XXXIII CONGRESSO NAZIONALE AIRO

AIRO2023

BOLOGNA,
27-29 OTTOBRE 2023
PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

# Sessione AIRB - Microbiota e Radioterapia

## TESTA COLLO

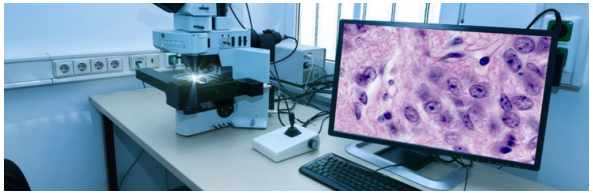
**Monica Mangoni**

**Università degli Studi di Firenze**

Associazione Italiana
Radioterapia e Oncologia clinica

# AIRO2023

Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti



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microbiota

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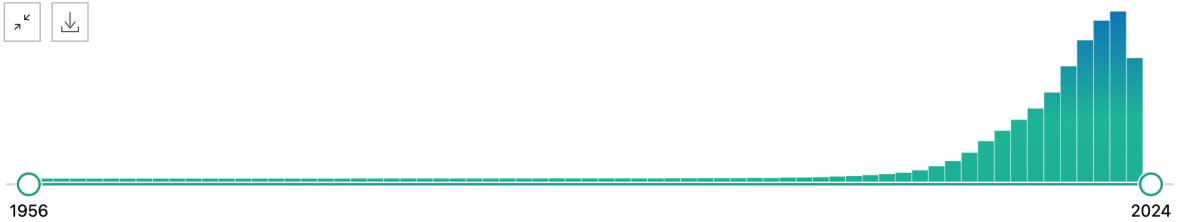
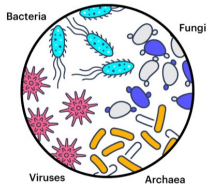


# Microbiota vs microbiome

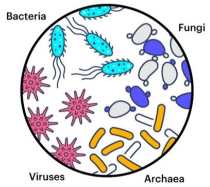
## Microbiota

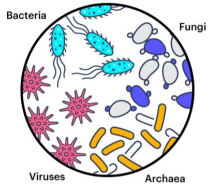
Microorganisms (by type) living in a specific environment



# Microbiota vs microbiome

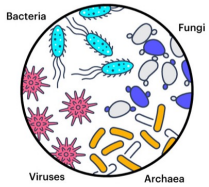
| Microbiome | Microbiota |
| --- | --- |
| Microorganisms (and their genes) living in a specific environment | Microorganisms (by type) living in a specific environment |

