

Dysbiosis – what are you going to do about it?

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Gut microbiota (microbiome).

NATURE | COMMENT



Microbiology: Microbiome science needs a healthy dose of scepticism

William P. Hanage

20 August 2014



Jonathan Eisen

<http://phylogenomics.blogspot.co.nz/search/label/overselling%20the%20microbiome%20award>

Causation and Correlation: do you know the difference?

Obesity: Jeff Gordon (2013) says "... obesity is a very complex puzzle with lots of parts - how much food we consume, how much exercise we do each day. The question was, could our microbial communities, which are tasked with the responsibility of transforming the foods that we eat into metabolic products that shape our biology and our biological differences, what role do they play?"

Diabetes: Henry Tilg (2014) says "..... suggest that patients with T2D show evidence of gut dysbiosis. ... available studies can only be considered as a starting point."

Inflammatory bowel diseases: Harry Sokol (2014) says "In some circumstances, the tolerance toward the intestinal microbiota is broken, leading to inappropriate immune response and intestinal or extra-intestinal inflammation...This is the case in inflammatory bowel diseases (IBD) such as Crohn's disease (CD) and ulcerative colitis In IBD a deviation of the gut microbiota composition called dysbiosis has been repeatedly pointed out."

Dysbiosis: the relative abundances of bacterial groups are altered compared to the situation in health.

Possible solutions: boosting particular populations of bacteria by adding probiotics or prebiotics to the diet.

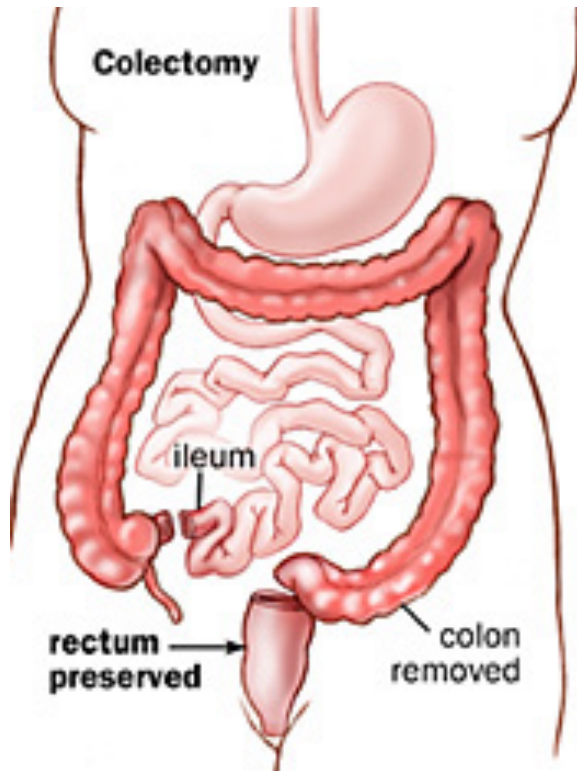
Probiotics: "Live microorganisms which when administered in adequate amounts confer a health benefit on the host." (Joint FAO/WHO Working Group, 2002).

Prebiotic: "A non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, that can improve the host health." (Gibson & Roberfroid, 1995).

To say nothing about **faecal transplants (transpoosions)**.

