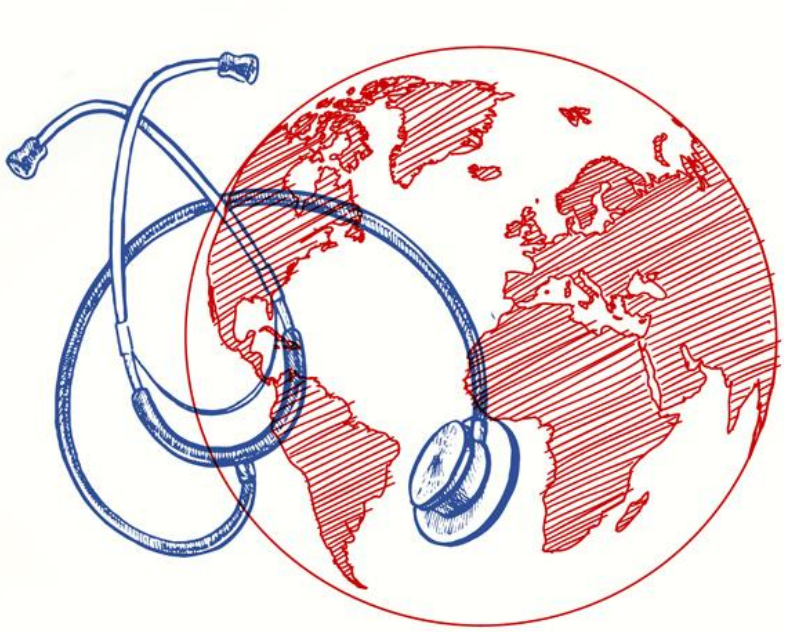
Global Health Cast 67

May 20, 2024



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What we talk about today

- *Fusobacterium* clade dominates colorectal cancer niche
- General mechanisms for bacteria – associated colon cancer
- Andrew Wakefield's "study": a powerful example of how misinformation can lead to significant public health challenges
- H5N1-update(s)
  - CDC, USA numbers
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Fusobacterium clade dominates colorectal cancer niche

Article

A distinct *Fusobacterium nucleatum* clade dominates the colorectal cancer niche

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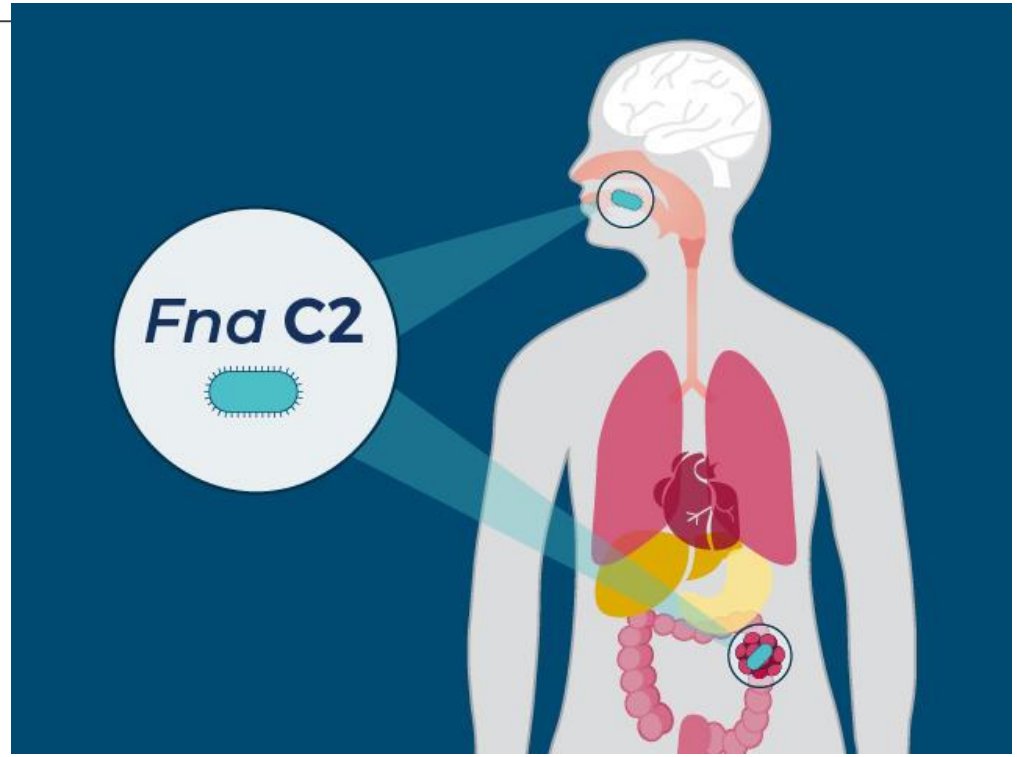
Fusobacterium nucleatum (*Fn*), a bacterium present in the human oral cavity and rarely found in the lower gastrointestinal tract of healthy individuals[1], is enriched in human colorectal cancer (CRC) tumours[2–5]. High intratumoural *Fn* loads are associated with recurrence, metastases and poorer patient prognosis[5–8]. Here, to delineate *Fn* genetic factors facilitating tumour colonization, we generated closed genomes for 135 *Fn* strains; 80 oral strains from individuals without cancer and 55 unique cancer strains cultured from tumours from 51 patients with CRC. Pangenomic analyses identified 483 CRC-enriched genetic factors. Tumour-isolated strains predominantly belong to *Fn* subspecies *animalis* (*Fna*). However, genomic analyses reveal that *Fna*, considered a single subspecies, is instead composed of two distinct clades (*Fna* C1 and *Fna* C2). Of these, only *Fna* C2 dominates the CRC tumour niche. Inter-*Fna* analyses identified 195 *Fna* C2-associated genetic factors consistent with increased metabolic potential and colonization of the gastrointestinal tract. In support of this, *Fna* C2-treated mice had an increased number of intestinal adenomas and altered metabolites. Microbiome analysis of human tumour tissue from 116 patients with CRC demonstrated *Fna* C2 enrichment. Comparison of 62 paired specimens showed that only *Fna* C2 is tumour enriched compared to normal adjacent tissue. This was further supported by metagenomic analysis of stool samples from 627 patients with CRC and 619 healthy individuals. Collectively, our results identify the *Fna* clade bifurcation, show that specifically *Fna* C2 drives the reported *Fn* enrichment in human CRC and reveal the genetic underpinnings of pathoadaptation of *Fna* C2 to the CRC niche.



