Microbiome and cancer
(oncobiome)

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Are intestinal bacteria bystander to the carcinogenic process?

R. Justin Davies, Richard Miller & Nicholas Coleman

*Nature Reviews Cancer* 5, 199-209 (March 2005)
Microbiota and Humans

Humans are a composite of microorganisms

**Leading Edge Commentary**

Are We Really Vastly Outnumbered? Revisiting the Ratio of Bacterial to Host Cells in Humans

Ron Sender,1 Shai Fuchs,2,3,* and Ron Milo1,*
Rapid colonization early in life set microbiota
Microbial composition varies according to the original seeding.
Microbial composition varies according to the original seeding

C-section

C-section + vaginal sponge

Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer

Maria G Dominguez-Bello1,2, Kassandra M De Jesus-Laboy3,
Nan Shen3, Laura M Cox1, Amnon Amir4, Antonio Gonzalez1,
Nicholas A Bokulich1, Se Jin Song4,5, Marina Hoashi1,6,
Juana I Rivera-Vinas3, Keimari Mendez7, Rob Knight4,8 &
Jose C Clemente5,9
The environment represents another important source of microbial exposure (seeding and transient)
Double threat phenomenon

Inside

Outside
Microbes and cancer: The infectious route

Outside

~4 X 10^{30} microbes on earth

10 organisms are designated as carcinogenic (International Agency for Cancer Research)

Epstein-Barr virus (EBV): Lymphomas
Human papillomavirus virus: Cervical cancer and other cancers
Human herpes virus: Kaposi’s sarcoma
Hepatitis B virus (HBV) and hepatitis C virus (HCV): non-Hodgkin lymphoma, liver cancer
Helicobacter species: stomach, biliary tract, and gallbladder cancer.
Microbes and cancer: Intestinal biota
Intestinal microbiota in health/diseases

- Diabetes
- Genetics
- Cancer
- Cardiovascular
- Diabetes
- Obesity
- Neurodisorders
- Rx response
- IBD-CRC
- Infection
- Rheumatoid arthritis

Diet
Life-style
Genetics

Bugs going global
Microbiota composition in colorectal cancer?

Next Generation Sequencing
State of microbial dysbiosis in CRC patients

**Enterococcus, Escherichia/Shigella, Klebsiella, Streptococcus, and Peptostreptococcus**


Burns, M.B., et al Virulence genes are a signature of the microbiome in the colorectal tumor microenvironment. 2015 Genome Medicine 1-12.

**Lachnospiraceae**

**Coriobacteridae, Roseburia, Fusobacterium, Providencia and Faecalibacterium**

**Adenocarcinoma**

**Adenoma**

**Functional impact of CRC-dysbiosis?**
Drilling down the microbiome world

Microbiome

Target

o’mics approaches
(metagenome, metatranscriptome,
proteome, metabolome)

Informative but associative results

Functional?

Gnotobiotics, humanized mice, microbial
gene manipulation, bioreactors,
structural chemistry, small molecules
How to dissect contribution of microbes in carcinogenesis?

Germ-free Next Generation Sequencing

"Humanized" mice

Next Generation Sequencing
The enemy within

Multiplicity

Invasion

Tumor # per mouse

Mice with invasion (%)

NC101 Δpks

NC101 Δpks

p = 0.0072

p = 0.031

Drilling down the microbiome world

ARTICLE
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DOI: 10.1038/ncomms5724

Microbial genomic analysis reveals the essential role of inflammation in bacteria-induced colorectal cancer

Janelle C. Arthur\textsuperscript{1,*}, Raad Z. Gharaibeh\textsuperscript{2,3,*}, Marcus Mühlbauer\textsuperscript{1}, Ernesto Perez-Chanona\textsuperscript{4,5}, Joshua M. Uronis\textsuperscript{1,†}, Jonathan McCafferty\textsuperscript{2}, Anthony A. Fodor\textsuperscript{2} & Christian Jobin\textsuperscript{5,6}

LETTERS
PUBLISHED: 11 JANUARY 2016 | ARTICLE NUMBER: 15009 | DOI: 10.1038/NMICROBIOL.2015.9

MATE transport of the \textit{E. coli}-derived genotoxin colibactin

Jarrod J. Mousa\textsuperscript{1†}, Ye Yang\textsuperscript{2†}, Sarah Tomkovich\textsuperscript{2}, Ayaka Shima\textsuperscript{3,4,5,6,7}, Rachel C. Newsome\textsuperscript{1}, Prabhanshu Tripathi\textsuperscript{1}, Eric Oswald\textsuperscript{3,4,5,6,7}, Steven D. Bruner\textsuperscript{1,*} and Christian Jobin\textsuperscript{2,8,*}
Microbial dysbiosis in CRC patients

