Diet, the Microbiota, Ethnic Differences, and Colon Cancer Risk

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University of Pittsburgh
The Power of Epidemiology

• Approximately 90% of GI cancers are due to differences in diet
  • Doll & Peto J Natl Cancer Inst 1981
Diet and Colon Cancer

- Epidemiological evidence
- Human interventions
- Animal experiments
- Cell biology
Protein
- Aminoacids
  - Arginine
  - Glutamine
  - Methionine
    - Immuno-stimulatory
    - Anti-Neoplastic
    - Anti-Proliferative

Fat
- Fatty Acids
  - n-6
  - n-3
    - Anti-inflammatory
    - Anti-Neoplastic
    - Anti-Proliferative

Carbohydrate
- Fibre/Resistant Starch
  - SCFAs (butyrate)
    - Immunosuppressive
    - Anti-inflammatory
    - Anti-Proliferative
# Diet and Colon Cancer Risk

<table>
<thead>
<tr>
<th>Increase Risk</th>
<th>Decrease Risk</th>
</tr>
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<tbody>
<tr>
<td>Red meat</td>
<td>Fiber</td>
</tr>
<tr>
<td>Animal fat</td>
<td>Vegetables</td>
</tr>
<tr>
<td>Processed meats</td>
<td>Calcium</td>
</tr>
<tr>
<td>Obesity</td>
<td>Fish oils</td>
</tr>
<tr>
<td>Inactivity</td>
<td>Antioxidants, selenium</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Folic acid</td>
</tr>
<tr>
<td>Cigarettes</td>
<td>Postmenopausal hormones</td>
</tr>
</tbody>
</table>
Meat and Fat

- Prospective study of 88,751 healthy women aged 34-59 (Nurses Health Study)
- Dietary questionnaire in 1980, follow-up 1986
- 150 incident cases of colon cancer
Meat and Fat

Results

- Significant influence on cancer risk:
  - Animal fat ↑
  - Beef, pork and lamb daily risk ↑ 2.5X
  - Processed meats and liver ↑
  - Fish and skinless chicken ↓
  - Red meat:chicken and fish ratio ↑ 2.5X (p=0.0005)
Red Meat

- Association confirmed by Norat’s EPIC study of 478,040 and Sandhu’s metanalysis (2005, 2001)

- Multiple actions based on its saturated fat, protein, heme and iron content, and the potential for ‘browning’ to produce carcinogenic heterocyclic amines
Mismatch Repair

- Dutch study: 184 sporadic colon cancer cases and 259 controls
- Red meat and alcohol enhanced the development of MSI-L/MSS and MSI-H tumors
- Fresh fruit reduced MSI-H cancers by epigenetically silencing hMLH1
  - Diergaarde et al. 2003
Fat

Relative Risk

Intake of Animal Fat (quintile)

Adapted from Willet et al. NEJM 1990 323 (24) 1669
Mechanisms

- High fat diet increases fecal bile acids
- 7-α-dehydroxylating bacteria convert colonic primary bile acids to secondary bile acids
- Secondary bile acids (deoxycholic acid) cytotoxic to colonic epithelial cells, mutagenic and anti-apoptotic in animal models¹
- Fecal and serum DCA levels are elevated in patients with colon cancer²

¹ Pereira et al. Cancer Lett. 2004
² Ochsenkun et al Cancer 1999
Fiber

- First attributed to low colon cancer prevalence in Africans by Burkitt

Conflicting Epidemiological Results

- EPIC study showed decreased risk of colonic adenomas and colorectal cancer with fiber (Bingham et al. Lancet 2003 361:1496)

- Nurses’ Health Study- no relationship between fiber and risk of colorectal cancer or adenoma (Fuchs et al. NEJM 1999 340:169)

  - Maybe explained by the complex nature of maldigested starch – which is the precursor for anti-neoplastic butyrate
Fiber & Vegetables

- 37 observational epidemiological studies and metanalysis of 16 case-control studies
- Overall protective effect of fiber-rich foods, with odds ratio of 0.57 comparing lowest and highest quantiles
- Most convincing for vegetables

- *Trock et al. JNCI 1990*
Critical Role of Butyrate

- **Chief energy source** for colonocytes

- **Chief regulator of epithelial growth:**
  - Suppresses epithelial proliferation, enhances differentiation
  - Suppresses the inflammatory response TNFα, NO
  - Tumor suppression p53, TGFβ
  - Increases apoptosis

