The ‘gut-skin’ axis in health and disease

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Can skin structure/function be modified via the gut?
The gut-skin axis is not a new concept

Stokes and Pillsbury 1930

- ‘A gut-brain-skin axis in Acne vulgaris’.

- *Lactobacillus acidophilus* as an intervention
The principle players in the gut-skin axis

<table>
<thead>
<tr>
<th>Gut Microbiome</th>
<th>Secretion of molecules, translocation, immune modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td>Direct effects or via gut microbiota</td>
</tr>
<tr>
<td>CNS/neuroendocrine interactions</td>
<td>Neurohormone/neuropeptide secretion by gut/skin</td>
</tr>
<tr>
<td>Metabolic interactions</td>
<td>Circulating metabolites generated by gut/skin</td>
</tr>
</tbody>
</table>
Does the gut microbiota influence skin?

Gut microbiota:

- Is the microbiota disturbed in skin disease?
- Does manipulation of the gut microbiota restore/improve skin health?
Is there evidence of gut dysbiosis in skin disease?

Atopic Dermatitis associated with:

1. **Decrease in Bifidobacteria**
   - Yes e.g. Bjorksten et al, 1999, 2000, Watanabe et al, 2003
   - No e.g. Kendler et al, 2006, Gore et al, 2008

2. **Increase in *E. coli* and Clostridia**
   - Yes e.g. Penders et al, 2006 (KOALA study, 700 subjects)
   - No e.g. Storro et al, 2011

3. **Decreased bacterial diversity**
   - Yes – e.g. Wang et al, 2008
   - No- e.g. Bisgaard et al 2011

AD is probably not all one disease
Severity of atopic disease inversely correlates with intestinal microbiota diversity and butyrate-producing bacteria

Nylund et al, 2015
Atopic dermatitis and sub-species level dysbiosis in *Faecalibacterium prausnitzii*

Song et al, JACI, 2016

- 132 subjects (90 AD patients)
- *F. prausnitzii* L2-6 strain dominates. A2-165 type depleted
- Low butyrate and propinoate
- AD microbiome enriched in genes for use of nutrients released from a damaged gut
Psoriasis

- Immune and barrier dysfunction
- Many co-morbidities (cardiovascular disease, arthritis)
- Increased depression and anxiety
- Increased suicide risk
Similar Depletion of Protective Faecalibacterium prausnitzii in Psoriasis and Inflammatory Bowel Disease, but not in Hidradenitis Suppurativa

Does manipulation of the gut microbiota using probiotics positively affect skin disease?

• AD – Probiotics probably don’t work in established disease

• Overwhelming evidence for probiotics in prevention of AD

  7 clinical studies e.g. Kalliomaki et al, 2003, Rautava et al, 2012

  Probiotics given to mother and baby in high risk groups
  AD rates significantly decreased.

• Rautava 2012 –
  Probiotics prevent AD if given to the mother during the last 3 months of gestation and
  continued on during breast feeding.

  Mechanism?
Probiotics and psoriasis

- 26 patient study
- Chronic plaque PASI<16
- $1 \times 10^{10}$ *B. infantis* daily for 8 weeks

Groeger et al 2013
A role for probiotics in healthy skin?
The ‘skinny, shiny, sexy’ mouse as an indicator of the gut skin axis

Increased folliculogenesis
More acidic skin
Increased sebocyte production
IL-10 driven

Randomised double-blind placebo-controlled study of the effects of *L. paracasei ST11*  
Gueniche et al, 2014
Can probiotics be used topically?
‘Topical’ probiotics protect human skin from the effects of *S. aureus*
Effects of probiotics on tight junction barrier function

O’Neill and Garrod 2011
Probiotic bacteria increase tight junction function

Sultanna et al, 2013
Lysates of probiotic bacteria increase tight junction protein expression in human skin

**con**

**BL**

**LGG**

![Bar chart showing mean pixel intensity for control (Con), BL, and LGG groups.](chart.png)

* indicates significant difference.
Testing the lysate on ‘wounded’ skin

<table>
<thead>
<tr>
<th></th>
<th>Day1</th>
<th>Day3</th>
<th>Day7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
</tr>
<tr>
<td>LGG LYSATE</td>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
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Excision wound
LGG lysate promotes re-epithelialisation in human skin
Summary

• Many studies suggest the existence of the ‘gut-skin’ axis

• This axis can be modified by probiotics in some instances

• Probiotics may have utility used topically

• Modulation of the gut may offer new therapeutic strategies for skin in health and disease