The Gut Microbiome (and HIV)

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• I have no relationships to declare with pharmaceutical, diagnostic, or such similar companies involved in HIV/STI related products for the preceding twelve months.
The gut microbiome
In numbers

• 100 trillions of microbes
  • 95% in the gut

• 5:1 viruses:bacteria

• 150 microbial genes for 1 human

• Unique fingerprint

Hug et al., 2016
Acquisition of the gut microbiome

Bäckhed et al. 2015

Kostic et al. 2013

Bäckhed et al. 2015
Shaping the gut microbiome
The gut microbiome and health

Nicholson et al., 2012

Jackson et al., 2018
Characterising the microbiome
Sampling the microbiome

• Faecal sample

• Swab

• Colonoscopy

• The gut is mostly anaerobic!

• Think carefully about:
  • Collection
  • Storage
  • …
Characterizing the microbiome – Culture -

• Most microbes in the gut are:
  • Anaerobes
  • Fastidious growth
  • May have very specific requirements
  • Depend on one another
Characterizing the microbiome – Sequencing-

- 16S rRNA -> who
  - Amplification step
  - ~ £30/sample

- Shotgun metagenomics -> who & what
  - Untargeted
  - ~ £200/sample
Data analysis

- **Alpha diversity**

- **Beta diversity**

- **Associations**

![Diagram showing data analysis with alpha and beta diversity plots and associations with specific bacteria.]
HIV and the gut microbiome
Unique gut microbiota signature

Fig. 1. Gut bacterial microbiota composition in HIV-infected VU subjects differs from that of HIV-uninfected risk-matched controls. P = 0.002

Vujkovic-Cvijin, 2013
Science Translational Medicine
Unique gut microbiota signature

Table 2. Comparison of Alpha Diversity in HIV-Positive and -Negative Individuals with and without ART Treatment

<table>
<thead>
<tr>
<th></th>
<th>Observed Species</th>
<th>Shannon</th>
<th>PD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV negative</td>
<td>508 ± 21.6</td>
<td>5.6 ± 0.19</td>
<td>27.9 ± 1.46</td>
</tr>
<tr>
<td>Chronic HIV, ART untreated</td>
<td>563 ± 30.5</td>
<td>6.3 ± 0.15</td>
<td>36.4 ± 1.31</td>
</tr>
<tr>
<td>Chronic HIV on long-term ART</td>
<td>469 ± 39.6</td>
<td>5.68 ± 0.16</td>
<td>28.69 ± 1.19</td>
</tr>
<tr>
<td>Recent HIV</td>
<td>517 ± 64.4</td>
<td>5.76 ± 0.49</td>
<td>31.7 ± 3.06</td>
</tr>
</tbody>
</table>

p value (ART untreated versus negative) t test

<table>
<thead>
<tr>
<th></th>
<th>p value</th>
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<tbody>
<tr>
<td>HIV negative</td>
<td>0.144</td>
<td>0.013</td>
<td>0.0003</td>
</tr>
<tr>
<td>Chronic HIV, ART untreated</td>
<td>0.070</td>
<td>0.016</td>
<td>0.0006</td>
</tr>
<tr>
<td>Chronic HIV on long-term ART</td>
<td>0.0006</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are given as mean ± SD.
Gut Microbiota Linked to Sexual Preference and HIV Infection