- **Promotes the growth** of probiotic species:
  e.g. *Lactobacilli*, which suppress proinflammatory and increase anti-inflammatory cytokines, displace pathogens, increase tight junctions
Calcium

Hypothesized that damaging effects of free fatty acids and bile acids could be reduced with supplemental calcium causing precipitation into calcium soaps

- In laboratory animals, increase in colonocyte proliferation after cholic acid or free fatty acid stimulation mitigated by calcium supplementation (Pence et al. Mutat Res 1993 290:87)
- There was a reduction of the abnormal colonic proliferation in patients with familial risk after 2-3 months to almost normal levels (Lipkin et al. NEJM 1985 313:381)
- RCT showed a significant reduction on recurrence of colorectal adenomas in 930 patients (Baron et al. NEJM 1999 340:101)
- NHS and HPFS cohorts showed an inverse association between higher total calcium intake and distal colon cancer (Wu et al. JNCI 2002 94(6): 437)
Selenium

Selenium is a component of glutathione peroxidase which may prevent free radical damage to tissue

- Low levels have been associated with an increased risk of colorectal neoplasia (Schrauzer et al. Bioinorganic Chem 1977 7:23)
- Significant inverse correlations found between selenium intake and colorectal cancer (Willett et al. Lancet 1983 2:130)
- A greater than 50% reduction in colorectal cancer incidence shown in patients taking selenium in the form of brewer’s yeast (Clark et al. JAMA 1996 276:1957.)
Folic Acid

Folate is essential for DNA synthesis and repair

- Epidemiological studies have provided evidence that the relationship between dietary folate and colon cancer risk assumes a bell-shaped curve, with very low intakes increasing risk as well as very high intakes

- *Kim YI. Role of folate in colon cancer development and progression. J Nutr. 2003;133:S3731–9*
Dietary factors associated with a low risk of colon cancer in colored west coast fishermen: SAfMJ 1997
Eicosapentaenoic acid reduces rectal polyp number and size in familial adenomatous polyposis

Nicholas J West,1 Susan K Clark,1 Robin K S Phillips,1 John M Hutchinson,2 Roger J Leicester,3 Andrea Belluzzi,4 Mark A Hul6

Figure 3  Comparison of the effects of eicosapentaenoic acid as the free fatty acid (EPA-FFA) and celecoxib in patients with familial adenomatous polyposis from this study and the study of Steinbach et al.6 (A) The percentage change in polyp number in a defined area of colorectal mucosa. (B) The change in global polyp burden measured by video panel assessment. Note that a positive difference between the baseline and 6 month examination implies a decreased global polyp burden ("better").

A

% change in polyp number from baseline to 6 months

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Active</th>
<th>Net change</th>
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<tr>
<td>9.7</td>
<td>3.1</td>
<td>6.6</td>
</tr>
<tr>
<td>-12.6</td>
<td>-22.5</td>
<td>-35.1</td>
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<tr>
<td>-22.4</td>
<td>-25.6</td>
<td>-33.0</td>
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B

change in mean score from baseline to 6 months

<table>
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<th>Active</th>
<th>Net change</th>
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<tbody>
<tr>
<td>-0.34</td>
<td>0.09</td>
<td>0.05</td>
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<tr>
<td>0.09</td>
<td>0.3</td>
<td>0.12</td>
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<tr>
<td>0.42</td>
<td>0.4</td>
<td>0.02</td>
</tr>
</tbody>
</table>
The Importance of a Balanced Diet

- The mutagenic effects of bile acids can be inhibited by increased butyrate production from high amylose resistant maize starch - McMillan et al. BiochemBiophys Res Comm 2000; 273:45–49.

- The effects of dietary casein and meat on DNA damage can also be prevented by the simultaneous consumption of resistant starch: Toden et al. Cancer BiolTher 2006; 5:267–272. Another important illustration of how beneficial dietary items can suppress carcinogenic factors


- The toxicity of heme can be annulled by chlorophyll
Relative Dietary Intakes of Items Know to Influence Colon Cancer Risk

<table>
<thead>
<tr>
<th>Item</th>
<th>% of RDA</th>
<th>Blacks</th>
<th>Whites</th>
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<tbody>
<tr>
<td>Energy</td>
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<td>Protein</td>
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<td>Fat</td>
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<tr>
<td>Calcium</td>
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<td></td>
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<tr>
<td>Vitamin A</td>
<td>**</td>
<td></td>
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<tr>
<td>Folate</td>
<td>**</td>
<td></td>
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<tr>
<td>Vitamin C</td>
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<tr>
<td>Fiber</td>
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</table>