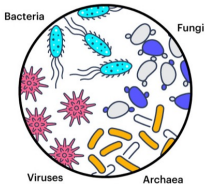


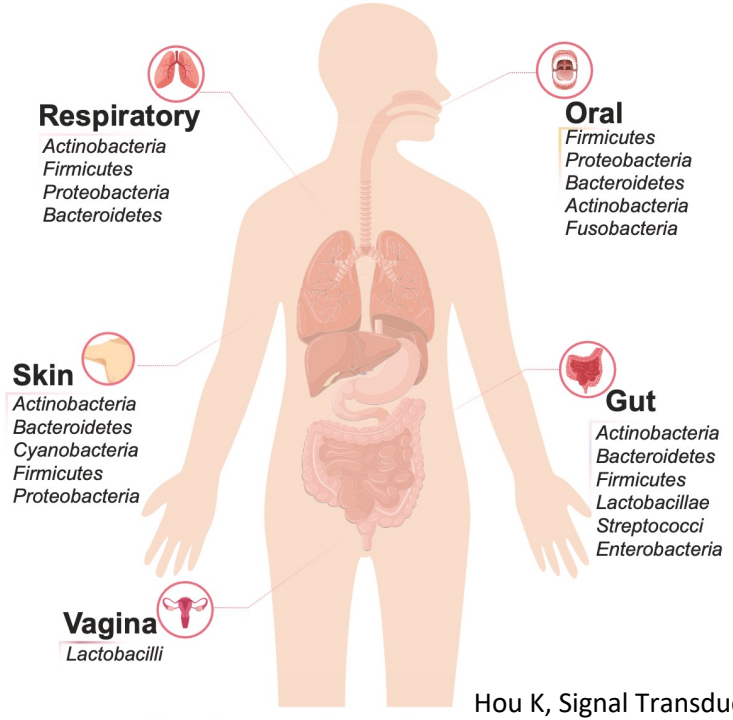
# Microbiota vs microbiome

| Microbiome | Microbiota | Metagenome |
|---|---|---|
| Microorganisms (and their genes) living in a specific environment | Microorganisms (by type) living in a specific environment | The genes of microorganisms in a specific environment |