Marc Noguera-Julian $^{a,b,c,1}$, Muntsa Rocafort $^{b,c,1}$, Yolanda Guillén $^{a,c}$, Javier Rivera $^{a,b}$, Maria Casadellà $^{a,c}$, Piotr Nowak $^{4}$, Falk Hildebrand $^{5}$, Georg Zeller $^{5}$, Mariona Parera $^{a}$, Rocio Bellido $^{a}$, Cristina Rodríguez $^{a}$, Jorge Carrillo $^{a,c,8}$, Beatriz Mothe $^{a,b,c,1}$, Josep Coll $^{a,1}$, Isabel Bravo $^{1}$, Carla Estany $^{1}$, Cristina Herrero $^{1}$, Jorge Saz $^{b}$, Guillem Sirera $^{1}$, Ariadna Torrela $^{1}$, Jordi Navarro $^{1}$, Manel Crespo $^{1}$, Christian Brandner $^{a,b,c,1}$, Eugènia Negredo $^{b,c,1}$, Julià Blanco $^{a,b,c}$, Francisco Guarner $^{5}$, Maria Luz Calle $^{b}$, Peer Bork $^{e,f,m}$, Anders Sönnerborg $^{g}$, Bonaventura Clotet $^{a,b,c,d}$, Roger Paredes $^{a,b,c,f,e}$.
Probably because:
Possible consequences
Resilience of the gut microbiome
The gut microbiome and HIV treatment
Vaccination?

HUTCH NEWS

Gut microbiome may have interfered with experimental HIV vaccines

Inoculating infants instead of adults could bypass problem, researchers say

July 30, 2015 | By Dr. Rachel Tompa / Fred Hutch News Service
Vaccination?

RESEARCH

RESEARCH ARTICLE

HIV-1 VACCINES

Diversion of HIV-1 vaccine–induced immunity by gp41-microbiota cross-reactive antibodies

Wilton B. Williams,1,6 Hua-Xin Liao,1,6 M. Anthony Moody,7 Thomas B. Kepler,2 S. Murim Alam,1 Feng Gao,1 Kevin Wiehe,1 Ashley M. Trama,1 Kathryn Jones,1 Ruijun Zhang,1 Hongzhao Song,1 Dawn J. Marshall,1 John F. Whitesides,1 Kaitlin Sawatzki,2 Azlin Hua,9 Pinghuang Lin,1 Matthew Z. Tay,1 Kelly E. Seaton,1 Xiaoying Shen,1 Andrew Foulds,1 Krisexy E. Lloyd,1 Robert Parks,1 Justin Pollara,1 Guido Ferrari,1 Jae-Sung Yu,1 Nathan Vandergrift,1 David C. Montefiori,1 Magdalena E. Sobieszczyk,3 Scott Hammer,1 Shelly Karuna,1 Peter Gilbert,6 Doug Grove,6 Nicole Grunenberg,4 M. Juliana McElrath,4 John R. Mascola,6 Richard A. Koup,6 Lawrence Corey,1 Gary J. Nabel,6 Cecilia Morgan,9 Gavin Churchyard,1 Janine Maenza,1 Michael Keefer,1 Barney S. Graham,9 Lindsey R. Baden,9 Georgia D. Tomaras,9 Barton F. Haynes3

Vaccination
with HIV-1 envelope

Human B cell repertoire

Vaccine-induced
HIV-1–reactive antibody response

gp120

gp41
(MPER)

Common B cells selected by microbiota that have B cell receptor cross-reactivity with microbiota and HIV-1 Env gp41

Dominant Env-microbiota antigen nonprotective antibody response

Rare B cells that can respond to HIV-1 Env protective antibody sites

No protective antibody response

Diversion of HIV-1 vaccine–induced immunity by Env gp41–microbiota cross-reactive antibodies. Immunization of humans with a vaccine containing HIV-1 Env gp120 and gp41 compo-
The microbiome & side effects
Side effects

Short-term:
• Feeling tired
• Nausea (upset stomach)
• Vomiting
• Diarrhea
• Headache
• Fever
• Muscle pain
• Occasional dizziness
• Insomnia

Long-term:
• Kidney problems, including kidney failure
• Liver damage
• Heart disease
• Diabetes
• An increase in fat levels in the blood
• Changes in how the body uses and stores fat
• Osteoporosis
• Nerve damage
• Insomnia & depression
Take home messages

• HIV patients have a distinct gut microbiome

• The gut microbiome could affect response to HIV treatment
  • Personalized medicine

• Could probiotic/prebiotic help minimizing long-term side effects?
Thank you!

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