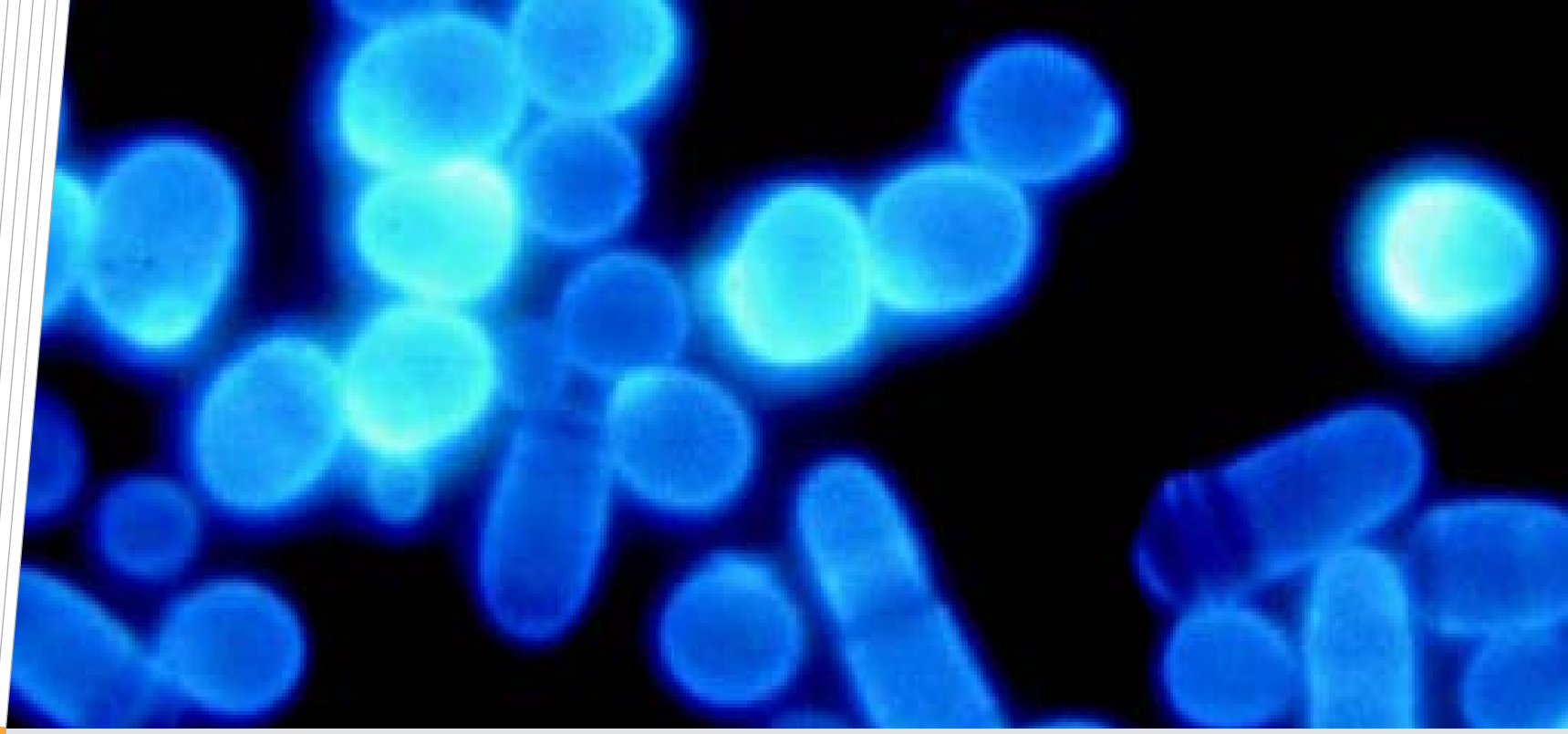

# *Structure-Function Analyses of the Human Gut Microbiota in Australian Subjects for Improved Risk Stratification and Clinical Management of IBD*

**Mark Morrison**
**OCE Science Leader, CSIRO Australia**
**Professor, The Ohio State University**

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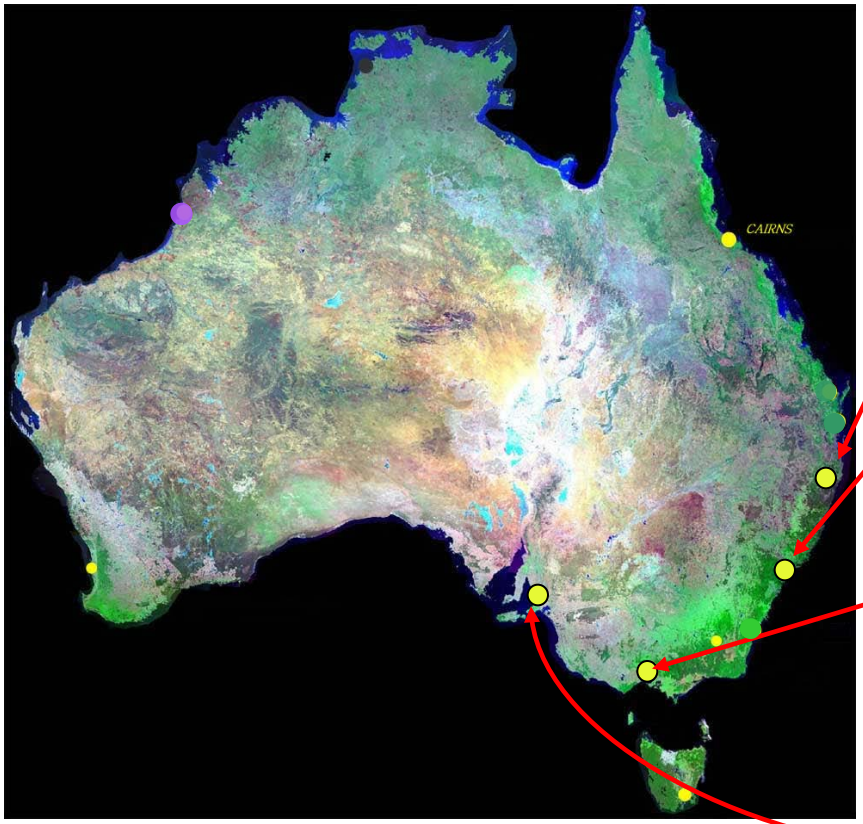
www.csiro.au