**symbiosis**



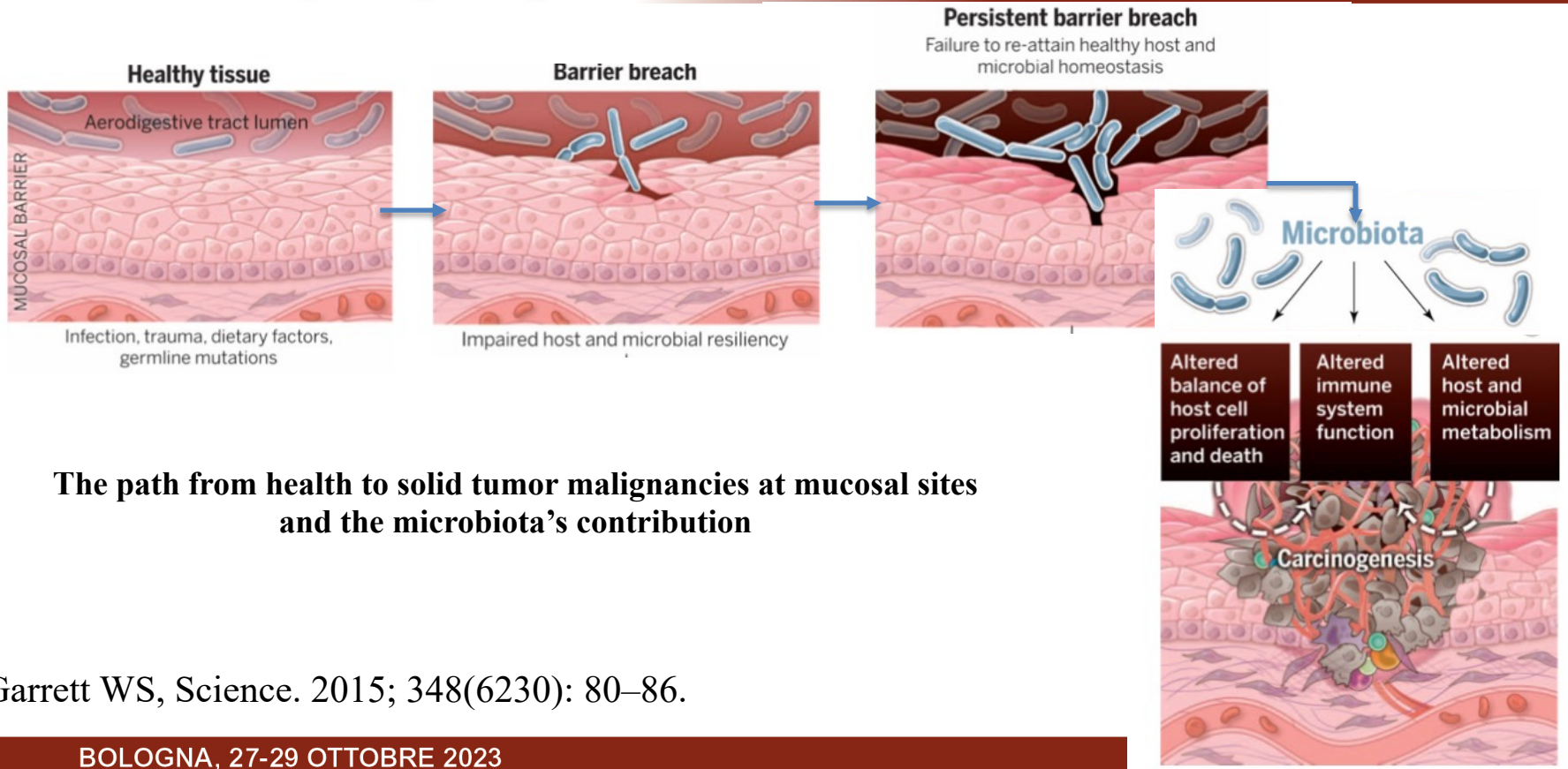

Hou K, Signal Transduction and Targeted Therapy (2022) 7:135

# Cancer and microbiota

- Tumor microbiota (tumorigenesis)
- Tossicity
- Response to treatment

# Cancer and microbiota

- **Tumor microbiota (tumorigenesis)**
- Tossicity
- Response to treatment




**The path from health to solid tumor malignancies at mucosal sites and the microbiota's contribution**

Garrett WS, Science. 2015; 348(6230): 80–86.

**the microbiota differs**
**between cancers**
**according to anatomical location**

Nejman D. et al. Science 2020; **368**

# Oral cavity

- Over 700 different bacterial species (any one individual around 350 in their mouth)
- Several microhabitats each with their own characteristic bacterial composition
- Environmental factors affect community composition
- Variations in oral hygiene practice contribute to the amount and composition of biofilms
- Complex inter-relationships between bacteria shape communities

**Poor oral hygiene** and associated oral diseases
**are associated with HN-SCC**
suggesting that **specific microbiota profiles**
**may associate with carcinogenesis**

Several clinical studies have attempted to characterise associations between the microbiome and HN-SCC→ ***contradictory results***

Rev in M. Reis Ferreira et al. Cancer Treatment Reviews 109 (2022) 102442

Several clinical studies have attempted to characterise associations between the microbiome and HN-SCC→ ***contradictory results***

→ tumours are often characterised by higher counts of fusobacteria

Rev in M. Reis Ferreira et al. Cancer Treatment Reviews 109 (2022) 102442

Several clinical studies have attempted to characterise associations between the microbiome and HN-SCC→ ***contradictory results***

→ tumours are often characterised by higher counts of fusobacteria

→tumour microbiome functionality is often characterised by increased pro-inflammatory and/or decreased xenobiotic degradation pathways