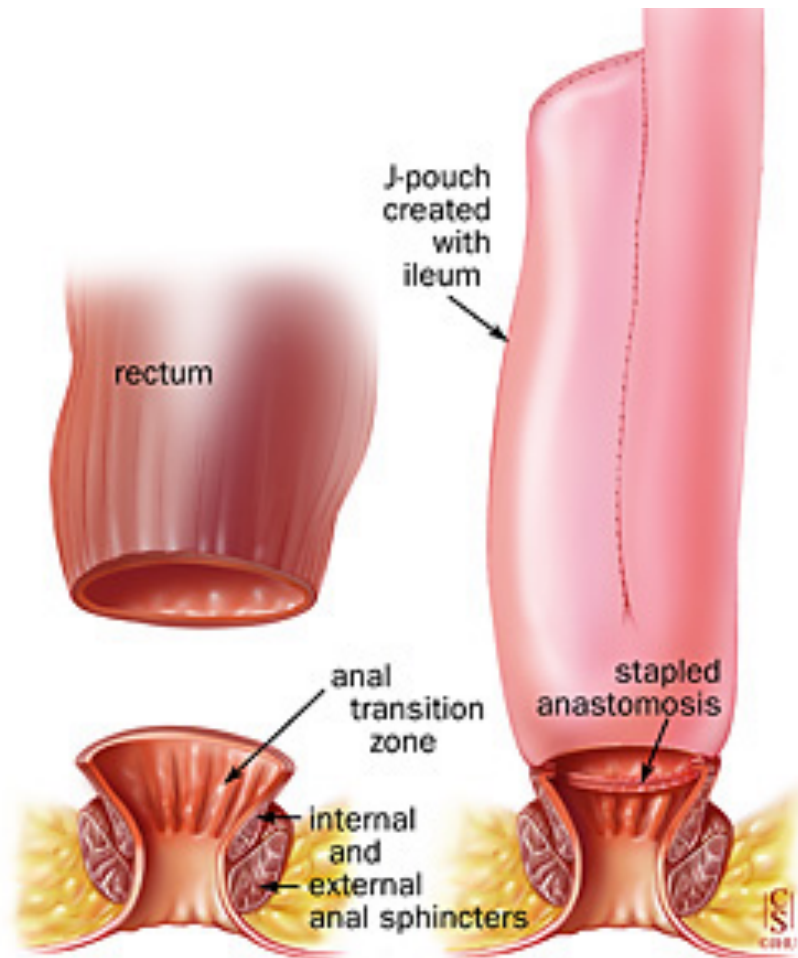
Ulcerative colitis

Ileal pouch-anal anastomosis.

