“Personalized Medicine, Colorectal Cancer and Gut Bacteria”

Invited Talk

City of Hope City Forum

Pasadena, CA

October 21, 2014

Dr. Larry Smarr

Director, California Institute for Telecommunications and Information Technology

Harry E. Gruber Professor,

Dept. of Computer Science and Engineering

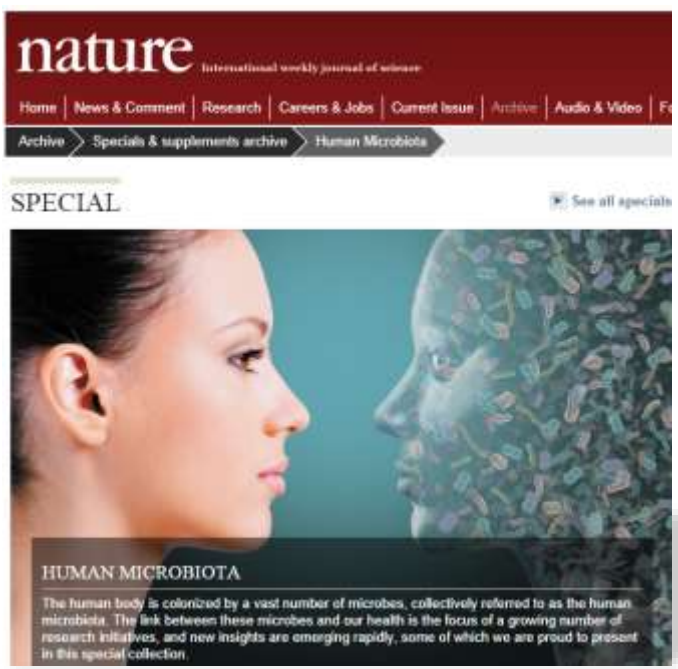
Jacobs School of Engineering, UCSD

http://lsmarr.calit2.net

Intense Scientific Research to Understand the Human Microbiome







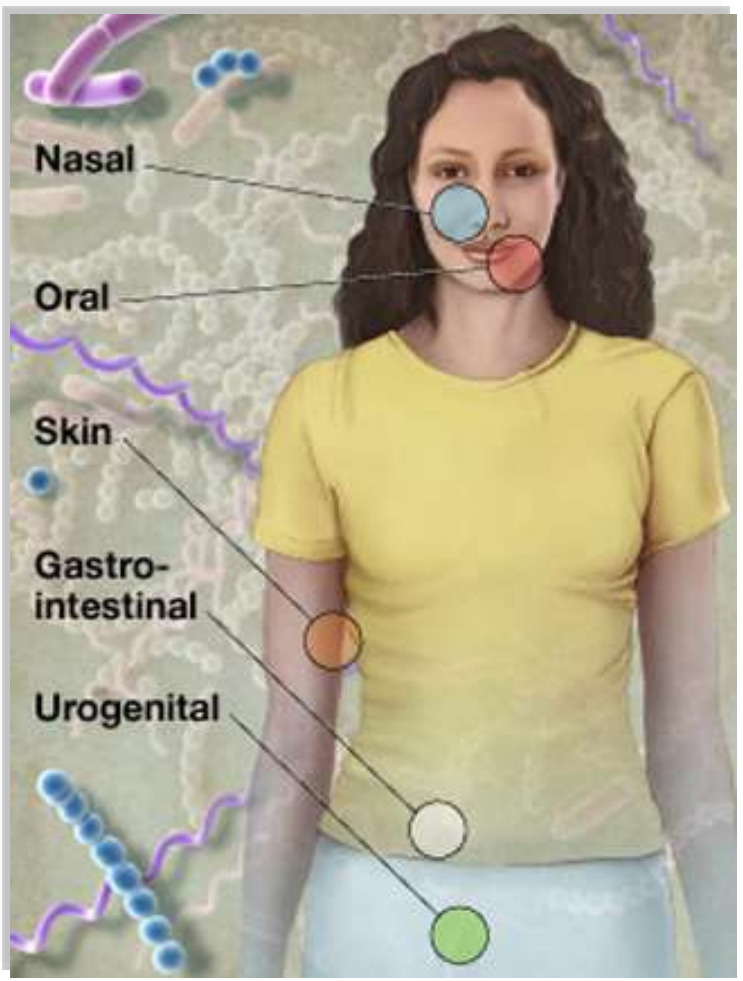
You Are a SuperOrganism

The Human Genome Contains <1% of the Bodies Genes

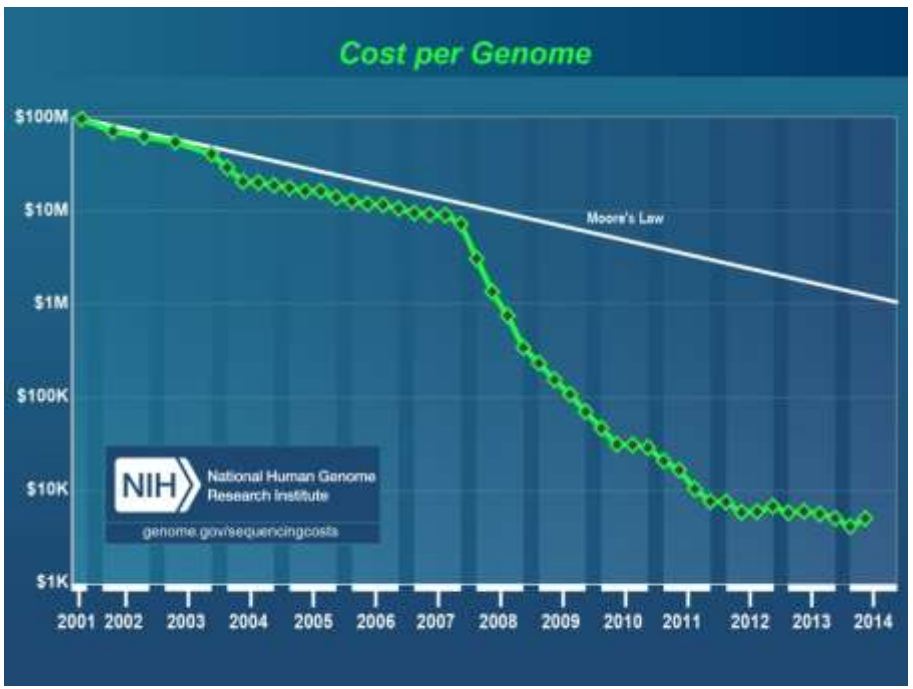