** p < 0.0005
* p < 0.0001

Geography and Ethnicity

International variation
DM Parkin

6334

Figure 5  Incidence of colorectal cancer in males
Cancer Survival Among US Whites and Minorities

A SEER (Surveillance, Epidemiology, and End Results) Program Population-Based Study


- **Methods:** Cancer-specific survival rates were analyzed for more than 1.78 million patients who resided in the 9 geographic areas and were diagnosed between 1975 and 1997 as having an incident invasive cancer.

- **Results:** Survival rates improved between 1988 to 1997 for virtually all racial or ethnic groups.

  - African American, American Indian and Alaskan native, and Hawaiian native patients tended to have higher relative risks of cancer death than the other groups.

  - American Indians and Alaskan natives generally exhibited the highest RRs of cancer death, except for colorectal cancer in males.
African-American and Caucasian disparities in colorectal cancer mortality and survival by data source: An epidemiologic review

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bDepartment of Epidemiology, University of Alabama at Birmingham, Birmingham, AL, USA
cDepartment of Pathology, University of Alabama at Birmingham, Birmingham, AL, USA

Abstract

Over the past four decades in the United States, there has been a divergent trend in mortality rates between African-Americans and Caucasians with colorectal cancer (CRC). Rates among Caucasians have been steadily declining, whereas rates among African-Americans have only started a gradual decline in recent years. We reviewed epidemiologic studies of CRC racial disparities between African-Americans and Caucasians, including studies from SEER and population-based cancer registries, Veterans Affairs (VA) databases, healthcare coverage databases, and university and other medical center data sources. Elevated overall and stage-specific risks of CRC mortality and shorter survival for African-Americans compared with Caucasians were reported across all data sources. The magnitude of racial disparities varied across study groups, with the strongest associations observed in university and non-VA hospital-based medical center studies, while an attenuated discrepancy was found in VA database studies. An advanced stage of disease at the time of diagnosis among African-Americans is a major contributing factor to the racial disparity in survival. Several studies, however, have shown that an increased risk of CRC death among African-Americans remains even after controlling for tumor stage at diagnosis, socioeconomic factors, and comorbidity. Despite advances in treatment, improvements in the standard of care, and increased screening options, racial differences persist in CRC mortality and survival. Therefore, continued research efforts are necessary to disentangle the clinical, social, biological, and environmental factors that constitute the racial disparity. In addition, results across data sources should be considered when evaluating racial differences in cancer outcomes.
Later diagnosis, worse survival

Stage Distribution (%)  Survival (%)
Figure 4
Per capita beef consumption by race/ethnicity

Migrant Studies

• In general migrants assume the cancer risk of their new countries
  • Japanese, Filipinos and Chinese to Hawaii and USA
  • Koreans and Vietnamese to USA

• However, risk is often lower for generations
  • Cultural or genetic???

• Within countries: ‘westernization’ in Alaska, Japan, Africa
The Microbiome

- ‘Black box’: difficult to culture, identify and characterize anaerobic bacteria
- *The Genomic era*: major breakthrough with culture-independent identification by high throughput gene sequencing and PCR of conserved regions of 16S rRNA
- Outnumber host cells 10:1, 800 species (increasing!), 7000 strains, number 100 trillion, weight 1-2Kg
- A vibrant mass of ‘foreign’ DNA
Lederberg (2000) has emphasized the importance of having a broad ecologic view of our relationships with microbes.

In this view, we are seen as superorganisms composed of an amalgam of both microbial and *H. sapiens* cells, where the survival of microbe and human is interdependent.
The Microbiota Composition

The majority of sequences are associated with only four phyla of the Bacteria:

- **Firmicutes** (49% of clones)
- **Bacteroidetes** (23%)
- **Proteobacteria** (21%)
- **Actinobacteria** (5%)

Only 1 Archaea species: *Methanobrevita Smithae*
The Microbiome Functions

- Self-survival: dependent on maldigested food
- Symbiotic: produce SCFAs, folate, biotin, vitamin K, thiamine, riboflavin, B12
- Affect energy balance, survival in intestinal failure, obesity risk
- ‘Educate’ the GALT
- Contrabiosis: H₂S, H₂, 2y bile salt production, *Strep bovis*, *H pylori*, *Strep faecalis*, SRBs
- Activate inflammation in IBD, colon cancer
- The ‘hygiene’ hypothesis: allergic disease, IBD
Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Carlotta De Filippoa, et al: PNAS 2010

16S rRNA gene surveys reveal a clear separation of two children populations investigated. (A and B) Pie charts of median values of bacterial genera present in fecal samples of BF and EU children.