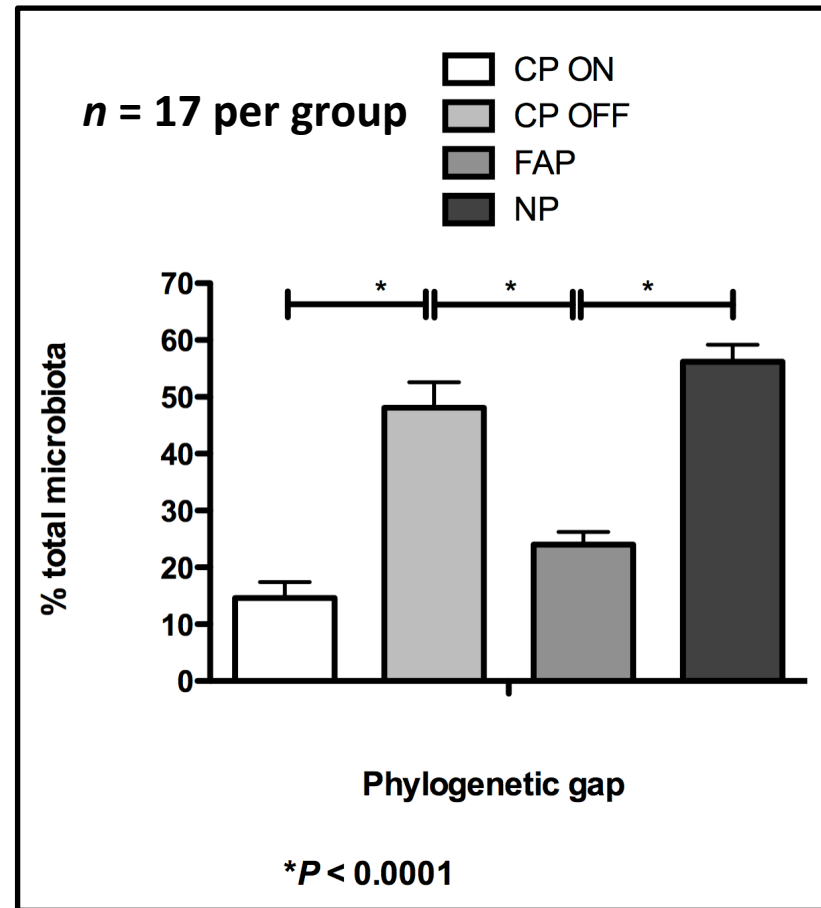
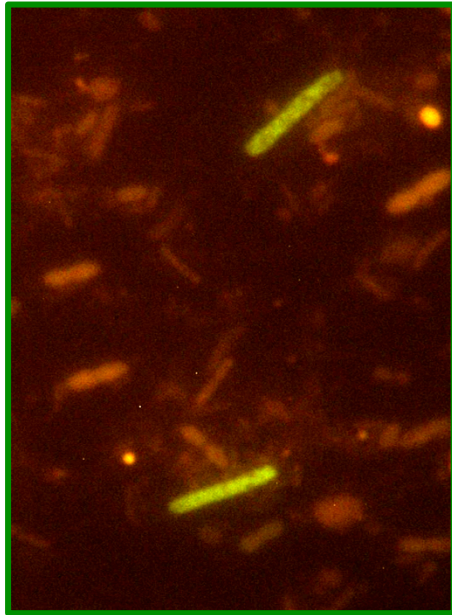