# *Major sites of p-Health research activity:*




Source: http://www.dragonglass.biz/a_contacts/images/MapAustralia.jpg

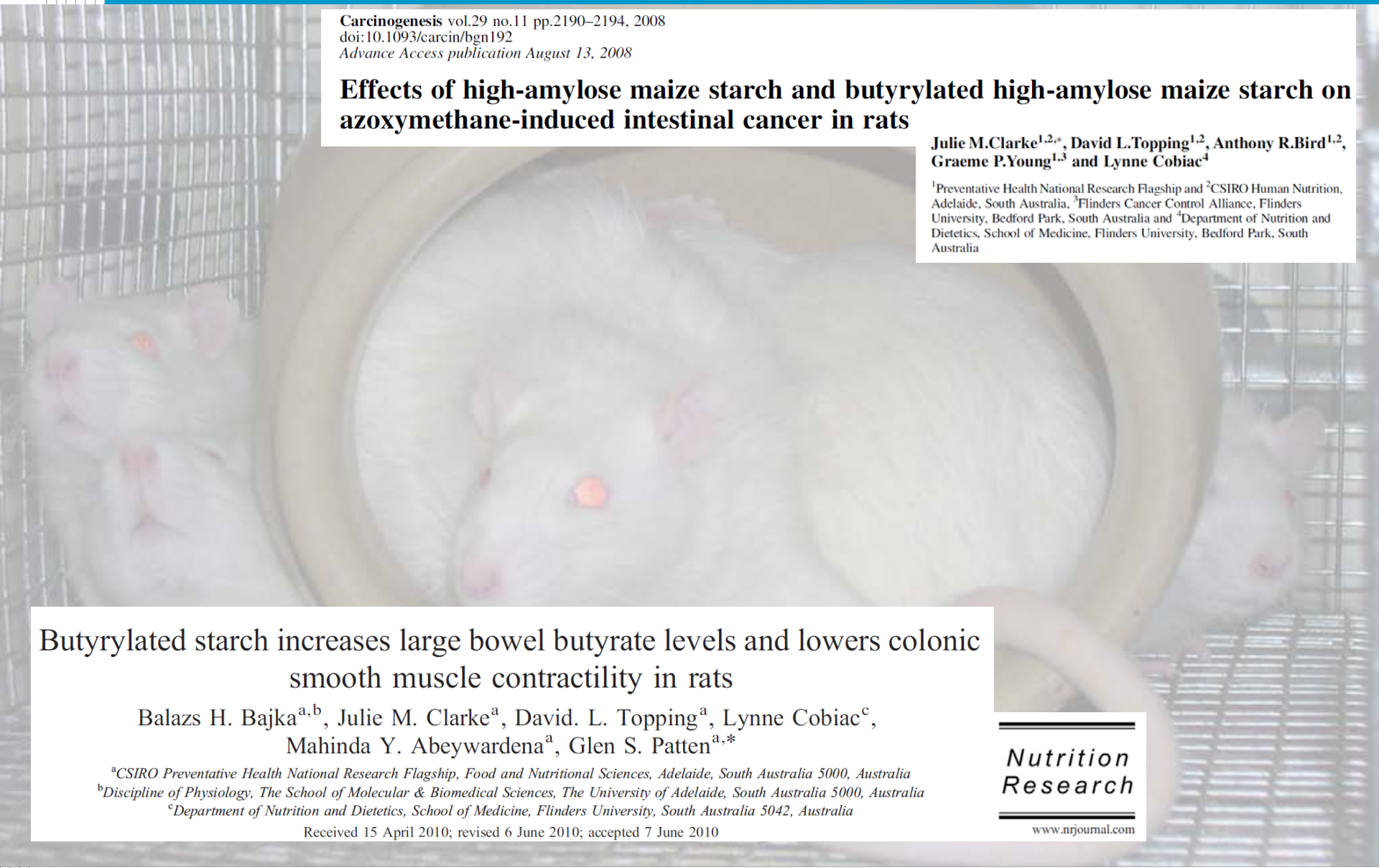
CSIRO Brisbane: Microbial ecology and genomics; QIMR and Mater Hospital: Colorectal cancer and IBD

CSIRO North Ryde: Theme leadership, human (epi)genetics and bioinformatics research

Royal Melbourne Hospital, Saint Vincent's Hospital and Ludwig Institute: Colorectal cancer and IBD research; proteomics and biomarker research

CSIRO Adelaide: Flagship headquarters. Human and animal trials, nutritional sciences and microbiology, biomarker research; Flinders and Queen Elizabeth Hospital: colorectal cancer and IBD research

# CSIRO Flagships' research on development of resistant starches and grains:



**Carcinogenesis** vol.29 no.11 pp.2190–2194, 2008
doi:10.1093/carcin/bgn192
*Advance Access publication August 13, 2008*

## Effects of high-amylose maize starch and butyrylated high-amylose maize starch on azoxymethane-induced intestinal cancer in rats

**Julie M.Clarke[1,2,*], David L.Topping[1,2], Anthony R.Bird[1,2], Graeme P.Young[1,3] and Lynne Cobiac[4]**

[1]Preventative Health National Research Flagship and [2]CSIRO Human Nutrition, Adelaide, South Australia, [3]Flinders Cancer Control Alliance, Flinders University, Bedford Park, South Australia and [4]Department of Nutrition and Dietetics, School of Medicine, Flinders University, Bedford Park, South Australia

## Butyrylated starch increases large bowel butyrate levels and lowers colonic smooth muscle contractility in rats

Balazs H. Bajka[a,b], Julie M. Clarke[a], David. L. Topping[a], Lynne Cobiac[c], Mahinda Y. Abeywardena[a], Glen S. Patten[a,*]

[a]*CSIRO Preventative Health National Research Flagship, Food and Nutritional Sciences, Adelaide, South Australia 5000, Australia*
[b]*Discipline of Physiology, The School of Molecular & Biomedical Sciences, The University of Adelaide, South Australia 5000, Australia*
[c]*Department of Nutrition and Dietetics, School of Medicine, Flinders University, South Australia 5042, Australia*

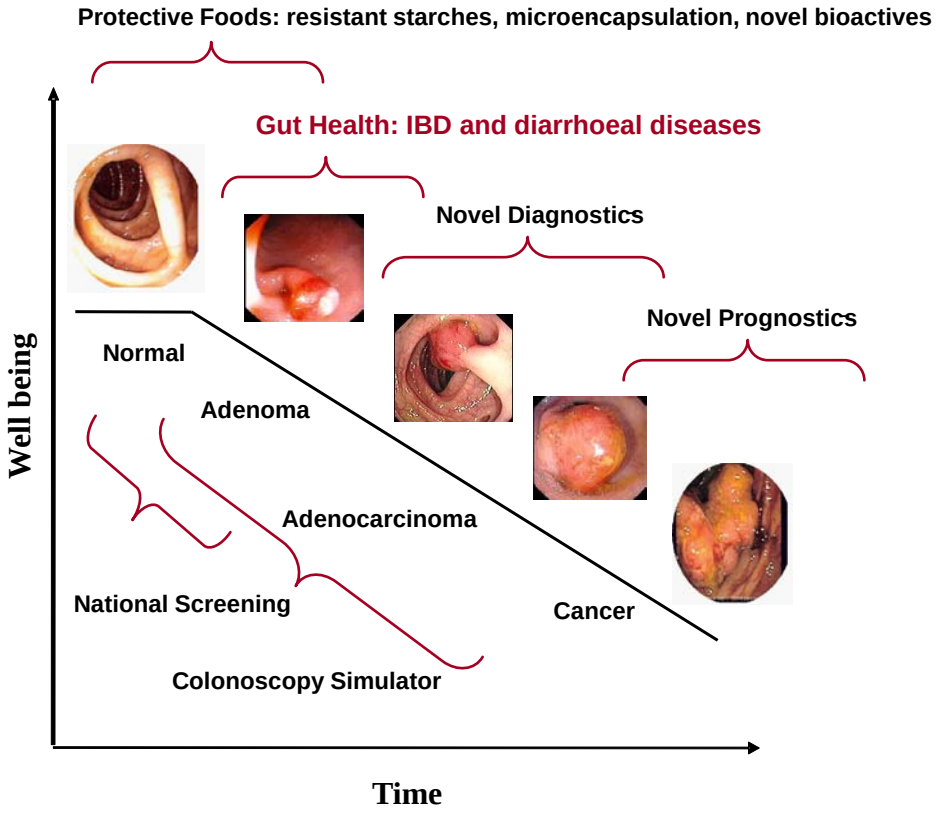
Received 15 April 2010; revised 6 June 2010; accepted 7 June 2010