C

D

E
The rarity of colon cancer in Africans is associated with low animal product consumption, high refined carbohydrate, *not fiber*

Differences in Colonic Fermentation

- Discovered by our studies on lactose intolerance examining breath hydrogen responses: >95% of Africans were LI; 80% were methane producers (O’Keefe et al. SAfMedJ 1983) compared to 20-40% westerners.

- 350ml drinks of whole milk were associated with mild abdominal symptoms in only 10%, in comparison to 50-80% of LI Americans, suggesting that Africans were more tolerant of malabsorbed carbohydrate (O’Keefe Eur J Clin Nutr 1990).

- Increased tolerance to lactose and milk associated with increased methanogenesis (O’Keefe et al AJCN 1991).
Why Do African Americans Get More Colon Cancer than Native Africans?\textsuperscript{1-3}

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\textsuperscript{4}Division of Gastroenterology and Pathology, University of Pittsburgh, Pittsburgh, PA 15213 and the \textsuperscript{5}University of Limpopo, Medunsa Campus, GaRanikwane, South Africa

Abstract

The incidence of colorectal cancer (CRC) is dramatically higher in African Americans (AAs) than in Native Africans (NAAs) (60:100,000 vs. <1:100,000) and slightly higher than in Caucasian Americans (CAs). To explore whether the difference could be explained by interactions between diet and colonic bacterial flora, we compared randomly selected samples of healthy 50- to 65-y-old AAAs (n = 17) with NAAs (n = 18) and CAs (n = 17). Diet was measured by 3-d recall, and colonic metabolism by breath hydrogen and methane responses to oral lactulose. Fecal samples were cultured for 7-wt dehydroxylating bacteria and \textit{Lactobacillus plantarum}. Colonoscopic mucosal biopsies were taken to measure proliferation rates. In comparison with NAAs, AAs consumed more ($P < 0.01$) protein (3.4 ± 9.3 g/d vs. 58 ± 4.1 g/d) and fat (11.4 ± 11.2 vs. 36 ± 3.6 g/d), meat, saturated fat, and cholesterol. However, they also consumed more ($P < 0.05$) calcium, vitamin A, and vitamin C, and fiber intake was the same. Breath hydrogen was higher ($P < 0.0001$) and methane lower in AAs, and fecal colony counts of 7-wt dehydroxylating bacteria were higher and of \textit{Lactobacilli} were lower. Colon crypt cell proliferation rates were dramatically higher in AAs (21.8 ± 1.1% vs. 3.2 ± 0.8% labeling, $P < 0.0001$). In conclusion, the higher CRC risk in mucosal proliferation rates in AAs than in NAAs were associated with higher dietary intakes of animal products and higher colonic populations of potentially toxic hydrogen and secondary bile-salt-producing bacteria. This supports our hypothesis that CRC risk is determined by interactions between the external (dietary) and internal (bacterial) environments. J. Nutr. 137: 1755–1823, 2007.
Colonic Epithelial Proliferation Rates

Split By: groups
Error Bars: ± 1 Standard Error(s)
<table>
<thead>
<tr>
<th></th>
<th>Native Africans</th>
<th>African Americans</th>
<th>Caucasian Americans</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>17</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Protein, g/d</td>
<td>58 ± 4</td>
<td>94 ± 9*</td>
<td>108 ± 10*</td>
</tr>
<tr>
<td>Meat protein, g/d</td>
<td>26 ± 2</td>
<td>65 ± 7**</td>
<td>77 ± 8***</td>
</tr>
<tr>
<td>Folate, μg/d</td>
<td>201 ± 23</td>
<td>481 ± 47**</td>
<td>526 ± 50***</td>
</tr>
<tr>
<td>Calcium, mg/d</td>
<td>228 ± 27</td>
<td>834 ± 100</td>
<td>1049 ± 112</td>
</tr>
<tr>
<td>Iron, mg/d</td>
<td>7.1 ± 0.5</td>
<td>18.3 ± 2.0***</td>
<td>18.9 ± 1.8***</td>
</tr>
<tr>
<td>Zinc, mg/d</td>
<td>6.7 ± 0.5</td>
<td>14 ± 1.5**</td>
<td>15.4 ± 1.3***</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM. Asterisks indicate different from Native Africans: *P < 0.05, **P < 0.005.
2 Reproduced from (1) with permission.
**TABLE 2**  Colonic evacuant contents of selected nutrients and the RBC folate concentration in African Americans, Caucasian Americans, and Native Africans

