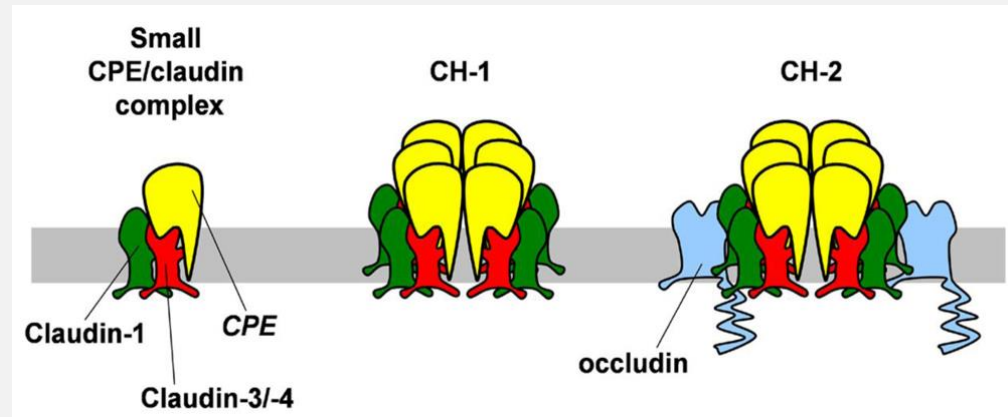


Modified from Elghannam et al., Infection, 2024 CC-BY-4.0

What about tumor suppression?

# Bacterial toxins with anti-cancer properties

- *Clostridium perfringens* enterotoxin (CPE) – highly specific to tight junctions Claudin-3 and -4



Mitchell et al., MDPI Toxins, 2010 CC-BY-4.0

## Rapid eradication of colon carcinoma by *Clostridium perfringens* Enterotoxin suicidal gene therapy

Research article | [Open access](#) | Published: 13 February 2017

Volume 17, article number 129, (2017) | [Cite this article](#)

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Jessica Pahle, Lutz Menzel, Nicole Niesler, Dennis Kobelt, Jutta Aumann, Maria Rivera & Wolfgang Walther ✉

## Molecular Oncology

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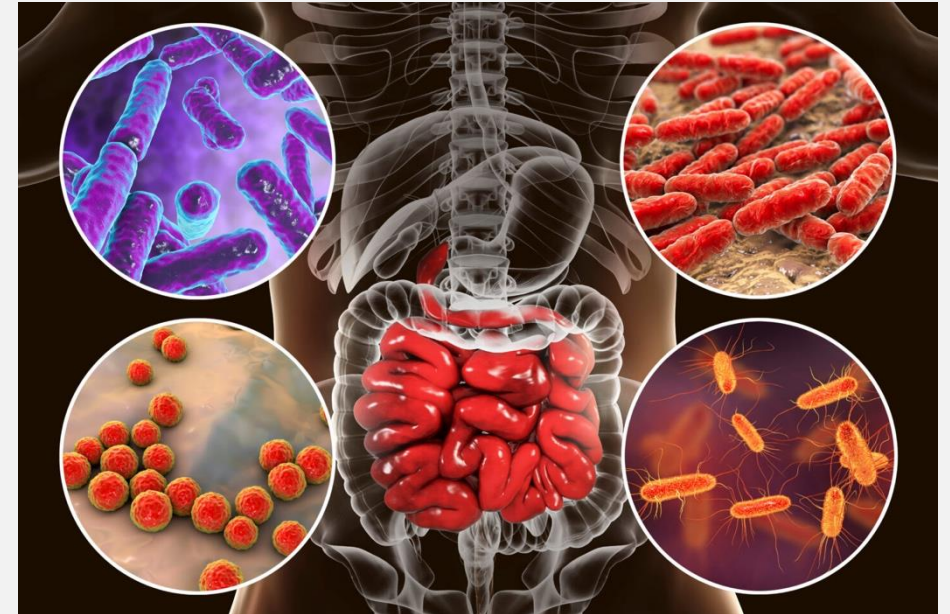
### Targeting claudin-overexpressing thyroid and lung cancer by modified *Clostridium perfringens* enterotoxin

Anna Piontek, Miriam Eichner, Denise Zwanziger, Laura-Sophie Beier, Jonas Protze, Wolfgang Walther, Sarah Theurer, Kurt Werner Schmid, Dagmar Führer-Sakel, Jörg Piontek ✉, Gerd Krause ✉

First published: 11 December 2019 | <https://doi.org/10.1002/1878-0261.12615> | Citations: 21

# The association of gut microbiota and cancer treatment

- Gut microbiota refer to diverse community of microbes that reside in the human gut.
- Number of studies have linked the association of gut microbiota and cancer.
  1. Cancer treatment resistance
  2. Cancer treatment response




<https://preventomics.eu/the-gut-microbiota-a-key-factor-in-metabolic-disorders-and-dietary-interventions/>

What are the implications of gut microbiota and cancer treatments?

