Skin microbiota transplant overview

Elizabeth A. Grice, PhD
Assistant Professor, Dept of Dermatology
University of Pennsylvania

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1.8 meters$^2$ of diverse habitat for microbes

- Barrier function
- Acidic, cool surface that is continually sloughed via terminal differentiation
- Appendages and invaginations
  - Hair follicle
  - Sebaceous glands (oils)
  - Sweat glands
- Varied topography
  - Folds
  - Thickness
  - Hair and gland density
  - Occlusion
Topographical variation of healthy human skin microbiota

- High intrapersonal and interpersonal variation
- Site-specific microbiomes

Grice and Segre (2011) Nature Reviews Microbiology
Data from Grice et al (2009) Science
Skin taxa partitioned by site microenvironment

Oh et al. *Nature* 2014
Not all of our skin microbiome is so micro!

Demodex:
• Small mites (Arachnids) that live in human pilosebaceous unit
• More common in older individuals
• Feed on sebum, dead skin cells
• They have their own microbiomes!
• Association with rosacea, some types of dermatitis
Skin microbiota in dermatological disease

Acne

Atopic Dermatitis

Psoriasis
Atopic dermatitis

- Chronic itchy, red skin
- 15% US—onset 6-12 months
- Genetic predisposition: genes responsible for barrier function
- Skewed immune response + low expression of endogenous antimicrobial peptides
- S. aureus colonization may amplify or in part cause inflammation
  - S. aureus infection linked with AD flares
  - 90% AD skin colonized by S. aureus
S. aureus colonizes during AD flares

Kong et al., Genome Research 2012
Features of the AD microbiome

- Flares associated with low bacterial diversity
- Treatments increase diversity
- Greater disease severity correlates with \textit{S. aureus}

Kong et al., \textit{Genome Research} 2012
Acne vulgaris

- Affects 80-90% of teenagers.
- Localized usually to oily/sebaceous skin
- Potential involvement of *Propionibacterium acnes*, which is also normally present on skin.
- Host immune response, as well as hormones, sebum production are also involved
- Commonly treated with antibiotics, spironolactone, isotretinoin, benzoyl peroxide, other topicals
P. acnes strains (ribotypes) are differentially abundant in acne vs. healthy skin

Fitz-Gibbon et al. JID 2013
Psoriasis:

- Affects ~3%
- Autoimmune, hyperproliferative disorder
- Elbows, knees, scalp, trunk
- Genetic + environmental factors. Microbes hypothesized to trigger or exacerbate disease.
- Antimicrobial peptides are highly expressed in lesions
- Guttate psoriasis associated w/ respiratory *Streptococcus* infection
- Treatments include topical corticosteroids, phototherapy, immunosuppresants (methotrexate), biologics (monoclonal antibodies targeting IL12/IL23, TNF-a)
The psoriasis-associated microbiome

17 Psoriasis + 15 Control subjects

Longitudinal analysis following treatment

Lesions have increased combined relative abundance of the skin microbes: *Staphylococcus*, *Propionibacterium*, *Corynebacterium*, *Streptococcus*
Status of skin microbiome transplants (SMT)

SMT for atopic dermatitis (UCSD, PI: Richard Gallo MD)

• AD skin is deficient in *S. epidermidis* strains that naturally inhibit *S. aureus*.

• Transplant *S. epidermidis* strains to AD skin.

• Evaluate ability to decrease *S. aureus* abundance on lesional skin; assess reduction in severity of AD

• Cream application (Cetaphil)
• Nitrosomonas: Gram negative bacteria that oxidize ammonia and urea to nitrite and nitric oxide (NO)
• Cosmetic application (Mother Dirt)
• Acne, rosacea, eczema, diabetic foot ulcers, bacterial vaginosis
• No published data
SCIENCE:
NER:D MASKS ARE GROWN, NOT MADE

Biocellulose - the wonder material in our masks - isn't built or woven; it's grown! This layer of polysaccharides (sugars!) develops using acetic acid bacteria (AABs) - the same method used for centuries in food and in modern medical treatments.

The family of AABs we use is Acetobacter Xylinum, and nobody but NER:D is using the same strain for cosmetics. We found it first.

TRANSLATION:
DEEP-DOWN BIOCELLULOSE NANOSTRUCTURE

We bred our strain of AAB to build the smoothest, most even pattern of microfibrils possible, because that's what works best on human skin. If the structure of these microfibrils is uneven, they can "clump" into loose bundles that reduce the mask's surface area at small scales. Look at a NER:D mask under a microscope and you'll see neat patterns - not clumps. A neat pattern means more surface area to adhere to your skin. And the greater the surface area, the more active ingredients the mask.
Gaps

• What are the beneficial microbes on the skin?
• What are the mechanisms of colonization resistance on the skin?
• What is the best way to transplant?
  – Topical application
  – Cream, spray
• How long does the transplant persist?
• Techniques to differentiate dead/alive, transient/resident
Risks, safety concerns, AEs

- Risk of infection, especially with broken skin
- Bacterial burden on skin is normally low. How will skin respond to higher burdens?
- Greater risk of inadvertent microbial transfer, especially if transplant is on hands.