*Nutrition Research*

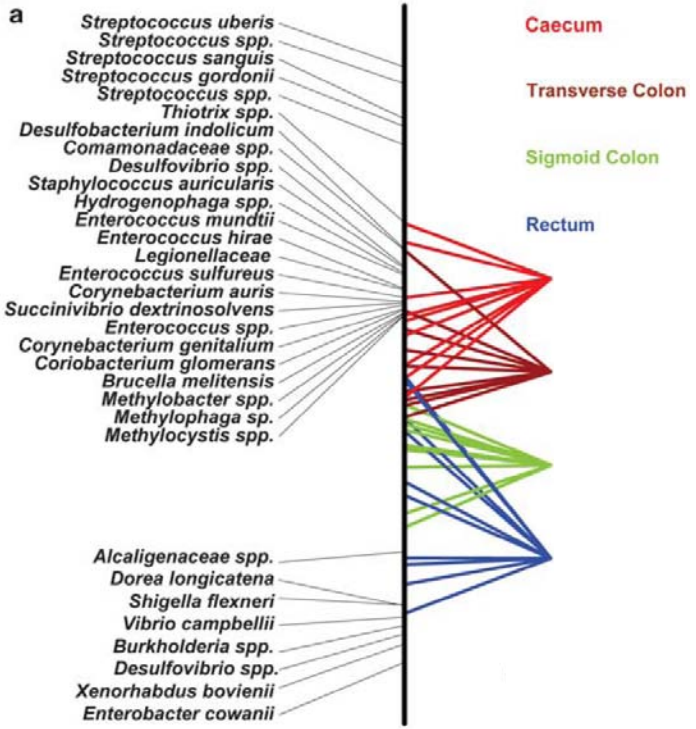
www.nrjournal.com

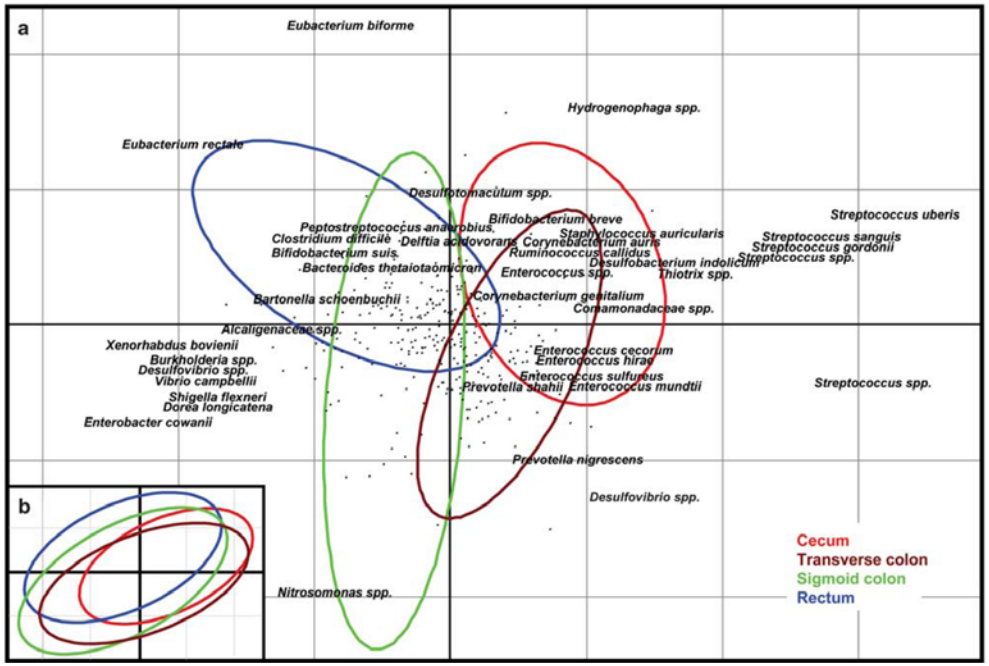
# *Colorectal Cancer and Gut Health Theme – Target Rationale and Achievements*

- **A multi-disciplinary approach with leading Australian clinicians and gastroenterologists.**
- Candidate Protective Food about to enter human clinical trial in CRC.
- Genes identified (and patented) for adenoma to adenocarcinoma in the human.
- Blood based protein panel identified to differentiate cancer from normal.
- Established a CRC biobank with the Ludwig Institute linked to data integration.
- Identified key drivers to increase the uptake in the national bowel screen.
- Developed a colonoscopy simulator.



# *Application of numerical ecology methods - Aguirre, O'Cuiv, Leggett* et al.:*




The ISME Journal (2010), 1–9

www.nature.com/ismej

**ORIGINAL ARTICLE**

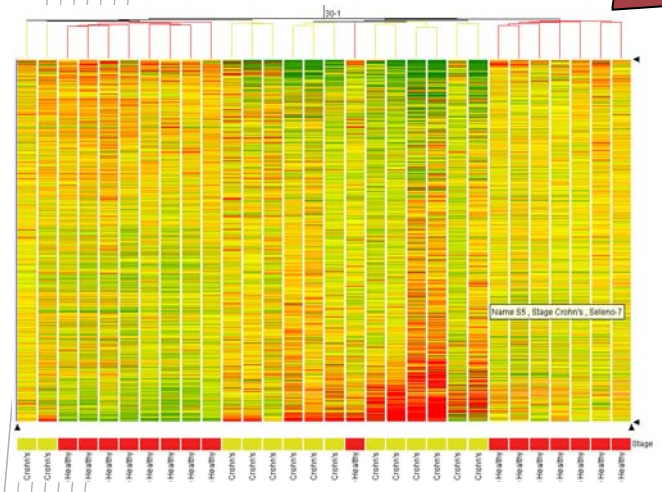
## Numerical ecology validates a biogeographical distribution and gender-based effect on mucosa-associated bacteria along the human colon

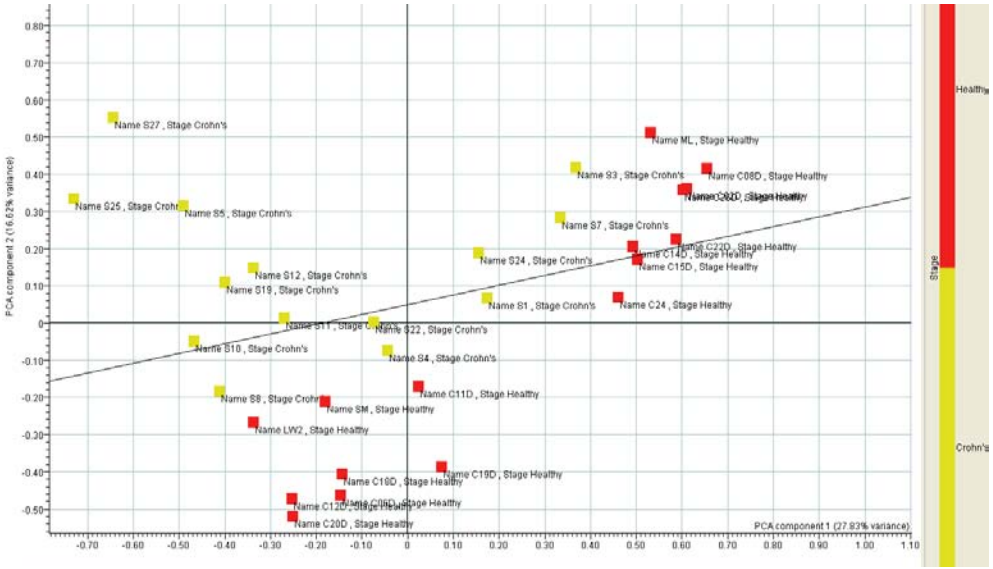
Daniel Aguirre de Cárcer[1], Páraic Ó Cuív[1], Tingting Wang[1,2], Seungha Kang[1], Daniel Worthley[3], Vicki Whitehall[3], Iain Gordon[4] and Chris McSweeney[1], Barbara Leggett[3] and Mark Morrison[1,5]