10X

MORE

Bacterial Cells
Than Human Cells
in Your Body



Cost of Sequencing a Human Genome



HAS FALLEN OVER 10,000X IN 10 YEARS

Enabling sequencing of Human and Microbial Genomes

Can the Gut Microbiome Intermediate Between Inflammation & the Development of Colorectal Cancer?

Colorectal cancer (CRC) is the most common cancer among inflammatory bowel disease (IBD) patients

However, IBD-related CRC is only 2% of all CRC

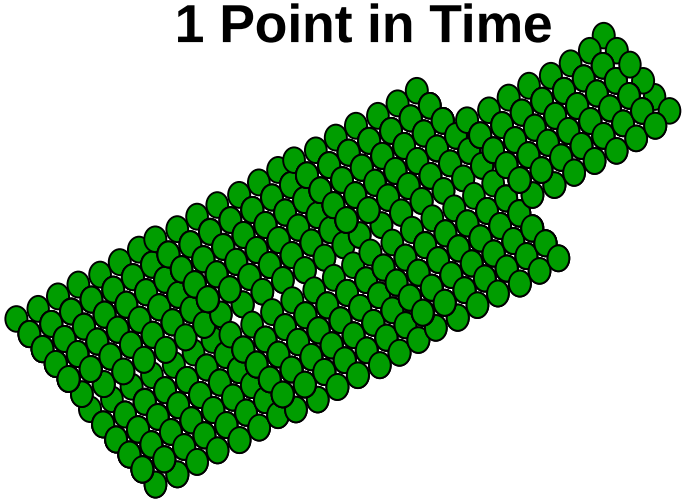
The root cause of Colorectal Cancer is unclear, but inflammation is a well-recognized risk factor*

(Wu et al. 2009; McLean et al. 2011)