<table>
<thead>
<tr>
<th></th>
<th>Native Africans</th>
<th>African Americans</th>
<th>Caucasian Americans</th>
</tr>
</thead>
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<tr>
<td><strong>n</strong></td>
<td>17</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td><strong>Colon contents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, g</td>
<td>1302 ± 108</td>
<td>1796 ± 181*</td>
<td>1694 ± 226</td>
</tr>
<tr>
<td>Calcium, mg</td>
<td>683 ± 119</td>
<td>1084 ± 143</td>
<td>1944 ± 260**</td>
</tr>
<tr>
<td>Nitrogen, mg</td>
<td>3131 ± 497</td>
<td>2459 ± 390</td>
<td>3054 ± 443</td>
</tr>
<tr>
<td>Iron, mg</td>
<td>28.9 ± 4.0</td>
<td>30.1 ± 6.2</td>
<td>39.2 ± 4.9*</td>
</tr>
<tr>
<td>Zinc, mg</td>
<td>6.1 ± 1.4</td>
<td>20.4 ± 5.2*</td>
<td>13.4 ± 5.2</td>
</tr>
<tr>
<td>Folate, μg</td>
<td>632 ± 95</td>
<td>699 ± 131</td>
<td>860 ± 129</td>
</tr>
<tr>
<td>Biotin, μg</td>
<td>91 ± 24</td>
<td>65 ± 21</td>
<td>183 ± 68</td>
</tr>
<tr>
<td><strong>Blood</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb, g/L</td>
<td>131 ± 10</td>
<td>138 ± 3</td>
<td>141 ± 3</td>
</tr>
<tr>
<td>MCV, fl</td>
<td>85 ± 4</td>
<td>90 ± 2</td>
<td>93 ± 2*</td>
</tr>
<tr>
<td>RBC folate, ng/mL</td>
<td>181.3 ± 20.0</td>
<td>328.2 ± 34.2**</td>
<td>341.4 ± 41.4**</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM, n = 10–14 randomly selected individuals from each group. Asterisks indicate different from Native Africans: *P < 0.05, **P < 0.005.

2 Hb, Hemoglobin; MCV, mean corpuscular volume.
Colonic Content of Short Chain Fatty Acids (mmol)

Error Bars: ± 1 Standard Error(s)

- Acetate mmol
- Propionate
- Butyrate

- African American
- Caucasian American
- Native African
Colonic Contents

Colonic 7-alpha Dehydroxylating Bacteria

![Graph showing the counts of 7-alpha dehydroxylating bacteria (bacteria/gm) split by groups (African vs. African American). Error bars indicate ±1 Standard Error(s).]

Colonic Lactobacillus pp Bacteria

![Graph showing the counts of lactobacillus (bacteria/gm) split by groups (African vs. African American). Error bars indicate ±1 Standard Error(s).]
Products of the Colonic Microbiota Mediate the Effects of Diet on Colon Cancer Risk\textsuperscript{1,2}

Stephen J. D. O’Keefe,\textsuperscript{3}\* Junhai Ou,\textsuperscript{3} Susanne Aufreiter,\textsuperscript{4} Deborah O’Connor,\textsuperscript{4} Sumit Sharma,\textsuperscript{3} Jorge Sepulveda,\textsuperscript{3} Tsutomu Fukuwatari,\textsuperscript{5} Katsumi Shibata,\textsuperscript{5} and Thomas Mawhinney\textsuperscript{6}

\textsuperscript{3}University of Pittsburgh, Pittsburgh, PA 15213; \textsuperscript{4}University of Toronto, Toronto M5G 1X8, Canada; \textsuperscript{5}University of Shiga Prefecture, Hikone, 522-8533, Japan; and \textsuperscript{6}University of Missouri, Columbia, MO 65211

\textit{Butyrate, secondary bile salts, folate, biotin.........}
Critical Role of Butyrate