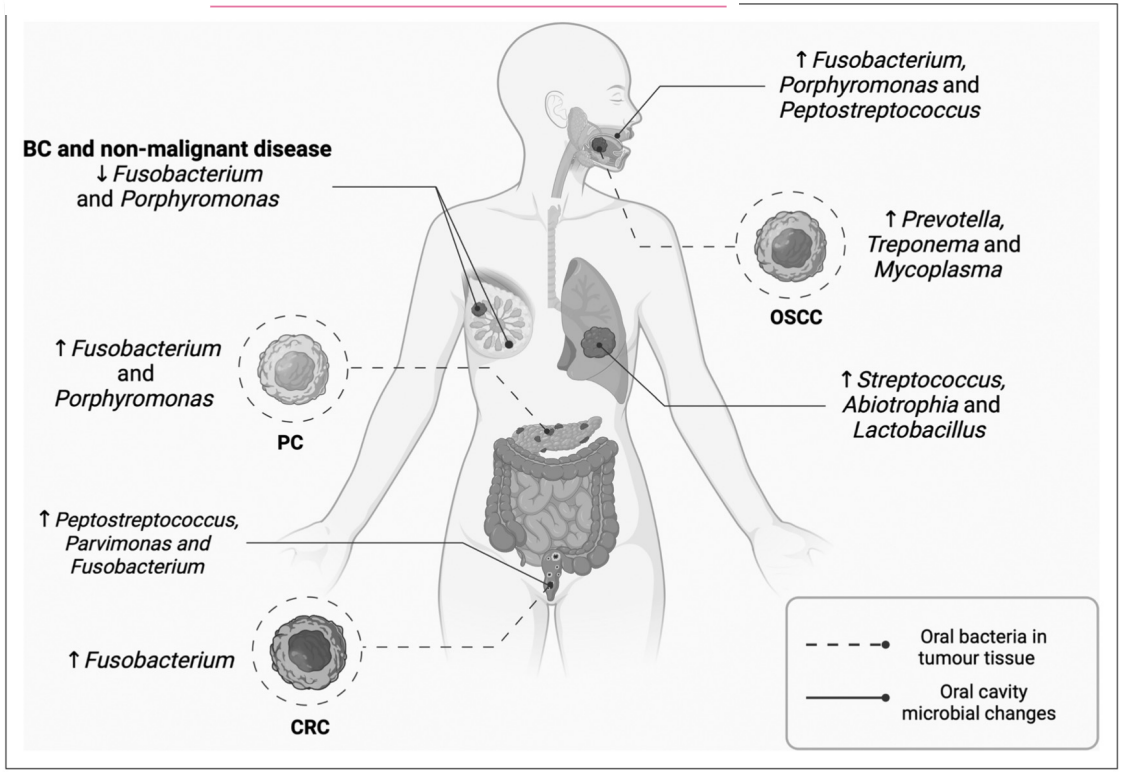
Rev in M. Reis Ferreira et al. Cancer Treatment Reviews 109 (2022) 102442

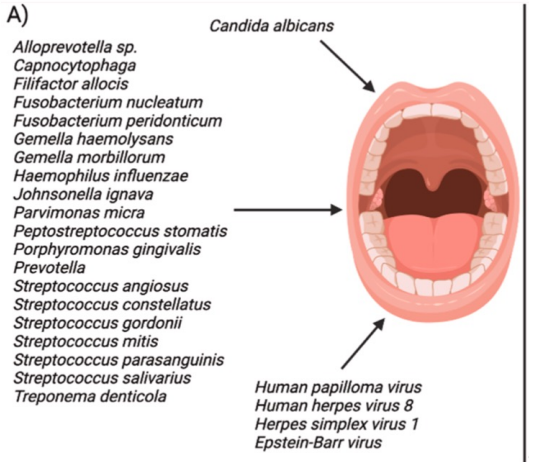
CURRENT OPINION

# Oral microbiome as a new research-target for supportive care and precision oncology

*Julia Stephanie Bruno and Eduardo Rodrigues Fregnani*






Stasiewicz M,
Seminars in Cancer Biology (2022) 633–642

# Bacteria can promote cancer proliferation, invasion, metastasis, angiogenesis, inhibit apoptosis and anti-tumour immunity.

Immunity

CellPress

Volume 42, Issue 2, 17 February 2015, Pages 344-355

Article

## Binding of the Fap2 Protein of *Fusobacterium nucleatum* to Human Inhibitory Receptor TIGIT Protects Tumors from Immune Cell Attack

Chamutal Gur [1,2], Yara Ibrahim [3], Batya Isaacson [1], Rachel Yamin [1], Jawad Abed [3],

ONCOIMMUNOLOGY
2019, VOL. 8, NO. 6, e1581531 (6 pages)
https://doi.org/10.1080/2162402X.2019.1581531

Taylor & Francis
Taylor & Francis Group

BRIEF REPORT

Check for updates

## *Fusobacterium nucleatum* supresses anti-tumor immunity by activating CEACAM1

Chamutal Gur[#a], Naseem Maalouf[#b], Amjad Shhadeh[b], Orit Berhani[a], Bernhard B. Singer[c], Gilad Bachrach[#b], and Ofer Mandelboim[#a]