Enterococcus, Escherichia/Shigella, Klebsiella, Streptococcus, and Peptostreptococcus

Lachnospiraceae

Biofilm correlates with 5X increase CRC rates

Microbiota organization is a distinct feature of proximal colorectal cancers

Christine M. Dejea\textsuperscript{a}, Elizabeth C. Wick\textsuperscript{b}, Elizabeth M. Hechenbleikner\textsuperscript{b}, James R. White\textsuperscript{c,1}, Jessica L. Mark Welch\textsuperscript{d}, Blair J. Rossetti\textsuperscript{d}, Scott N. Peterson\textsuperscript{e,2}, Erik C. Snepsrud\textsuperscript{e,3}, Gary G. Borisy\textsuperscript{d}, Mark Lazarev\textsuperscript{f}, Ellen Stein\textsuperscript{f}, Jamuna Vadivelu\textsuperscript{g}, April C. Roslan\textsuperscript{h}, Ausuma A. Malik\textsuperscript{h}, Jane W. Wanyiri\textsuperscript{f}, Khean L. Goh\textsuperscript{i}, Iyadorai Thevambiga\textsuperscript{g}, Kai Fu\textsuperscript{j}, Fengyi Wanj\textsuperscript{j,k}, Nicolas Llosa\textsuperscript{l}, Franck Housseau\textsuperscript{k}, Katharine Romans\textsuperscript{m,n}, XinQun Wu\textsuperscript{f}, Florencia M. McAllister\textsuperscript{k}, Shaoguang Wu\textsuperscript{f}, Bert Vogelstein\textsuperscript{m,n}, Kenneth W. Kinzler\textsuperscript{m,n}, Drew M. Pardoll\textsuperscript{f,k}, and Cynthia L. Sears\textsuperscript{a,f,k,4}

Firmicutes, Bacteroidetes, Fusobacterium and Proteobacteria

Adenoma
How to dissect contribution of microbe in carcinogenesis?

“Humanized” mice
Microbes and cancer: Bacteria as therapeutic adjuvant?
Microbes and cancer therapy

Commensal *Bifidobacterium* promotes antitumor immunity and facilitates anti-PD-L1 efficacy

Ayelet Sivan,1 Leticia Corrales,1 Nathaniel Hubert,2 Jason B. Williams,1 Keston Aquino-Micaelis,2 Zachary M. Earley,2 Franco W. Benyamin,1 Yuk Man Lei,2 Bana Jabri,2 Maria-Luisa Alegre,2 Eugene B. Chang,4 Thomas F. Gajewski1,4

CANCER IMMUNOTHERAPY

Forbes / Pharma & Healthcare

Fighting Cancer With Microbes, Flagship Bets on a $35M Startup
Microbes and cancer: Now what?

Prebiotics-Probiotics
Dietary manipulation
Anti-cancer adjuvant
Bacteriotherapy

Potential of fecal microbiota for early-stage detection of colorectal cancer

Georg Zeller1,*, Julien Tap1,*, Anita Y Voigt1,*, Shinichi Sunagawa3, Jens Roat Kultima3, Paul I Costea3, Aurélien Amiot3, Jürgen Böhm3, Francesco Brunetti3, Nina Habermann3, Rajna Hercog3, Moritz Koch3,*, Alain Luciani3, Daniel R Mende3, Martin A Schneider3,*, Petra Schrotz-King3,*, Christophe Tournigand1,*, Jeanne Tran Van Nhieu1,*, Takuji Yamada1,*, Jürgen Zimmermann3, Vladimir Beneš3, Matthias Kloos3,*, Cornelia M Ulrich6,*, Magnus von Knebel Doeberitz3,*, Iraj Sobhani1,*, & Peer Bork1,*,

Research Article
See related article by Narayanan et al., p. 1108

The Human Gut Microbiome as a Screening Tool for Colorectal Cancer

Joseph P. Zackular1, Mary A.M. Rogers2, Mack T. Ruffin IV2, and Patrick D. Schloss1

Weight Gain After Fecal Microbiota Transplantation
Neha Alang1 and Colleen R. Kelly1
BRIEF REPORT • OFID • 1

Alleviating Cancer Drug Toxicity by Inhibiting a Bacterial Enzyme
Bret D. Wallace,† Hongwei Wang,† Kimberly T. Lane,† John E. Scott,† Jillian Orans,‡ Je Seol Koo,‡ Madhukumar Venkatesh,§ Christian Jobin,∥ Li-An Yeh,∥ Sridhar Mani,∥ Matthew R. Redinbo,¶,†,‡,*

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Jobin Lab
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  Jillian Pope
Ernesto Perez-Chanona
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