Chronic pouchitis.

Pouchitis can be treated with antibiotics (antibacterial).



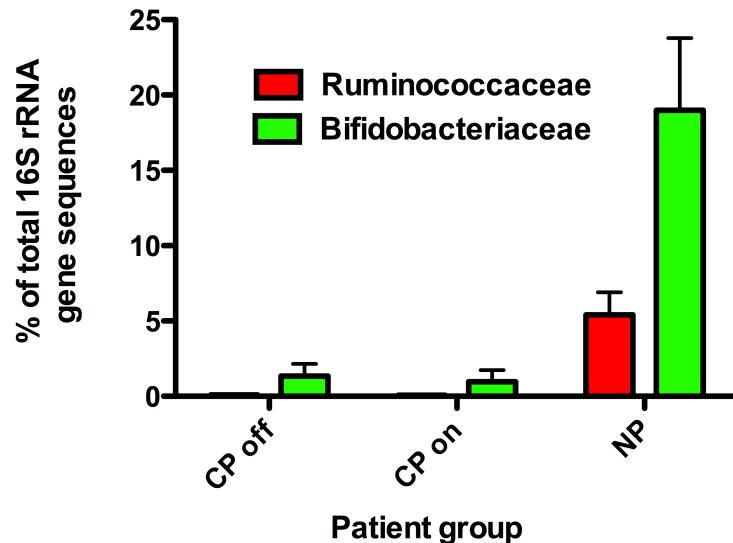
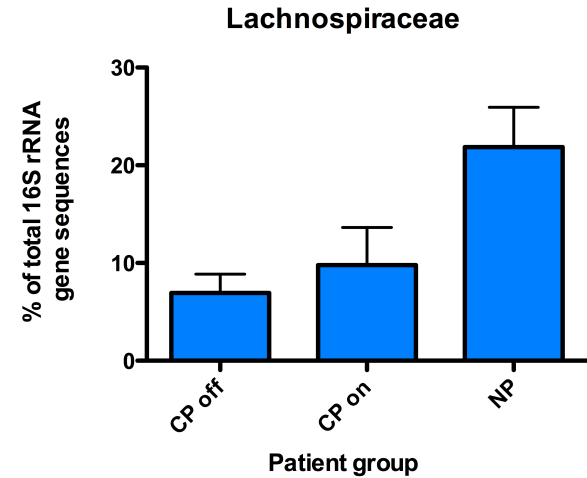
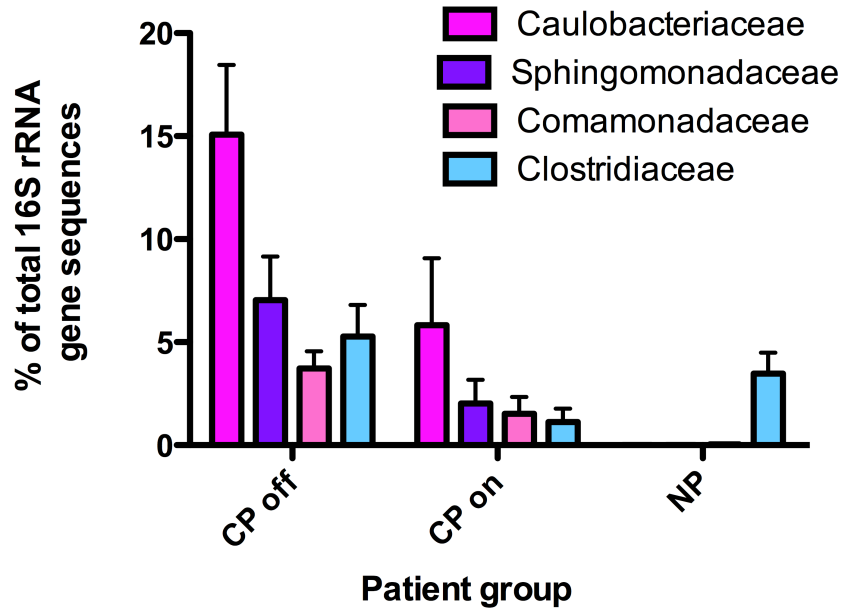
Fluorescent oligonucleotide probes to quantify bacterial groups