JOURNAL OF ORAL MICROBIOLOGY
2020, VOL. 13, 1849493
https://doi.org/10.1080/20002297.2020.1849493

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

OPEN ACCESS Check for updates

## Fusobacteria modulate oral carcinogenesis and promote cancer progression

Amani M. Harrandah[a,b], Sasanka S. Chukkapalli[a,c], Indraneel Bhattacharyya[d], Ann Progulske-Fox[a,c] and Edward K. L. Chan[a]

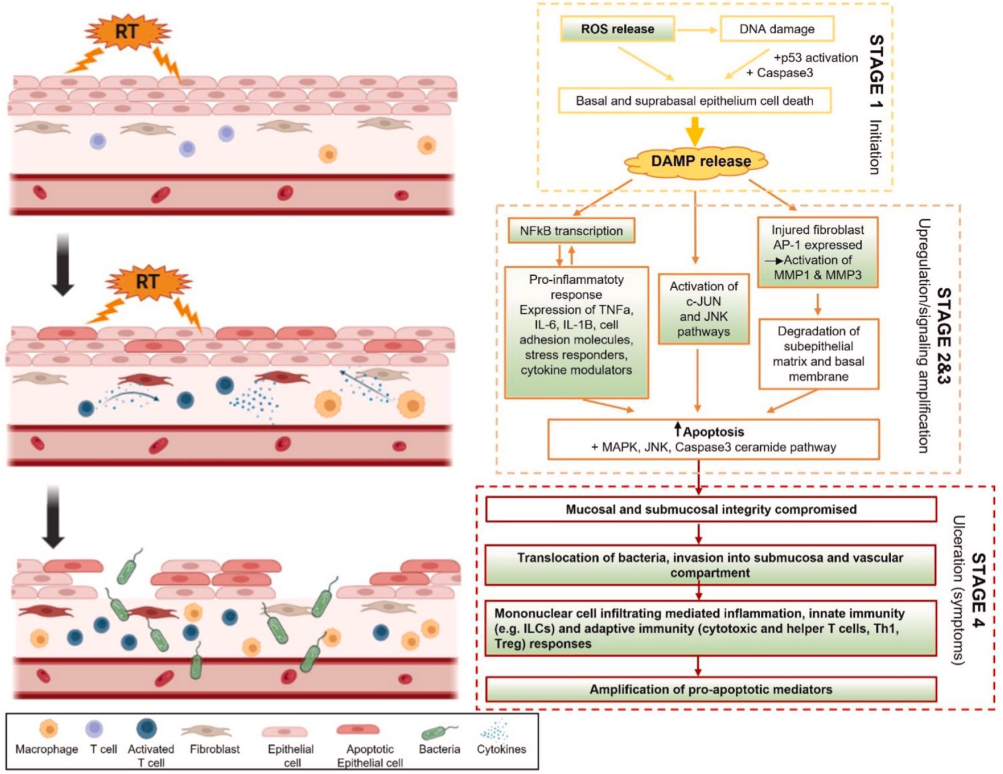
# Cancer and microbiota

- Tumor microbiota (tumorigenesis)
- **Tossicity**
- Response to treatment

# Impact of radiotherapy on the microbiota

**shift by the bacterial community**
**to a pro-cariogenic/pro-inflammatory-one**
**after radiotherapy**

## radiation-induced acute oral mucositis




Rev in M. Reis Ferreira et al.
Cancer Treatment Reviews 109 (2022) 102442

# Bacteriotherapy to prevent mucositis

EUROPEAN JOURNAL OF CANCER 48 (2012) 875–881

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

ELSEVIER


## *Lactobacillus brevis* CD2 lozenges reduce radiation- and chemotherapy-induced mucositis in patients with head and neck cancer: A randomized double-blind placebo-controlled study ☆☆☆

*Atul Sharma [a,*], G.K. Rath [b], S.P. Chaudhary [a], Alok Thakar [c], Bidhu Kalyan Mohanti [b], Sudhir Bahadur [c]*

