Skin Microbiome

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DNA sequencing is a powerful microscope for microbial identification.

454 XLR or MiSeq

Pyrosequencing
Direct sequencing vs. culture-based methods

Diversity from direct sequencing

Diversity from culture
Skin Bacterial Genomic Data: Direct Sequence vs Culture

![Graph showing relative abundance of bacterial genera across direct sequence and culture samples from different locations (Alar Crease (Side of nose) and Umbilicus (Navel)). The graph compares Actinobacteria, Bacteroidetes, Cyanobacteria, Firmicutes, Proteobacteria, and divisions contributing less than 1% to the overall abundance.]
Skin Microbial Biomass

Swab: 10,000/cm²
Scrape: 50,000/cm²
Punch: 1,000,000/cm²

Grice E, Kong,…Segre, GenRes 2008
Human Skin Sites Survey

Grice E, Kong,…Segre, Science 2009
Inter-personal site variation
Exploring fungal diversity

- Develop DNA prep that breaks open fungi. If you don’t lyse it, you don’t sequence it.
- Test 18S rRNA and ITS primers for amplification and diversity
- Populate ITS database and develop phylogenetic classification at genus and species level
Summary of Human Skin Microbial Diversity

• Greater bacterial diversity than appreciated by pure culture studies;

• Skin is an ecosystem with bacterial diversity dependent on site (oily, dry, moist crease). Bacterial and fungal diversity may be shaped by different forces.;

• Does this begin to explain the predilection of skin disorders for stereotypical sites?
Alterations to the Skin Microbiome

• Age (Newborn to 1 year old, Transition through puberty, geriatric aging)

• Disease State (Atopic Dermatitis)
Shift in Skin and Nare Microbiome Community during transition through puberty

Tanner 1 is pre-pubescent, Tanner 3 is cusp of puberty; Tanner 4 is emerging through puberty

Oh, …Segre, Kong
Gen Med 2012
Shift in Skin and Nare Microbiome Community during transition through puberty

![Graph showing microbiome community changes across different stages of puberty.](image)

**Figure 3A legend**
- **Actinobacteria** (other)
- Corynebacteriaceae
- Propionibacteriaceae
- Bacteroidetes
- Firmicutes (other)
- Staphylococcaceae
- Streptococcaceae
- Clostridia
- Other
- Proteobacteria (other)
- Alphaproteobacteria
- Betaproteobacteria
- Gammaproteobacteria

Oh, …Segre, Kong
Gen Med 2012
Increased Prevalence of Atopic Dermatitis

• Currently affects 15% of US Children
• 2-fold increase in last 30 years
• “Hygiene hypothesis”
  – Increased incidence of atopic disorders is related to decreased exposure to common infections in early life
• Increased prevalence of atopic disorders in westernized countries

Strachan et al. BMJ 1989
AD disease severity

Staphylococcus aureus increases during AD flares

Kong, Oh … Segre, Gen Res 2012
S. aureus associated with decreased microbial diversity and flare

**Diagram:**
- **Left Panel:**
  - Scatter plot showing the proportion of S. aureus against the Shannon Diversity Index.
  - Correlation coefficient: $r = 0.69$, $P < 3.9e-06$.

- **Right Panel:**
  - Scatter plot showing the proportion of S. aureus.
  - Correlation coefficient: $r = 0.59$, $P < 2.1e-04$.

**Legend:**
- **Baseline:** Yellow circles
- **Flare (no trt.):** Orange circles
- **Flare (intermittent trt.):** Blue circles
- **Postflare:** Cyan circles

**Objective ScorAD**
AD microbiome progression hypothesis
Skin Microbiome Studies

- AD: Disease state affects microbial diversity, *S. aureus* prevalence. What is the driver?
- Age affects microbial composition. Is it increase in sebum? Hormones?
- Immune status alters microbiome, but not as profoundly as one might imagine

![Diagram showing the relationship between immune status, skin barrier, and microbes](image-url)
Future Directions

• METAGENOMICS: Limited by skin biomass (same for proteomics, metabolomics)
• NEGATIVE CONTROLS: Given limited starting material, are samples ‘clean’ enough?
• EXPLORE OTHER MICROBES: VIRUSES, MITES
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NIH Common Fund: Human Microbiome Project

Longitudinally assess microbial diversity of 250 healthy subjects at 5 major body sites

http://commonfund.nih.gov/hmp/

Signature Taxa for each major body site, large variation between subjects