Tannock GW, Lawley B, Munro K, Lay C, Taylor C, Daynes C, Baladjay L, McLeod R, Thompson-Fawcett M. 2012. Comprehensive analysis of the bacterial content of stool from patients with chronic pouchitis, normal pouches, or familial adenomatous polyposis pouches. *Inflamm Bowel Dis.* 18:925-934.

Crohn's and Colitis Foundation of America

Sequencing the 16S rRNA genes amplified from pouch stool DNA reveals potential probiotic product.



Safety and acceptability trial with pouch patients

**Otago Innovation Ltd.
(A University of Otago Company)**

Prebiotic studies with rats

Wayne Young



Enterprise Ph.D.
Scholarship from the
Tertiary Education
Commission.

Changes in Bowel Microbiota Induced by Feeding Weanlings Resistant Starch Stimulate Transcriptomic and Physiological Responses. Wayne Young et al. Appl. Environ. Microbiol. (2012) 78:6656.

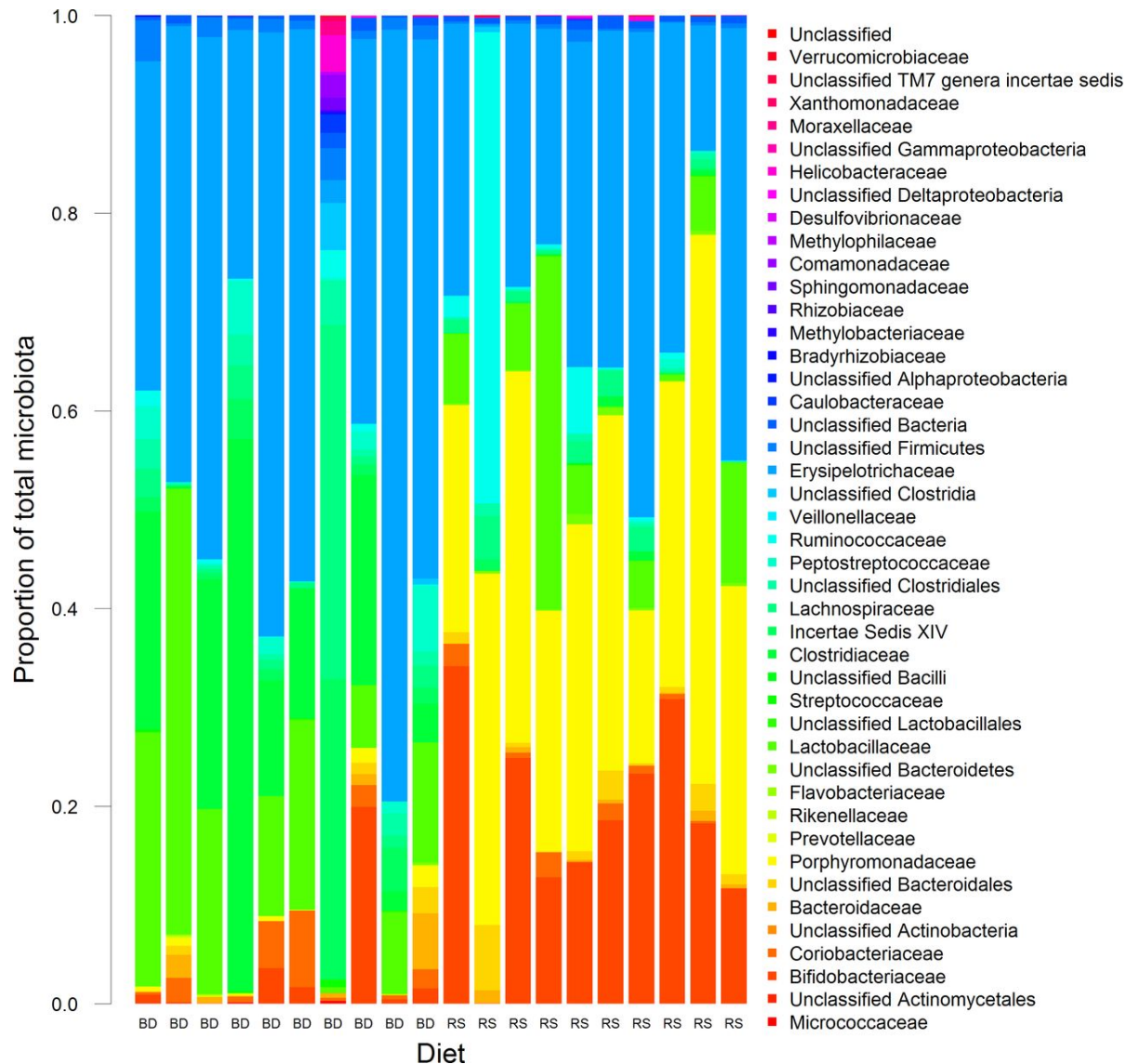
Bowel Microbiota Moderate Host Physiological Responses to Dietary Konjac in Weanling Rats. Wayne Young et al. J. Nutr. (2013) 143: 1052.

Weanling rats, basal diet or basal diet plus 'prebiotic', 28 days.