In this new study, published in *Nature*, NCI-funded researchers have pinpointed a single type of *F. nucleatum* that appears to be the cancer-fueling culprit scientists have been searching for.

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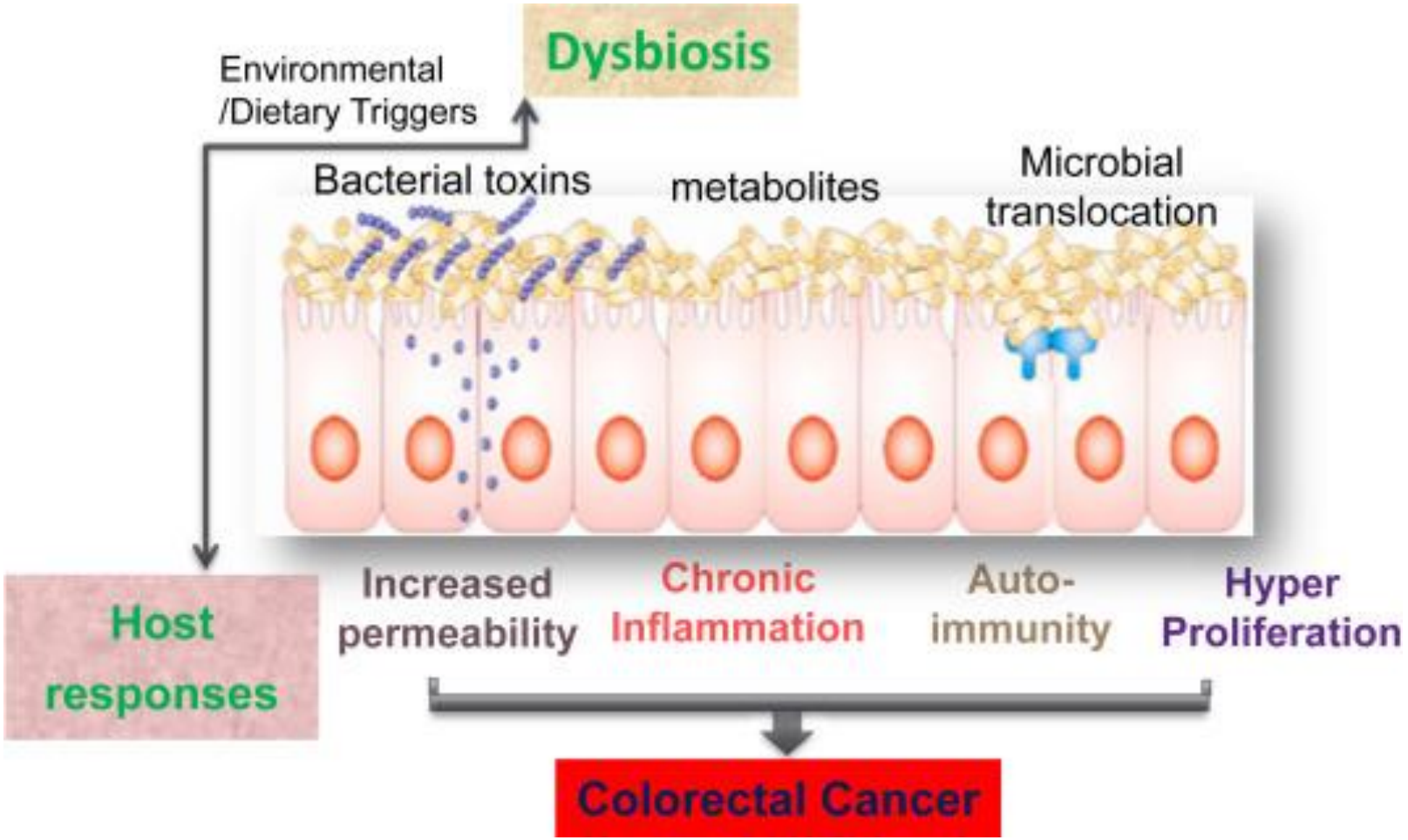
Working models of general mechanisms for bacteria – associated (or induced) colon cancer.