Compared My Gut Microbiome Ecology with NIH Human Microbiome Project

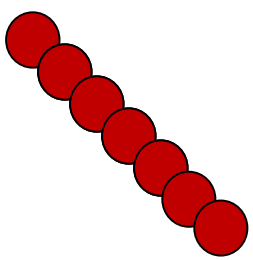
"Healthy" Individuals

250 Subjects
1 Point in Time



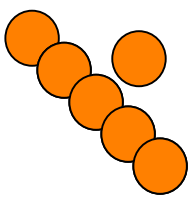
Larry Smarr

7 Points in Time

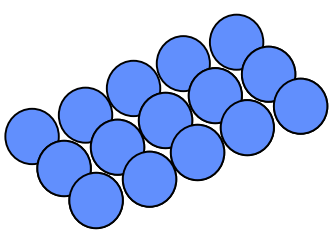


IBD Patients

2 Ulcerative Colitis Patients,
6 Points in Time

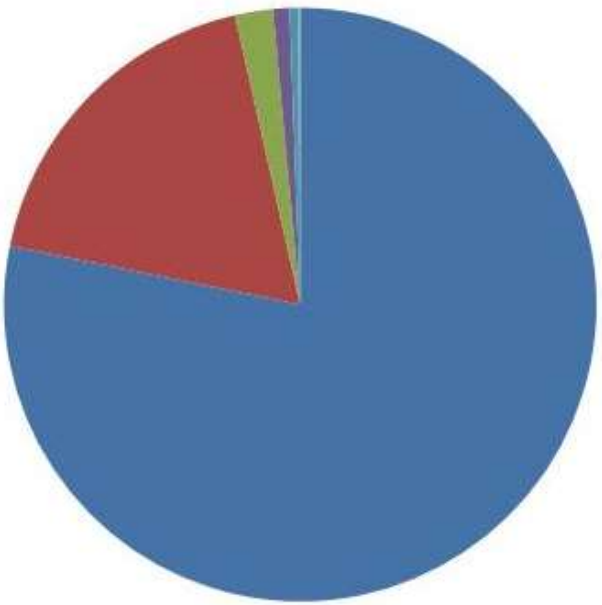


5 Ileal Crohn's Patients,
3 Points in Time

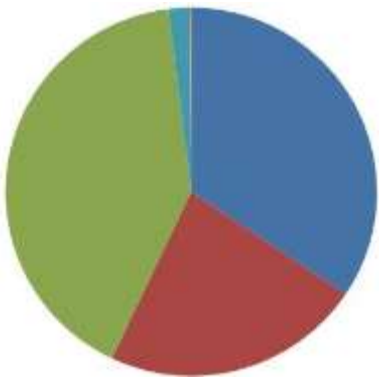


Major Shifts in Microbial Ecology Phyla Between Healthy and Two Forms of IBD

Average Healthy

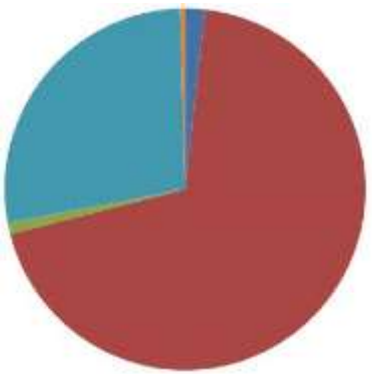


Average Ulcerative Colitis



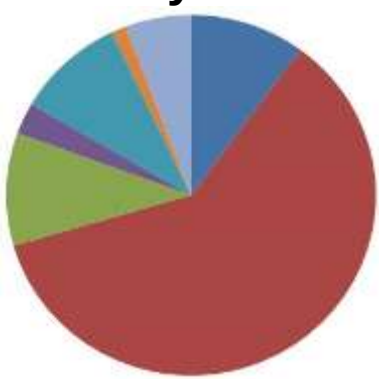
Explosion of Proteobacteria

Average Crohn's Disease



Collapse of Bacteroidetes
Explosion of Actinobacteria

Average Larry Smarr



Hybrid of UC and CD
High Level of Archaea

Emerging Role of the Human Gut Microbiome in the Transition to Colorectal Cancer

"Inflammation is thought to induce or promote intestinal cancer through the effects of immune cells on epithelial cells, leading to oxidative stress, DNA damage, and cell turn-over. However, the notion that chronic inflammation can lead to the accumulation of cancer-promoting bacteria begins to shift greater attention toward the microbiota."