***A collaboration with Queensland Institute of Medical Research**

National Research FLAGSHIPS CSIRO

# *Microbial Profiling of IBD dysbiosis – Mondot, Kang, McSweeney, Leclerc*, et al.:*






ORIGINAL ARTICLE

## Highlighting New Phylogenetic Specificities of Crohn's Disease Microbiota

*S. Mondot, PhD,* S. Kang, PhD,† J.P. Furet, MS,* D. Aguirre de Carcer, PhD,† C. McSweeney, PhD,† M. Morrison, PhD,† P. Marteau, PhD,‡ J. Doré, PhD,* and M. Leclerc, PhD**

*(Inflamm Bowel Dis 2011;17:185–192)*

**Source: http://virtual.vtt.fi/virtual/proeuhealth/peuh5.pdf**

***A collaboration with INRA Jouy-en-Josas**

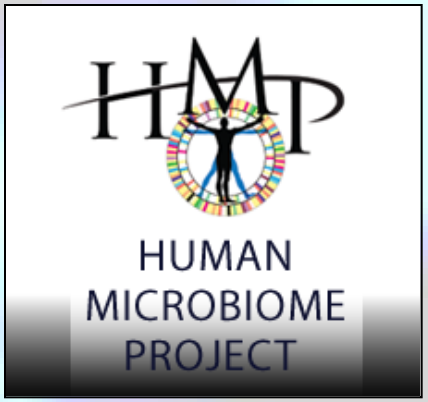
National Research FLAGSHIPS CSIRO

# *Bacterial isolation and genome sequencing – O'Cuiv, Klaassens, Nelson*, Torralba*, et al.:*

- ***Enterococcus faecium* PC4.1**
  - 2,811,160 bp assembled in 78 contigs
  - DNA G+C = 37%
  - 2739 genes

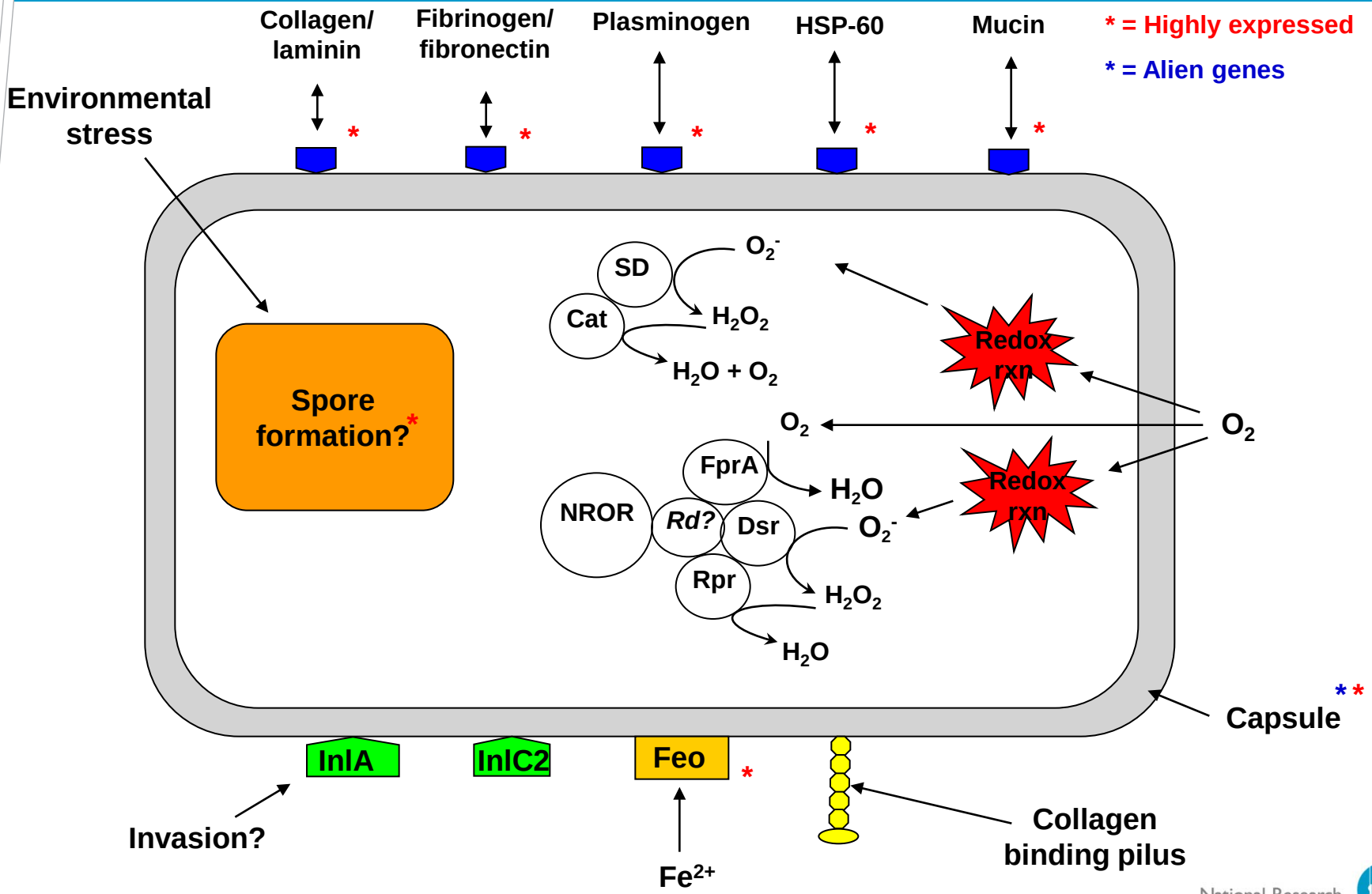
- ***Bacteroides vulgatus* PC510**
  - 4,781,702 bp assembled into 117 contigs
  - DNA G+C = 42%
  - 4019 genes

- ***Enterococcus faecalis* PC1.1**
  - 2,753,923 bp assembled into 79 contigs
  - DNA G+C = 37%
  - 2673 genes



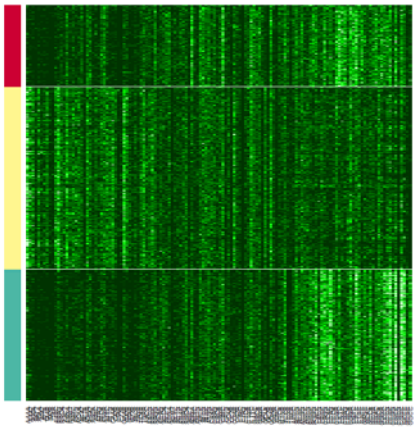

***In collaboration with J. Craig Venter Institute, please see http://www.hmpdacc.org**

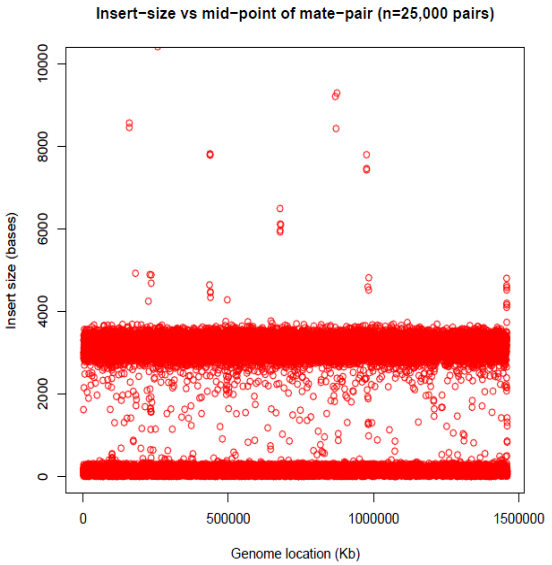
# *Genome analysis of Turicibacter sp. PC909 – O'Cuiv, Klaassens, Nelson*, Torralba*, et al.:*