Through enhancing toxic bacterial products, decreasing beneficial bacterial metabolites, disrupted tissue barriers, translocation of microbes, dysbiosis leads to abnormal immune activation, chronic inflammation, and hyperpreliferation that contribute to the colorectal cancer.

Host factor i.e., genetic defect, could enhance the dysbiosis along with the environment trigger and change of dietary

Sun J, Kato I. Gut microbiota, inflammation and colorectal cancer. Genes Dis. 2016 Jun;3(2):130-143. doi: 10.1016/j.gendis.2016.03.004. Epub 2016 Apr 13. PMID: 28078319; PMCID: PMC5221561.

Andrew Wakefield's "study": a powerful example of how misinformation can lead to significant public health challenges

THE LANCET

The Lancet, Volume 351, Issue 9103, Pages 637 - 641, 28 February 1998
doi:10.1016/S0140-6736(97)11096-0

This article was retracted

RETRACTED: Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

Dr AJ Wakefield FRCS a, SH Murch MB b, A Anthony MB a, J Linnell PhD a, DM Casson MRCP b, M Malik MRCP b, M Berelowitz FRCPsych c, AP Dhillon MRCPath a, MA Thomson FRCP b, P Harvey FRCP d, A Valentine FRCR a, SE Davies MRCPath a, JA Walker-Smith FRCP a

Summary

Background

We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods

12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic-resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

H5N1 in the USA on 2024-05-17

(H5N1 Bird Flu: Current Situation Summary | Avian Influenza (Flu) (cdc.gov)

Humans

- Total Reported Human Cases in the United States: **2** (since 2022)
  - **1** following exposure to dairy cows (reported on 4/01/2024) | Full Report >
  - **1** following exposure to poultry (reported on 4/28/2022) | Full Report >
- States with Reported Case(s): **2**

Wild Birds

Wild Birds Detected

9,352

as of 5/14/2024 | Full Report >

Jurisdictions with Bird Flu in Wild Birds

50

Poultry

Poultry Affected

90,892,846

as of 5/14/2024 | Full Report >

States with Poultry Outbreaks

48

Dairy Cattle

States with Outbreaks in Cattle

9

as of 5/16/2024 | Full Report >

Dairy Herds Affected

49

as of 5/16/2024 | Full Report >

Proactive surveillance for avian influenza H5N1 and other priority pathogens at mass gathering events

- Recurring **mass gatherings** at religious, sporting, or festival events are sources of infectious disease transmissions,
- **Advanced planning**, risk assessment, and updates on guidance to countries hosting the event,
- Most of the human avian influenza cases reported worldwide to date, have been avian influenza **A(H7N9), A(H5N1), and A(H5N6) viruses**.
- 2004, the emergence of the novel **Highly Pathogenic Avian Influenza (HPAI)** virus, A(H5N1), had focused attention of **Saudi Arabia's government** and of WHO because of the nearly **1.6 million pilgrims** from across the world expected for the annual Hajj pilgrimage at the time.
- Fortunately, there have been no major outbreaks from any mass gathering events.