Bacteria Deliver a Genotoxic Hit
Robert F. Schwabe and Timothy C. Wang
Science **338**, 52 (2012);
DOI: 10.1126/science.1229905

Fusobacteria Are Found To Be More Abundant In Colorectal Carcinoma Tissue

The New York Times

Two Cancer Studies Find Bacterial Clue in Colon

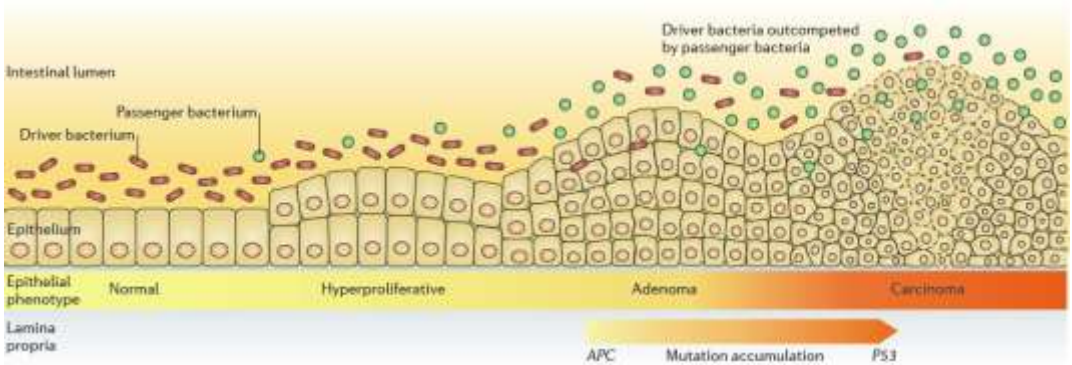
By GINA KOLATA
Published: October 17, 2011

Genomic analysis identifies association of *Fusobacterium* with colorectal carcinoma Aleksander D. Kostic et al.

Fusobacterium nucleatum infection is prevalent in human colorectal carcinoma Mauro Castellarin et al.

CSH PRESS GENOME RESEARCH

The Bacterial Driver-Passenger Model for Colorectal Cancer Initiation



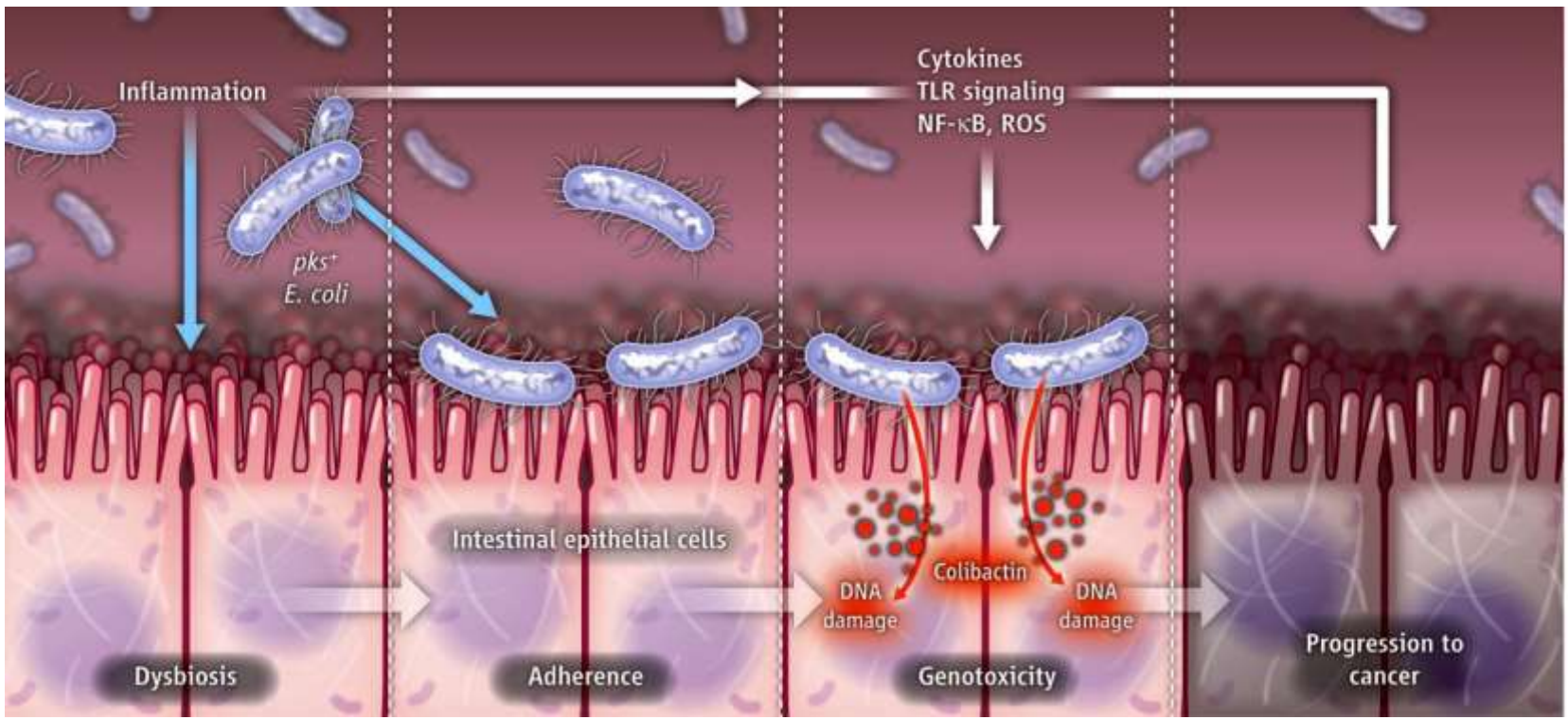
Is Fusobacterium nucleatum a "Driver" or a "Passenger"