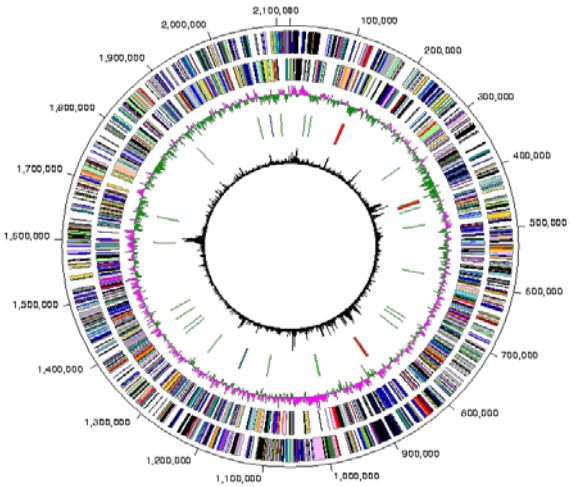


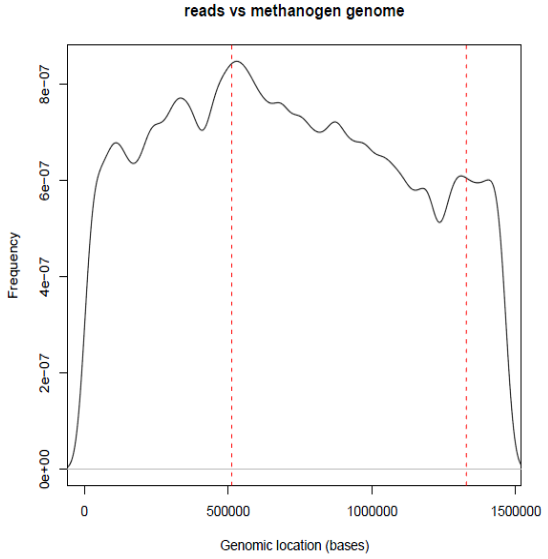

*In collaboration with J. Craig Venter Institute, please see http://www.hmpdacc.org

# *De novo genome assembly from enrichment cultures using "NGS" - Bragg, Denman et al.:*



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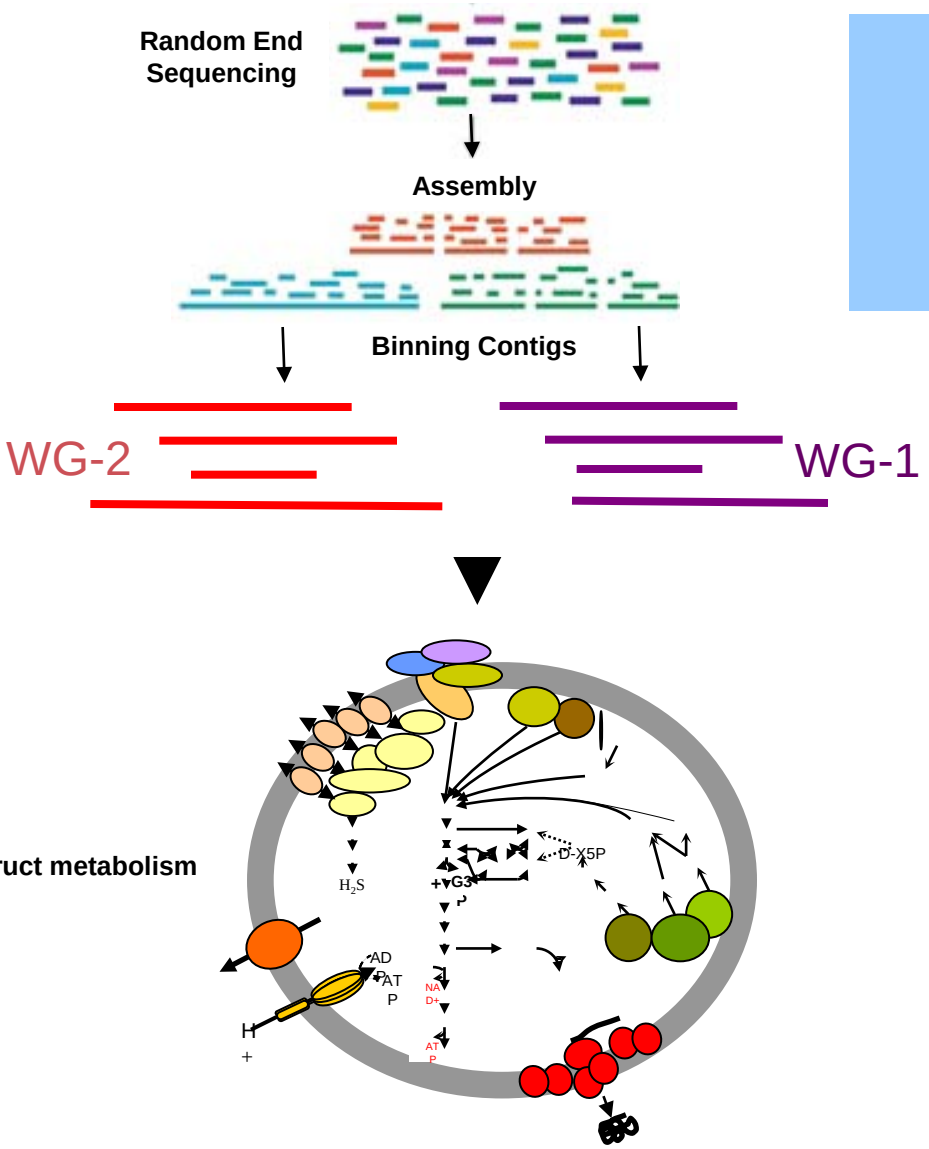
# *"Reverse metagenomics" – from sequence data to taxonomic binning and metabolic reconstruction:*




Assembly - phrap

JGI (USA)

Binning - GC content, depth, PhyloPythia

max planck institut (Germany)

Annotation - IMG/M

JGI/CSIRO (AUS)