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Pathogens with *epidemic* potential of concern at 2024 mass gathering events

Viral pathogens

WHO Blueprint Priority pathogens list

- Crimean–Congo haemorrhagic fever virus
- Ebola virus
- Marburg virus
- Lassa fever virus
- MERS-CoV
- SARS-CoV
- SARS-CoV-2
- Nipah virus and henipaviruses
- Rift Valley fever virus
- Zika virus
- Monkeypox virus

Other re-emerging viruses of concern

- Highly pathogenic avian Influenza virus (H5N1)
- HIV (antiretroviral resistant strains)
- Non-polio enteroviruses (EV-71, EV-68)
- Influenza A and variants
- Dengue virus
- Yellow fever virus
- Rabies virus
- Equine encephalitis virus
- Other

***Bacterial* pathogens**

WHO priority AMR pathogens list

Critical priority

- *Acinetobacter baumannii* (carbapenem-resistant)
- *Pseudomonas aeruginosa* (carbapenem-resistant)
- Enterobacteriaceae (carbapenem-resistant, ESBL-producing)
- *Mycobacterium tuberculosis* (multidrug-resistant, extensively drug-resistant, and totally drug-resistant)

High priority

- *Enterococcus faecium* (vancomycin-resistant)
- *Staphylococcus aureus* (meticillin-resistant, vancomycin-intermediate, and vancomycin-resistant)
- *Helicobacter pylori* (clarithromycin-resistant)
- *Campylobacter* spp (fluoroquinolone-resistant)
- *Salmonellae* spp (*Typhi* and non-typhoidal; fluoroquinolone-resistant)
- *Neisseria gonorrhoeae* (penicillin-resistant, cephalosporin-resistant, and fluoroquinolone-resistant)

Medium priority

- *Streptococcus pneumoniae* (penicillin non-susceptible)
- *Haemophilus influenzae* (ampicillin-resistant, azithromycin-resistant, ceftriaxone-resistant)
- *Shigella* spp (fluoroquinolone-resistant)
- *Bordetella pertussis* (macrolide-resistant)
- *Vibrio cholerae* (resistant to ampicillin, nalidixic, chloramphenicol, and tetracycline)

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Building global preparedness for avian influenza

Diagnostics

Commercial assays for human influenza can likely detect A(H5N1) viruses in respiratory specimens because they target conserved proteins,[29] but will not identify H5 specifically but as influenza A positive; H5 specific tests are needed for confirmation. Pipelines for rapid test development are needed for pandemic control, since rapid tests greatly aid in prevention and disease control, such as the implementation of guidelines for isolation and treatment; however, PCR confirmation might still be needed to enhance detection of infections.

Virological assessments

Continued genetic virological analyses should help identify changes in A(H5N1) that may impact adaptability and transmissibility. So far, genetic changes in A(H5N1) enhance lower respiratory tract replication in some mammals, but there is no evidence of increased transmissibility to humans through changes in upper respiratory tract receptor binding.[29] Continued monitoring of A(H5N1) for susceptibility to antivirals is needed with genotype and phenotype analysis.

Vaccine development and production

WHO works with WHO Collaborating Centres, the World Organisation for Animal Health, and the Organisation for Animal Health/Food and Agriculture Organization of the United Nations Network of Expertise on Animal Influenza and other modellers twice a year to review circulating influenza viruses and match to available vaccines during the vaccine composition meetings where vaccine components are proposed. These candidate vaccine viruses are only for human use. There are other candidate vaccine viruses to reduce animal-to-human transmission for poultry. Communication and collaboration between world governing bodies, governments, and industry should enable production and vaccine deployment in case of sustained human-to-human transmission of avian influenza. Additionally, due to challenges with the Pandemic Treaty,[30] preset agreements should be made to ensure equitable access to medical countermeasures, including vaccines, for low-income and middle-income countries.

Public communication and engagement

Clear and transparent communication with the public and community leaders is needed to disseminate up-to-date information with special emphasis on first responders and those most at risk, including farmers, farm workers, cullers, veterinarians, and health-care professionals. Early and continuous engagement and trust building is needed to have effective channels of communication.

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