"Early detection of Colorectal Cancer (CRC) is one of the greatest challenges in the battle against this disease & the establishment of a CRC-associated microbiome risk profile could aid in the early identification of individuals who are at high risk and require strict surveillance."

Tjalsma, et al. Nature Reviews Microbiology v. 10, 575-582 (2012)

Chronic Inflammation Can Accumulate Cancer-Causing Bacteria in the Human Gut

Escherichia coli Strain NC101



Bacteria Deliver a Genotoxic Hit
Robert F. Schwabe and Timothy C. Wang
Science **338**, 52 (2012);
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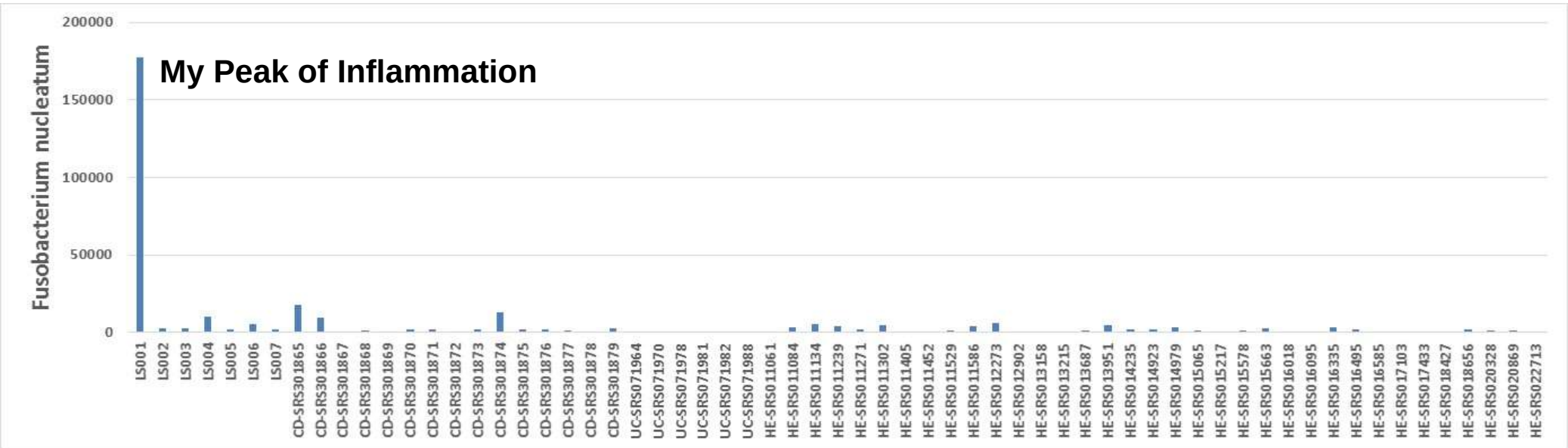
E.Coli Claims the Driving Seat for Cancer