- **Chief energy source** for colonocytes

- **Chief regulator of epithelial growth:**
  - Suppresses epithelial proliferation, enhances differentiation
  - Suppresses the inflammatory response TNFα, NO
  - Tumor suppression p53, TGFβ
  - Increases apoptosis

- **Promotes the growth** of probiotic species:
  e.g. *Lactobacilli*, which suppress proinflammatory and increase anti-inflammatory cytokines, displace pathogens, increase tight junctions
Microbiotal H₂ Production

- End-product of anaerobic fermentation
- In excess, toxic to all living cells, including microbes
- Expansion of microbiotal diversity to include specific H₂ consuming organisms:
  - *Methanogens*: Convert H₂ to CH₄, non-toxic: Permit massive rates of butyrate-SCFA generation to feed not only the mucosa, but the whole animal
High Meat Diet

- Stimulates the growth of sulfate-reducing bacteria (SRBs)
- SRBs outcompete methanogens for hydrogen disposal
  - S U Christl, G R Gibson, J H Cummings: Gut 1999
- SRBs convert hydrogen to gentoxic $\text{H}_2\text{S}$
Phylogeny of Methanogens and *Desulfovibrio*: Carbone and Gaskins

12 stool samples from Native Africans (NA) and 12 from African Americans (AA)
All subjects were positive for *Desulfovibrio* 16S and Sulphate reducing bacteria functional gene.

For methanogen functional gene and methanogen 16S, 75% of NA were positive, only 25% AA were positive

148 clones sequenced for *Desulfovibrio* 16S: at least 5 different clusters, 2 major clusters 1 mostly AA, 1 mostly NA

66 clones sequenced Methanogens 16S: at least 4 different clusters also 1 cluster NA and 1 cluster AA
16S rRNA genes were used for all bacteria, *Bifidobacterium* spp., *Clostridium* cluster IV and *Faecalibacterium prausnitzii*, but methyl coenzyme-M reductase A gene (mcrA) and dissimilatory sulfite reductase gene (dsrA) were used for detecting methanogen and sulfate reducing bacteria.
But there are other bugs that do other things....... 

- *Enterococcus faecalis* is unique in generating superoxide: Tissue culture model demonstrated EF superoxide stimulated macrophage COX-2 production and the promotion of chromosomal instability
  - Wang et al: Gastroenterology 2007

- A human colonic commensal, Enterotoxigenic *Bacteroides fragilis*, promotes colon tumorigenesis via activation of T helper type 17 T cell responses.
Infection, Inflammation, and Cancer

- Similar biological mediators, cytokines, chemokines, “cancer is like an infection that never heals”
- Chronic infection triggers proliferation
  - H pylori and gastric MALT and cancer
  - Bacteria and IPSID, MALT
  - Virus and Burkitt’s lymphoma, HCC, cervical cancer
- *Strep bovis* and colon cancer??
- Ulcerative colitis and colon cancer (x5)
- NSAIDs reduce colon cancer risk 40-50%
FOOD

DIGESTION

AMINO ACIDS
GLUCOSE
FATTY ACIDS
VITAMINS

RESIDUES

HI MEAT
$H_2 + H_2S$

FERMENTATION

HI FIBER
BUTYRATE
FOLATE
BIOTIN

MUCOSAL INFLAMMATION - CANCER RISK↑
Summary and Conclusions

- It is the *milieu interieur* that determines colonic health
- The composition of the *milieu* is dependent on the diet and the microbiota
- The *milieu* determines the balance between nutritive metabolites and toxic metabolites
- >90% of colon cancer is preventable by dietary or bacterial manipulation
- *Intense effort has to be directed to preventing dietary practices associated with ‘westernization’ being adopted by ‘developing’ counties*
Diet, the Microbiota, and Colon Cancer Risk in African Americans and Rural Africans

Acronym: ‘ELSA’

- NIH-NCI sponsored
- Collaborators
  - Rex Gaskins: UIUC
  - Erwin Zoetendal: Wageningen Univ, Holland
  - Keith Newton: Univ KwaZulu-Natal, South Africa
The ELSA Study
Typical South African Zulu Diet

SAMP & BEANS
High Complex CHO
High Resistant Starch

PHUTU/
STIFF MAIZE
PORRIDGE
High Red Meat
High Fat

GROUND BEEF, SAUSAGE, LIVER, PORK CHOPS, SPARERIBS, HAM

Typical African American Diet
Rural Africans love Fast Food!
Thank you all

and acknowledgements to the AICR and NCI for support