ANTICANCER RESEARCH *39*: 1935-1942 (2019)
doi:10.21873/anticanres.13303

## *Lactobacillus brevis* CD2 for Prevention of Oral Mucositis in Patients With Head and Neck Tumors: A Multicentric Randomized Study

VITALIANA DE SANCTIS[1], LILIANA BELGIOIA[2], DOMENICO CANTE[3], MARIA R. LA PORTA[3], ORIETTA CASPIANI[4], ROBERTA GUARNACCIA[4], ANGELA ARGENONE[5], PAOLO MUTO[5], DANIELA MUSIO[6], FRANCESCA DE FELICE[6], FRANCESCA MAURIZI[7], FEISAL BUNKHELIA[7], MARIA G. RUO REDDA[8], ALESSIA REALI[8], MAURIZIO VALERIANI[1], MATTIA F. OSTI[1], DANIELA ALTERIO[9], ALMALINA BACIGALUPO[10] and ELVIO G. RUSSI[11]

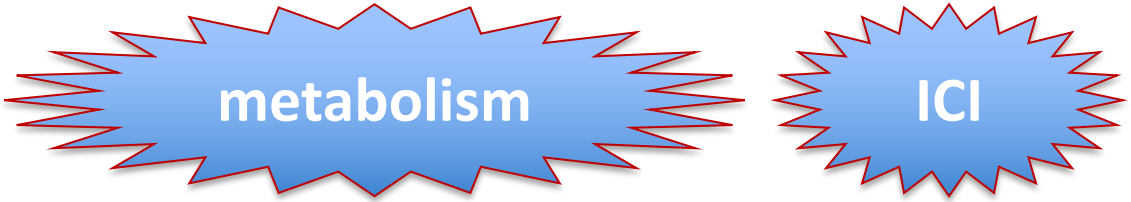
# Cancer and microbiota

- Tumor microbiota (tumorigenesis)
- Tossicity
- **Response to treatment**

Published in final edited form as:
*Cancer Cell*. 2018 April 09; 33(4): 570–580. doi:10.1016/j.ccell.2018.03.015.

# The influence of the gut microbiome on cancer, immunity, and cancer immunotherapy

**Vancheswaran Gopalakrishnan**[1,*], **Beth A. Helmink**[1,*], **Christine N. Spencer**[2], **Alexandre Reuben**[1], and **Jennifer A. Wargo**[1,2]



Published in final edited form as:

*Cancer Cell*. 2018 April 09; 33(4): 570–580. doi:10.1016/j.ccell.2018.03.015.

# The influence of the gut microbiome on cancer, immunity, and cancer immunotherapy

Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study

Barbara Burtness, Kevin J Harrington, Richard Greil, Denis Soulières, Makoto Tahara, Gilberto de Castro Jr, Amanda Psyrri, Neus Basté, Prakash Neupane, Åse Bratland, Thorsten Fuereder, Brett G M Hughes, Ricard Mesía, Nuttapong Ngamphaiboon, Tamara Rordorf, Wan Zamaniah Wan Ishak, Ruey-Long Hong, René González Mendoza, Ananya Roy, Yayan Zhang, Burak Gumuscu, Jonathan D Cheng, Fan Jin, Danny Rischin, on behalf of the KEYNOTE-048 Investigators*

**Summary**

**Background** Pembrolizumab is active in head and neck squamous cell carcinoma (HNSCC), with programmed cell death ligand 1 (PD-L1) expression associated with improved response.

*Lancet* 2019; 394: 1915–28 Published Online October 31, 2019

N Engl J Med 2016;375:1856-67.