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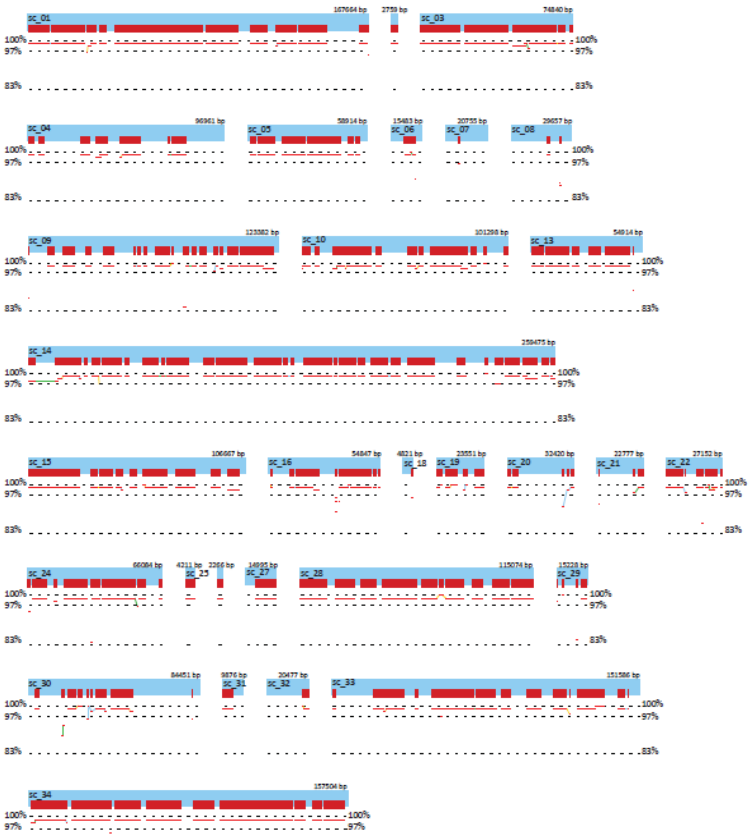
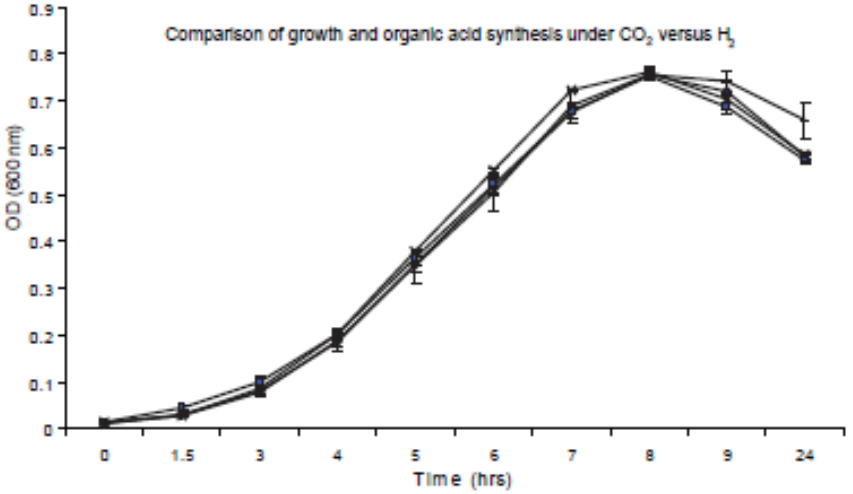
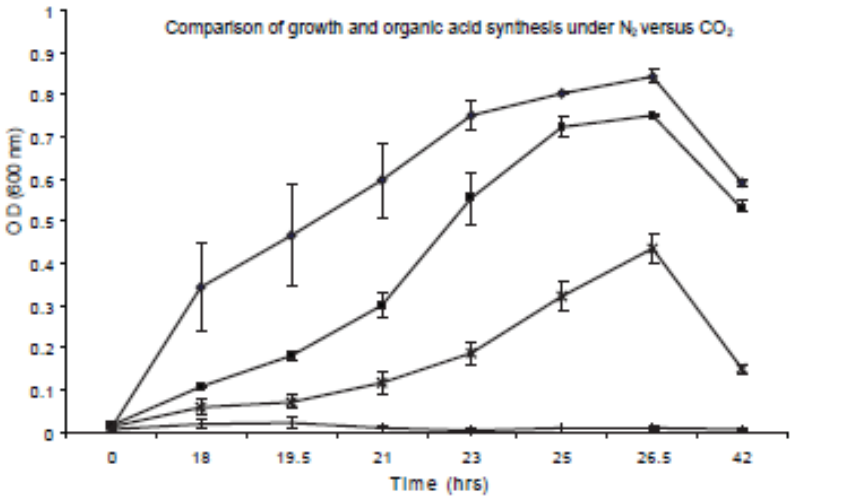
# *Reverse metagenomics – "culturing the unculturable" Pope, Smith et al.:*






- 454 data with axenic culture
- Sanger reads recovered with Phylopythia

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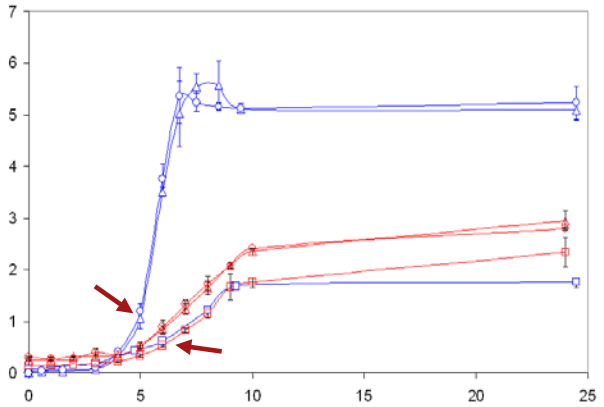
# *Moving from structure to function, transcriptomics – Klaassens, Toll, Wang*, et al.*

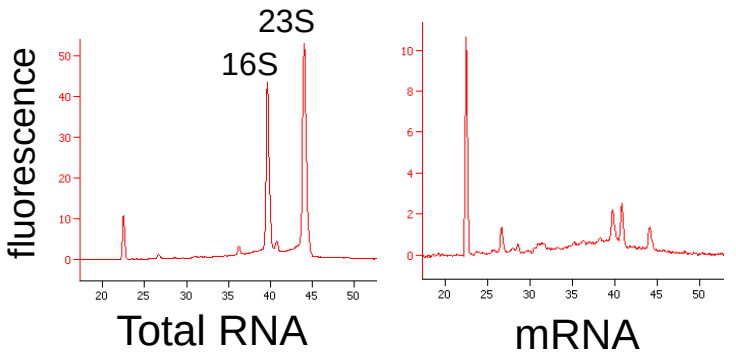
- *E. faecium* PC4.1

CDM + 5 % BHI | CDM + FW S | CDM + FW C | CDM + Water

- *B. vulgatus* PC510

BHI + Water | BHI + FW S | BHI + FW C




CDM: Chemically defined medium
BHI: Brain Heart Infusion medium
FW: Fecal water
S: IBD patient (subject)
C: Healthy subject (control)

*Special thanks to the Chinese Scientific Council and Shanghai Jiao Tong University

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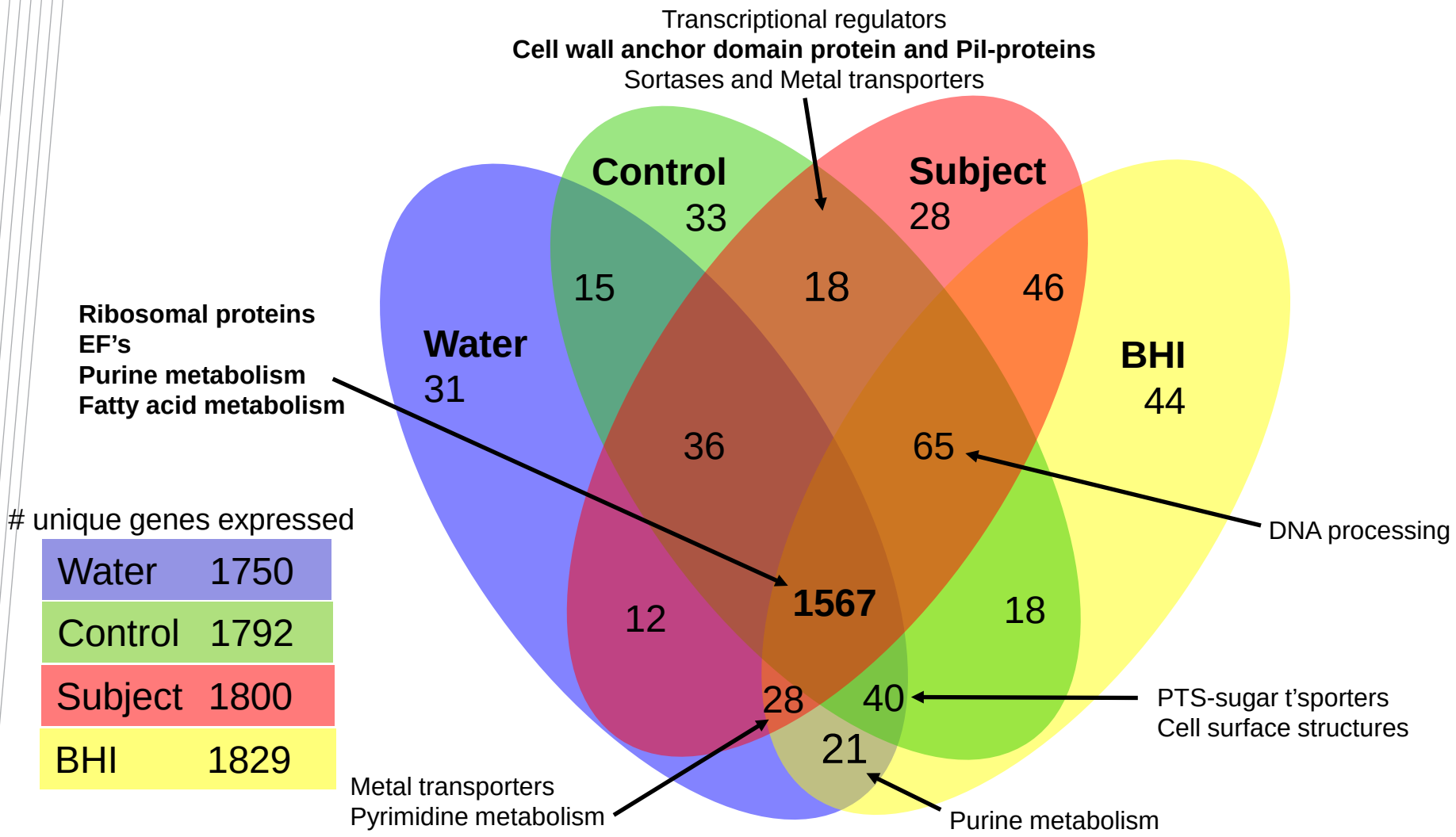
# *Differential gene expression in fecal waters – Klaassens, Toll, Wang*, et al.:*