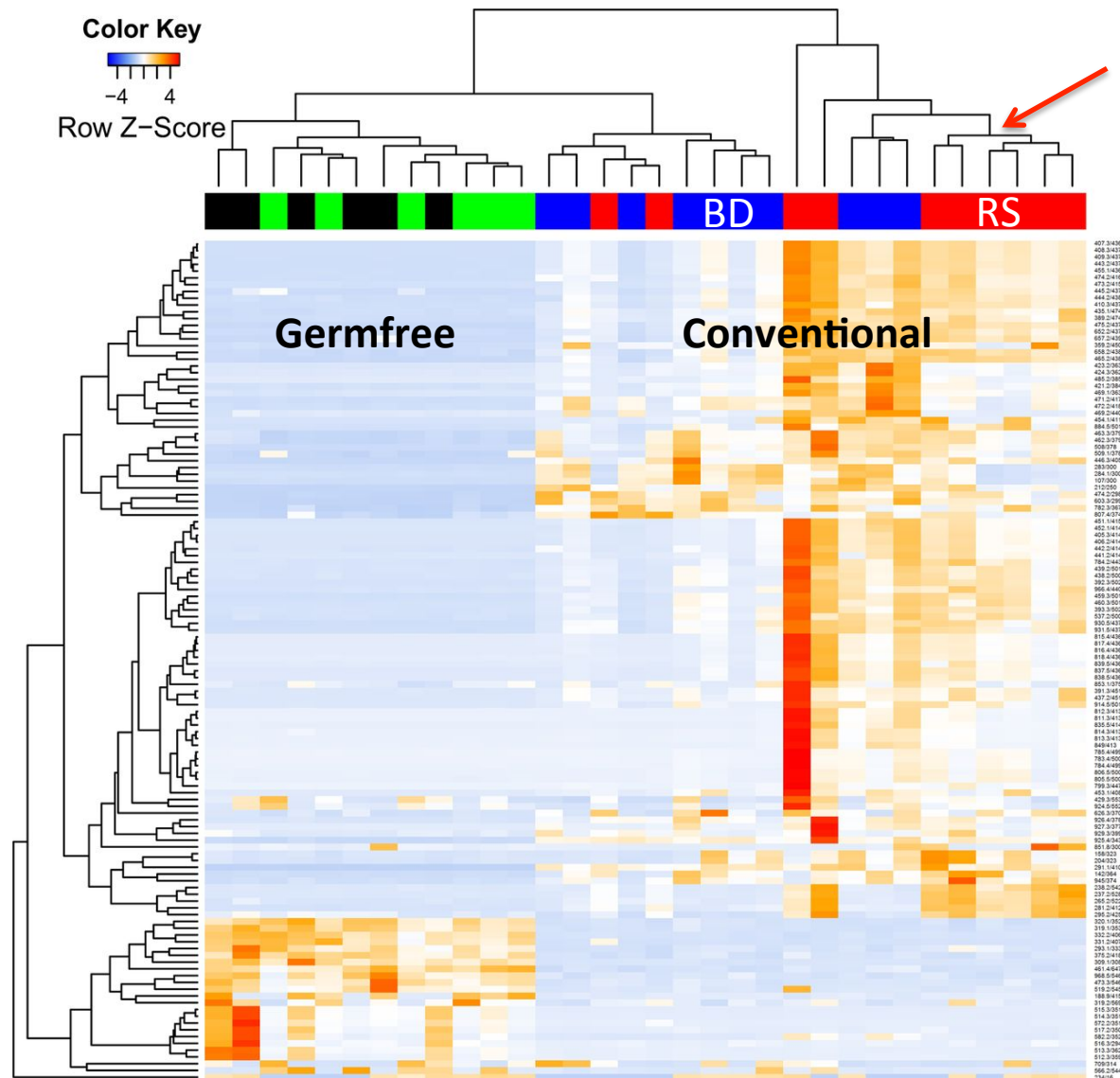
N = 10 per group.

Large bowel microbiota, mucosal gene expression, mucosal histology, serum metabolite profiles.

Abundances of family level taxa as a proportion of total bacterial sequences identified from the colonic digesta of individual conventional rats fed BD or **Resistant Starch (Hi-Maize) 5%** for 28 days using high-throughput sequencing of 16S rRNA gene amplicons.



Cluster analysis and heat map of serum metabolite ion signal intensities from conventional and germ-free rats fed BD or RS for 28 days, using metabolites that show the top 15% of variation across all samples. Determined by LC-MS.



Serum metabolites in conventional and germfree rats fed BD or BD + **konjac.**

Ion/time	Identification (simplified nomenclature)	Conventional rats*	Germfree rats*
437.2/421	Lysophosphatidic acid	2.8	NS
438.2/407	Lysophospholipid	2.4	NS
465.4/345	Sterol lipid	1.7	3.1
478.3/326	Glycerophospholipid	1.6	1.9
429.4/456	Sterol lipid	1.9	NS
251.1/353	Formylkynurenine	NS	4.6

***Fold increase KJ-5 relative to BD.
NS = no statistically significant difference.**

**Laurenson Fund,
Otago Medical Research Foundation.
Andrew Day and Richard Gearry (Gastroenterologists, Christchurch).
Blair Lawley & Anna Otal (Otago).**

There are at least 3079 detectable metabolites in **human urine**, of which 1350 have been quantified. At least **72 of these compounds are of microbial origin**, 1453 are endogenous while 2282 are considered exogenous (note some compounds can be both exogenous and endogenous), coming from **diet**, drugs, cosmetics or environmental exposure.