ORIGINAL ARTICLE

## Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck

R.L. Ferris, G. Blumenschein, Jr., J. Fayette, J. Guigay, A.D. Colevas, L. Licitra, K. Harrington, S. Kasper, E.E. Vokes, C. Even, F. Worden, N.F. Saba, L.C. Iglesias Docampo, R. Haddad, T. Rordorf, N. Kiyota, M. Tahara, M. Monga, M. Lynch, W.J. Geese, J. Kopit, J.W. Shaw, and M.L. Gillison

ABSTRACT

**BACKGROUND**

Patients with recurrent or metastatic squamous-cell carcinoma of the head and neck after platinum chemotherapy have a very poor prognosis and limited therapeutic options. Nivolumab, an anti–programmed death 1 (PD-1) monoclonal antibody, was assessed as treatment for this condition.

Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study

*Ezra E W Cohen, Denis Soulières, Christophe Le Tourneau, José Dinis, Lisa Licitra, Myung-Ju Ahn, Ainara Soria, Jean-Pascal Machiels, Nicolas Mach, Ranee Mehra, Barbara Burtness, Pingye Zhang, Jonathan Cheng, Ramona F Swaby, Kevin J Harrington, on behalf of the KEYNOTE-040 investigators**

**Summary**

**Background** There are few effective treatment options for patients with recurrent or metastatic head-and-neck squamous cell carcinoma. Pembrolizumab showed antitumour activity and manageable toxicity in early-phase trials. We aimed to compare the efficacy and safety of pembrolizumab versus standard-of-care therapy for the treatment of head-and-neck squamous cell carcinoma.

Radiotherapy and Oncology 164 (2021) 83–91

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

# The baseline oral microbiota predicts the response of locally advanced oral squamous cell carcinoma patients to induction chemotherapy: A prospective longitudinal study

Mengyu Rui [a,b,c], Xinyi Zhang [a,d], Jinyun Huang [a,b,c], Dongliang Wei [a,b,c], Zhi Li [a,d], Ziyang Shao [a,b,c,*], Houyu Ju [a,b,c,*], Guoxin Ren [a,b,c,*]

**Novel potential biomarkers for response to TPF:**

Fusobacterium and Mycoplasma were more enriched in the nonresponsive group
Slackia was more enriched in the responder group

AIRO2023

European Journal of Cancer 131 (2020) 9–15

ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

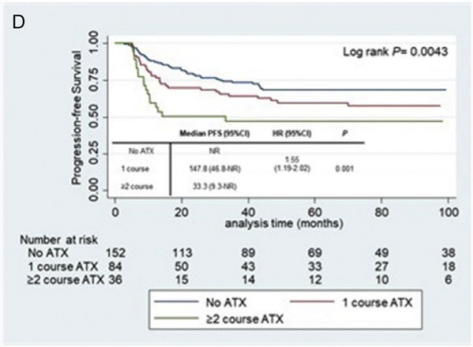
journal homepage: www.ejcancer.com

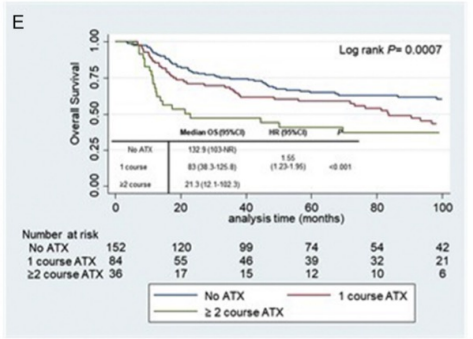

Original Research

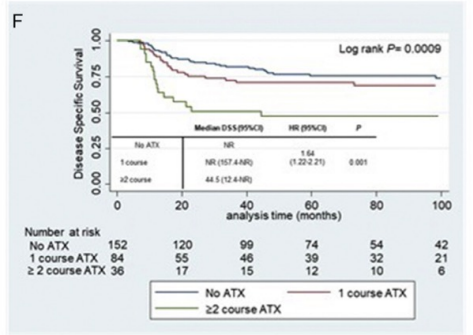
# Impact of antibiotic use during curative treatment of locally advanced head and neck cancers with chemotherapy and radiotherapy

Pablo Nenclares [a,*], Sheerang A. Bhide [a,b], Helena Sandoval-Insausti [c], Pierre Pialat [d], Lucinda Gunn [a,b], Alan Melcher [a,b], Kate Newbold [a,b], Christopher M. Nutting [a,b], Kevin J. Harrington [a,b]

**preponderant local effect!**



Published in final edited form as:
*Cancer Cell*. 2018 April 09; 33(4): 570–580. doi:10.1016/j.ccell.2018.03.015.