# unique genes expressed

| | |
|---|---|
| Water | 1750 |
| Control | 1792 |
| Subject | 1800 |
| BHI | 1829 |

*Special thanks to the Chinese Scientific Council and Shanghai Jiao Tong University

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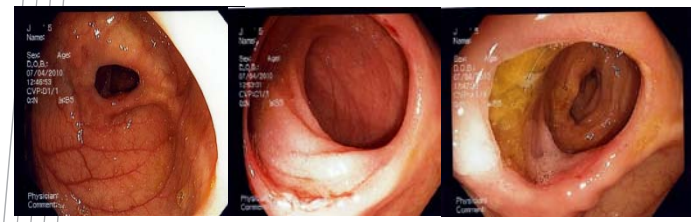
# *Collaborative clinical studies – Post-Operative Crohn's Endoscopic Recurrence (POCER) Study:*

- A collaborative study with Prof. Michael Kamm (Saint Vincent's and Royal Melbourne Hospitals) and Murdoch Children's Research Institute
- Patient recruitment supported by the Australian and New Zealand IBD Consortium
- Longitudinal endoscopic monitoring of Crohn's disease post-operatively:
  - ✓ endoscopic disease progression
  - ✓ recurrent clinical symptoms &
  - ✓ need for further surgery
- Standard best drug care v endoscopy & $R_x$ step-up
  - ✓ $1^0$ end-point – endoscopic recurrence at 18 months
  - ✓ $2^0$ end-point – clinical & surgical recurrence at 18 months

# *Restoration Ecology of the Anastomoses – Kang, McSweeney, Kamm*, et al.:*

**27 y.o. female: Low risk 3/12 metronidazole**



**At 6/12 Asymptomatic (CDAI 43 & CRP 5)**
**Rutgeert's score = i1**
**Step up – No**




- **Healthy controls**
- **Baseline surgery**
- **Recurrent, 6 months**
- **Non-recurrent, 6 months**

**23 y.o. male: High risk 3/12 metronidazole + thiopurine**

**At 6/12: Asymptomatic (CDAI 5 & CRP 5)**
**Rutgeert's score = i4**
**Step up – Anti-TNF + (thiopurine)**

***In collaboration with Saint Vincent's and Royal Melbourne Hospitals, and Murdoch Children's Res. Inst.**

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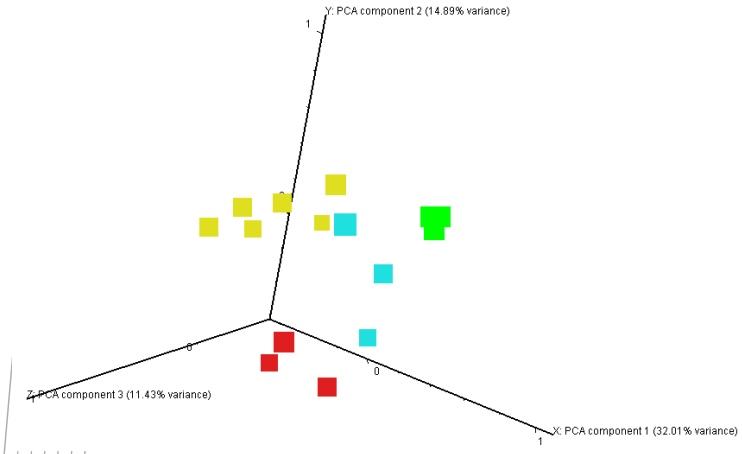
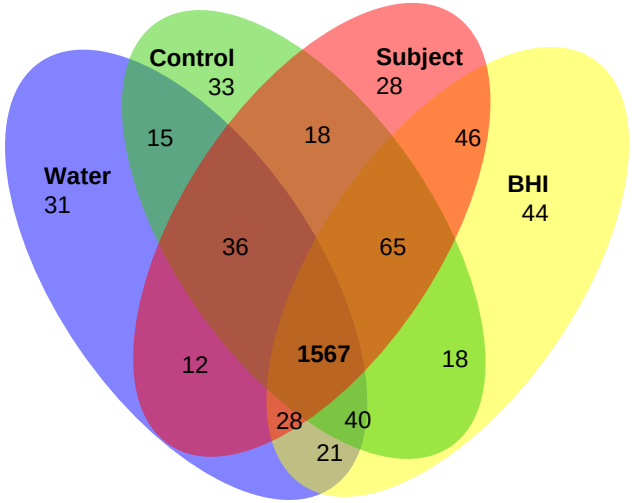
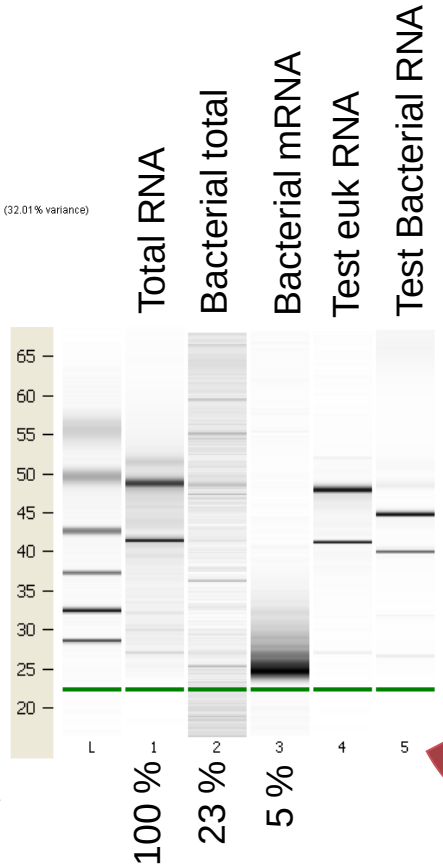
# *Metagenomic analyses of biopsy µRNA – Klaassens, de Cruz, Prideaux, Kamm*, et al.:*




*In collaboration with Saint Vincent's and Royal Melbourne Hospitals, and Murdoch Children's Res. Inst.