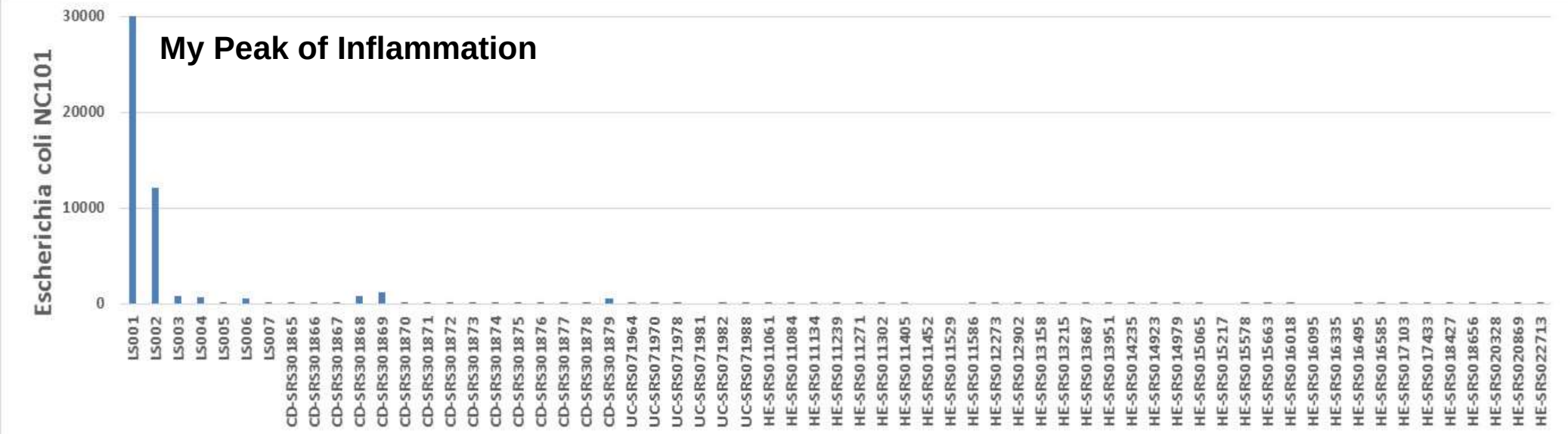
"Arthur *et al.*
provide evidence that
inflammation alters the intestinal microbiota
by favouring the proliferation of genotoxic commensals, and that the
Escherichia coli **genotoxin colibactin promotes colorectal cancer."**

Christina Tobin Kåhrström
Associate Editor,
Nature Reviews Microbiology

VOLUME 12 | OCTOBER 2012
NATURE REVIEWS | CANCER

I Discovered I Had the Highest Values of E. coli NC101 and Fusobacterium nucleatum of All My Subjects





National Programs Are Underway: Inflammation, Microbiome, & Cancer

NYU CANCER INSTITUTE
AN NCI-DESIGNATED CANCER CENTER

The Microbiome: Friend or Foe?

NYUCI Scientists Study Inflammation, Bacteria, and Cancer

MAYO CLINIC

CENTER FOR INDIVIDUALIZED MEDICINE

MICROBIOME PROGRAM

COLON CANCER

This project makes the assumption that the diet and resulting intestinal microbiome communities create metabolites that can harm bowel cells an produce DNA damage, leading to cancer development. Two metabolic pathways with toxic potential are being tested, including sulfate-reducing bacteria and methanogens.



MICROBIOME: BACTERIA AND OUR BODIES

Heidi Nelson, M.D., director, provides an overview of the Microbiome Program, Center for Individualized Medicine.

Predictive, Personalized, Preventive & Participatory Medicine

Newsweek

A Doctor's Vision of the Future of Medicine

Leroy Hood
NEWSWEEK

From the magazine issue dated Jul 13, 2009



PIONEER 100
HUNDRED PERSON WELLNESS PROJECT
Institute for Systems Biology

Will Grow to 1000, then 10,000

Thanks to Our Great Team!

UCSD Metagenomics Team

Weizhong Li
Sitao Wu

JCVI Team

Karen Nelson
Shibu Yooseph
Manolito Torralba

Calit2@UCSD Future Patient Team

Jerry Sheehan
Tom DeFanti
Kevin Patrick
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