**The influence of the gut microbiome on cancer, immunity, and cancer immunotherapy**

# Association of Prior Antibiotic Treatment With Survival and Response to Immune Checkpoint Inhibitor Therapy in Patients With Cancer

David J. Pinato, MD, MRes, PhD[1,2]; Sarah Howlett, MD[2]; Diego Ottaviani, PhD[2]; Heather Urus[2]; Aisha Patel, MD[2]; Takashi Mineo[1,3]; Cathryn Brock, PhD[4]; Danielle Power, MD[2]; Olivia Hatcher, MD[2]; Alison Falconer, MD[2]; Manasi Ingle, MD[2]; Anna Brown, PharmD[2]; Dorothy Gujral, PhD[2]; Sarah Partridge, MD[2]; Naveed Sarwar, PhD[2]; Michael Gonzalez, PhD[2]; Maggie Bendle, PharmD[4]; Conrad Lewanski, MD[2]; Thomas Newsom-Davis, PhD[4]; Elias Allara, MD[1,5]; Mark Bower, PhD[4]

» Author Affiliations | Article Information

*JAMA Oncol*. 2019;5(12):1774-1778. doi:10.1001/jamaoncol.2019.2785

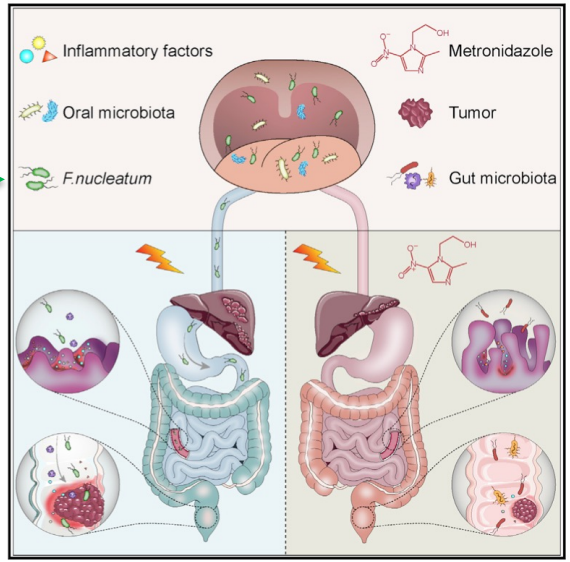
Article

Cell Reports

# Oral microbiota affects the efficacy and prognosis of radiotherapy for colorectal cancer in mouse models

Fusobacterium nucleatum

## Graphical abstract




## Authors

Jiali Dong, Yuan Li, Huiwen Xiao, ..., Yiliang Li, Saijun Fan, Ming Cui

## Correspondence

fansaijun@irm-cams.ac.cn (S.F.), cuiming0403@bjmu.edu.cn (M.C.)

## In brief

Dong et al. report that oral microorganisms such as *Fusobacterium nucleatum* can colonize colorectal cancer (CRC) sites and impair the therapeutic efficacy of radiotherapy and prognosis for primary rectal cancer and CRC liver metastases. Metronidazole, a *Fusobacterium*-killing antibiotic, is a potential radiosensitizer for the treatment of gastrointestinal tumors.

Dong et al., 2021, Cell Reports 37, 109886

# Summary

- ✓ microbiota can impact cancer treatment through direct and indirect mechanisms
- ✓ microbiota is likely to become as impactful in radiotherapy as it has in systemic therapies
- ✓ bidirectional effect between radiotherapy and oral microbiota