1. Enhance cancer treatment efficacy
2. Reduce cancer treatment-related toxicities




## FMT of treatment-responding patients improve treatment efficacy in non-responsive patients

Unknown status 

### Fecal Microbiota Transplant and Pembrolizumab for Men With Metastatic Castration Resistant Prostate Cancer.

ClinicalTrials.gov ID  NCT04116775

Sponsor  Julie Graff, MD

Information provided by  Julie Graff, MD, Portland VA Medical Center (Responsible Party)

Last Update Posted  2022-06-23

### Fecal microbiota transplant promotes response in immunotherapy-refractory melanoma patients

EREZ N. BARUCH  , ILAN YOUNGSTER  , GUY BEN-BETZALEL  , RONA ORTENBERG  , ADI LAHAT  , LIOR KATZ  , KATERINA ADLER  , DANIELA DICK-NECULA  ,

STEPHEN RASKIN  , [...], AND BEN BOURS   +22 authors [Authors Info & Affiliations](#)

SCIENCE • 10 Dec 2020 • Vol 371, Issue 6529 • pp. 602-609 • DOI: 10.1126/science.abb5920

- Aimed to enhance immunotherapy efficacy with FMT
- FMT were from donors of prostate cancer patients with response to treatment
- FMT delivered via endoscopy
- FMT + re-induction of immunotherapy promoted intratumoral immunity activity

# Improved levels of MAIT cells near primary tumor, enhancing efficacy of immunotherapy

Active, not recruiting ⓘ

**Preventing Toxicity in Renal Cancer Patients Treated With Immunotherapy Using Fecal Microbiota Transplantation (PERFORM)**

ClinicalTrials.gov ID ⓘ NCT04163289

Sponsor ⓘ Lawson Health Research Institute

Information provided by ⓘ Lawson Health Research Institute (Responsible Party)

Last Update Posted ⓘ 2023-12-19

[Home](#) > [Cancer Immunology, Immunotherapy](#) > Article

## Improved MAIT cell functions following fecal microbiota transplantation for metastatic renal cell carcinoma

Research | Published: 18 November 2022

Volume 72, pages 1247–1260, (2023) [Cite this article](#)

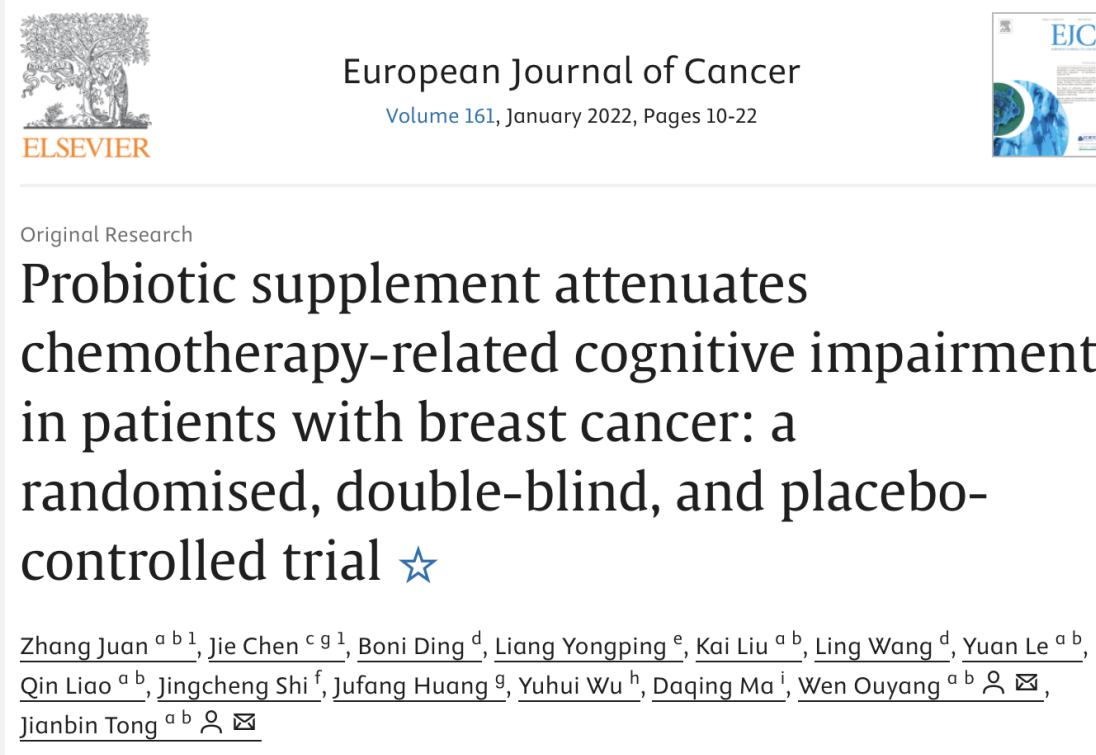
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Marina Ninkov, Crystal L. Schmerk, Manoosh Moradizadeh, Seema N. Parvathy, Rene Figueredo, Jeremy P. Burton, Michael S. Silverman, Ricardo Fernandes, Saman Maleki Vareki ✉ & S. M. Mansour Haeryfar



- Mucosal-associated invariant T cell (MAIT) cells
- Exhaustion of MAIT cells make patients prone to bacterial and viral infections
- Enhance immunotherapy efficacy + protect patients from opportunistic infections while undergoing cancer treatment.

# Partial recovery of chemo-related gut microbiota dysbiosis



- Prior to treatment, dysbiosis detected in breast cancer patients
- After treatment with probiotic + chemotherapy, higher abundance of enterococcus than placebo group



### Future Direction:

- Further bacteria strains exhibiting anti-cancer activity could be further explored
- Validate molecular mechanism of gut microbiotas' role as anti-cancer agents

### Challenges:

- Microbiota heterogeneity is one major challenge for clinical translations in cancer patients.
- Lack of standardized procedures (i.e. sample collection, technology, reproducibility)

## Conclusion

- Further comprehend the influence of gut microbiota in cancer.
- The current clinical trials of modulating gut microbiota for cancer treatment are to enhance efficacy and reduce toxicities.
- The study of gut microbiota could open more doors for other treatment strategies, not limited to cancers.

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