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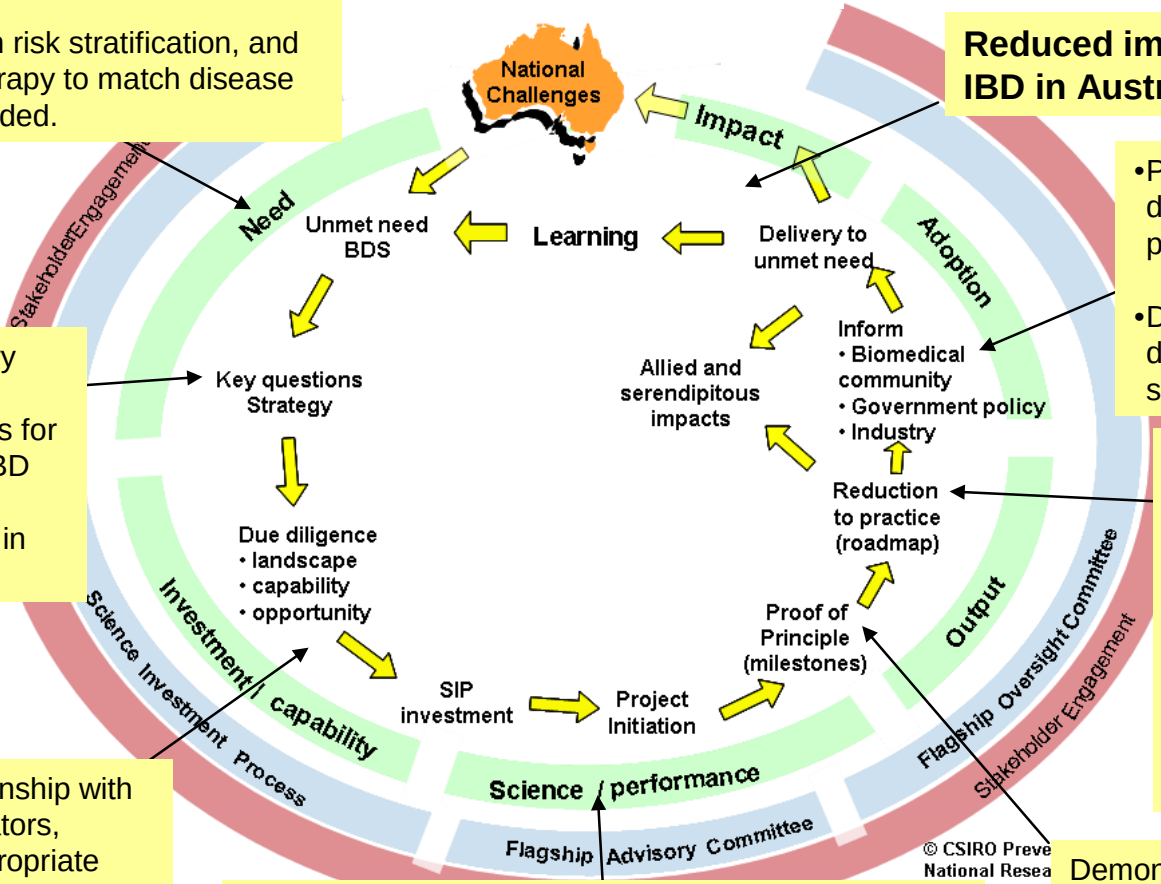
# *Inflammatory Bowel Diseases (IBD) - Overview*

- IBD affects ~60,000 Australians, has increased in incidence and prevalence, and increases risk of colorectal cancer.
- Improvements in risk stratification, and tailoring IBD therapy to match disease are urgently needed.

**Reduced impact of IBD in Australia**




Use contemporary microbiology to generate methods for identification of IBD and intervention through changes in diet

- Partner with industry to develop commercial products (diagnostic/diet)
- Develop and communicate diet and lifestyle advice strategies

- Diagnostic based on microbiological and gene profiling for IBD to guide therapy
- Dietary interventions that will favourably alter profiles, truncate disease and/or prolong remission

Maximise relationship with clinical collaborators, bringing the appropriate basic science together with the clinical sciences

- Clinical collaborators / access to IBD patients
- Establish and use metagenomic methods
- Identify candidate diets and dietary interventions

Demonstrate association of bacterial profiles with IBD and favourable shift in those profiles with dietary intervention

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# *Acknowledgements:*


- INRA, Jouy-en-Josas
  - Marion Leclerc
  - Joel Dore
  - Stanislas Mondot
- Shanghai Jiao Tong University
  - Liping Zhao
    - Tingting Wang
- Murdoch Children's Res. Inst.
  - Carl Kirkwood
    - Josef Wagner
- J. Craig Venter Institute
  - Karen Nelson
    - Manolito Torralba
    - A. Scott Durkin
- University of Melbourne
  - Finlay Macrae
- St Vincents Hospital, Melbourne
  - Michael Kamm
    - Peter de Cruz
    - Lani Prideaux
- Univ. of Queensland (QIMR)
  - Barbara Leggett
    - Vicki Whitehall
    - Daniel Worthley
- Queen Elizabeth Hospital, Adelaide
  - Ian Roberts-Thomson


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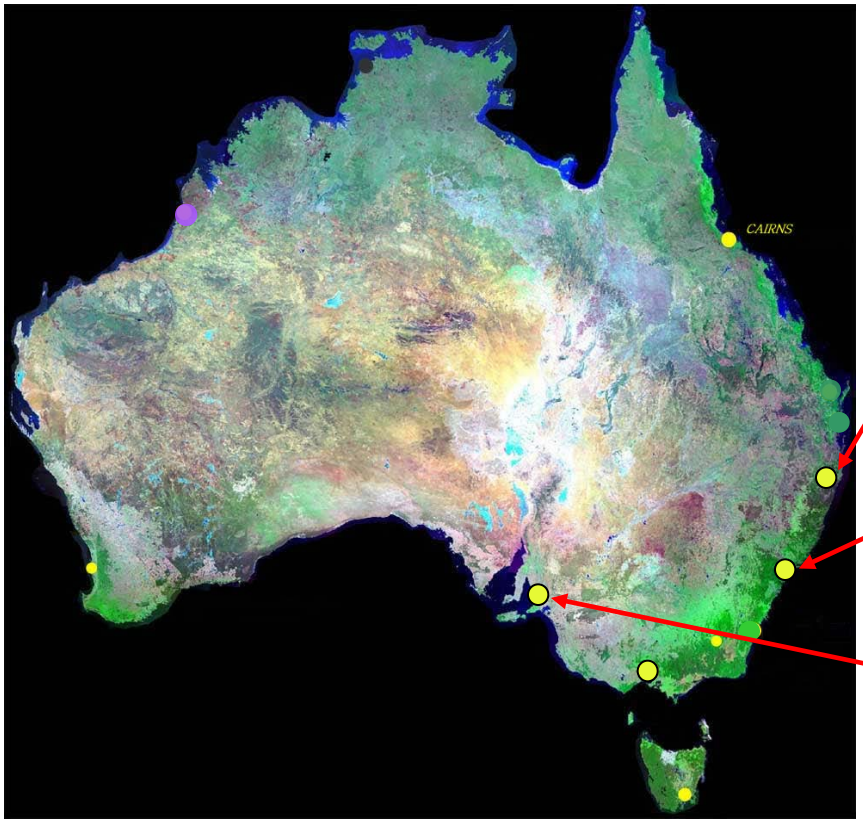
# *Key CSIRO scientists:*




Source: http://www.dragonglass.biz/a_contacts/images/MapAustralia.jpg

**Brisbane:**

Eline Klaassens
Seungha Kang
Paraic O'Cuiv
Daniel Aguirre
Chris McSweeney

**Sydney:**

Caroline Kerr
Rob Dunne
Trevor Lockett

**Adelaide:**

Michael Conlon
Claus Christophersen
Julie Clarke
David Topping

- **OCE Science Leader Program**
- **Transformational Biology Capability Platform**