Diet-Microbiota Interactions and The Elderly

Ian Jeffery
Dept. Microbiology, Univ. College Cork, Ireland
Alimentary Pharmabiotic Centre, Univ. College Cork, Ireland

http://apc.ucc.ie
http://eldermet.ucc.ie
The human gut microbiota

- ~10 times more bacterial cells in GIT than human cells in body

- ~150 times more bacterial genes than human genes

- Perform a number of beneficial functions

- Variations in the gut microbiota in disease
Diseases with microbiota linkages

Healthy Colon  Ulcerative Colon

Irritable Bowel Syndrome

Obesity
“Gut microbiota as an indicator and agent for nutritional health in elderly Irish subjects”

Why elderly?

- Increasing proportion in population
- Increased susceptibility to infection
- Increased inflammatory status (Inflamm-aging)
- Changes in microbiota composition and activity
- Prospect of dietary modulation
Eldermet dataset

Data:

- 178 elderly (≥65yrs) Irish subjects
  - 83 Community-dwelling
  - 20 Day hospital (out-patient)
  - 15 Rehabilitation (≤6 weeks)
  - 60 Long-stay (≥6 weeks)
  - (13 Young healthy controls)

- Metabolomics (NMR)
  - 16S rDNA amplicons (454) & shotgun (Illumina) sequencing

- Clinical Variables
  - BMI, frailty
  - malnourishment,
  - depression
  - cognitive function
  - dementia

- No antibiotics treatment ≤1 month prior sampling

- Dietary data
  - 168 elderly subjects
  - food frequency questionnaire (FFQ), 147-item, weighted by 10 consumption frequencies
Subjects separate by community location

5.4 million 16S rDNA reads => 47,500 OTUs

Unweighted UniFrac OTU PCoA

Community  Day Hospital  Rehab  Long-stay  Young control
Subjects separated by community location

Hierarchical Ward-linkage clustering based on Spearman correlation coefficients of the proportion of OTUs for each subject
What impact has diet on microbiota?

**Food Frequency Questionnaire (FFQ)**

- *Long-term dietary habits*
- *FFQ data for 96% elderly subjects*
- *147 food types (beef/apples/white rice/potatoes/milk/porridge etc)*
- *Healthy Food Diversity (HFD): how diverse AND healthy a diet is*
FFQ multivariate analysis

Correspondence analysis

Complete-linkage clustering based on Euclidean distances to PC1

DG1: “low fat / high fibre”
DG2: “moderate fat and fibre”
DG3: “moderate fat / low fibre”
DG4: “high fat / moderate fibre”
Microbiota & diet by community location

Unweighted UniFrac PCoA vs. FFQ PCA

Weighted UniFrac PCoA vs. FFQ PCA

Diet
Community  Day Hospital  Rehab  Long-stay

Microbiota
Microbiota & diet by duration in long-stay care

N/A (C+DH)

Year1+
Diversity of microbiota and diet

• Healthy Food Diversity index (HFD) showed that it positively correlated with microbial diversity indices.

• Significant differences across the four groups, suggest that a healthy diverse diet promotes a more diverse gut microbiota.
Separation of residence location by faecal water NMR metabolome

Long-stay Community
Rehab Community

Dr. Martina Wallace and Dr. Lorraine Brennan, Univ. College Dublin
Integrating metabolome, metabolites & genus-level microbiota

Co-inertia of microbiota & metabolome → by location

NMR spectrum metabolite PCA
Shotgun metagenome: differentially abundant SCFA genes

- BCoAt: Butyryl-CoA transferase/Acetyl-CoA hydrolase
- ACS: Acetate-formyltetrahydrofolate synthetase/Formate-tetrahydrofolate ligase
- PCoAt: Propionyl-CoA:succinate-CoA transferase/Propionate CoA-transferase

Microbiota-health correlations

**Health/clinical markers**
- BMI: Body Mass Index
- CC: Calf Circumference
- MAC: Mid-Arm Circumference
- SBP: Systolic Blood Pressure
- DBP: Diastolic Blood Pressure
- CCI: Charlson Index of Comorbidity
- Barthel Index of Activities of Daily Living
- FIM: Functional Independence Measure
- MMSE: Mini-Mental State Exam
- MNA: Mini-Nutritional Assessment

**Possible confounders**
- Antibiotics:
  - Exclude <1mo
  - >1mo had no sign. effect on µ-biota (α- or β-diversity)
- Quantile regression model adjusted for:
  - Age
  - Gender
  - Location
  - Medication
Following adjustment for age/gender/location/medication, microbiota correlates significantly with e.g. frailty and inflammation. Prospective studies needed to establish causality.
Microbiota separation correlates with health measures
Location-specific unweighted UniFrac PCoAs

Following adjustment for age/gender/location/medication, microbiota correlates significantly with e.g. frailty and inflammation.
Prospective studies needed to establish causality.
Microbiota clustering correlates with health measures

Unweighted UniFrac OTU PCoA
Microbiota clustering correlates with health measures

Barthel Index

Functional Independence Measure

Unweighted UniFrac OTU PCoA
Microbiota clustering correlates with health measures

Unweighted UniFrac OTU PCoA
Summary
(Claesson, Jeffery et al., 2012 Nature)

- Microbiota in elderly is different depending on community location
- Driven by habitual diet
- Microbiota alterations correlate with health changes especially in long-stay

Diet shapes gut microbiota, which may impact on health in elderly people

May lead to carefully designed dietary interventions to promote healthier aging
n = 1,250

UK, NL, FR, IT, PL

$T_0$ 12 mo.’s

5 x 25 subjects
Challenges

- *Microbiota modulation / restoration*
  - Prospective / longitudinal studies
  - Interventions
- *Integrated metabolomics, nutritional and microbial datasets*
- *Dietary guidelines informed by microbiota needs*
Acknowledgements

Paul O’Toole  
Anthony Fitzgerald  
Denis O’Mahony  
Paul Ross  
Catherine Stanton  
Gerald Fitzgerald  
Fergus Shanahan  
Ted Dinan  
Martina Wallace  
Julian Marchesi  
Lorraine Brennan  
Michael O’Connor  
Douwe van Sinderen  
Colin Hill  
Cillian Twomey  
Kieran O’Connor  
Lorraine Brennan  
Denise Lynch  
Eileen O’Herlihy

Marcus Claesson  
Eibhlis O’Connor  
Siobhán Cusack  
Hugh Harris  
Susana Conde  
Jennifer Deane  
Orla O’Sullivan  
Mary Rea  
Colm Henry  
Mairead Coakley  
Patricia Egan  
Susan Power  
Karen O’Donovan  
Ann O’Neill  
Norma Harnedy  
Bhuna Laks  
Martina Wallace

The Cork City Geriatrians Group
Microbiota clustering correlates with health measures

Unweighted UniFrac OTU PCoA