Microbiome and biofilm 101

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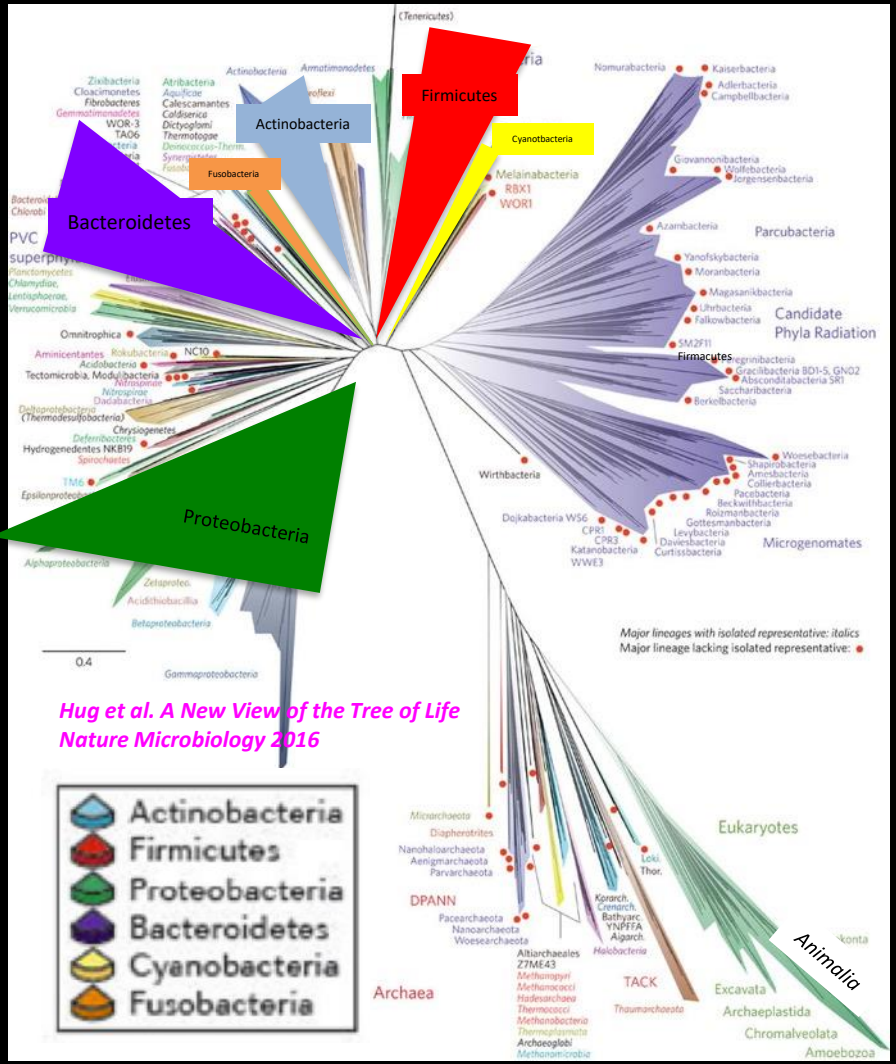
Microbiome:

“the collection of cells, genes, and metabolites from the bacteria, eukaryotes, and viruses that inhabit the human body……“


Actinobacteria
Firmicutes
Proteobacteria
Bacteroidetes
Cyanobacteria
Fusobacteria
Candidate Phyla Radiation
Parcubacteria
Microgenomates
Eukaryotes
Archaea
Animalia
Major lineages with isolated representative: italics
Major lineage lacking isolated representative:
0.4
Hug et al. A New View of the Tree of Life
Nature Microbiology 2016
Actinobacteria
Firmicutes
Proteobacteria
Bacteroidetes
Cyanobacteria
Fusobacteria

Relative abundance

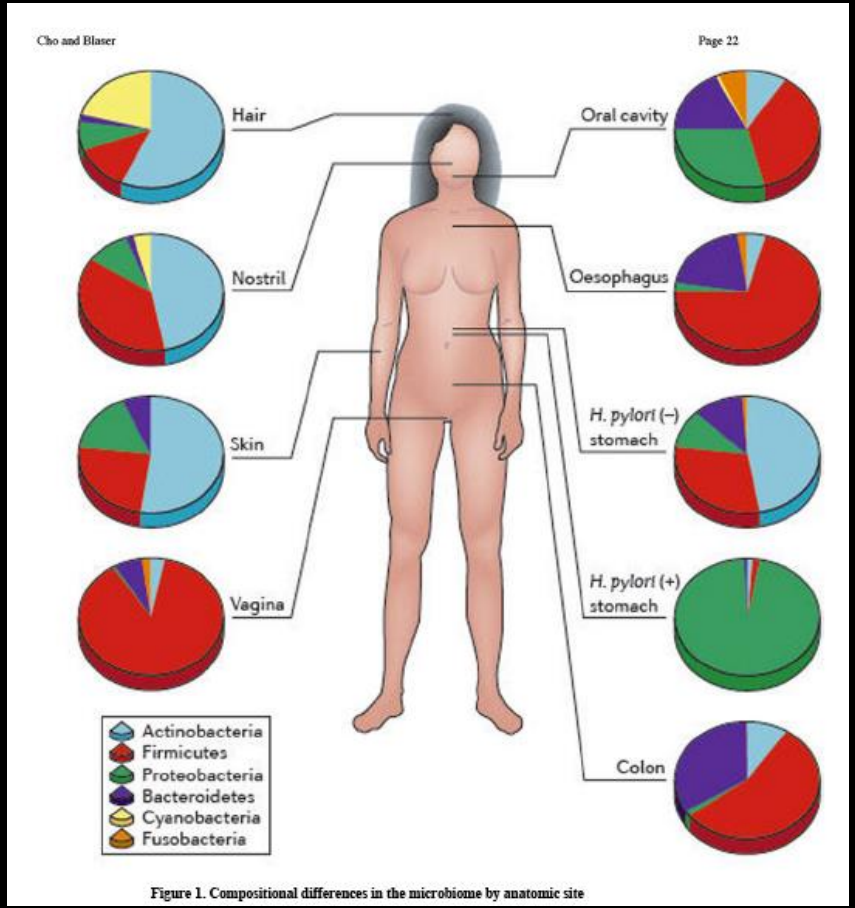
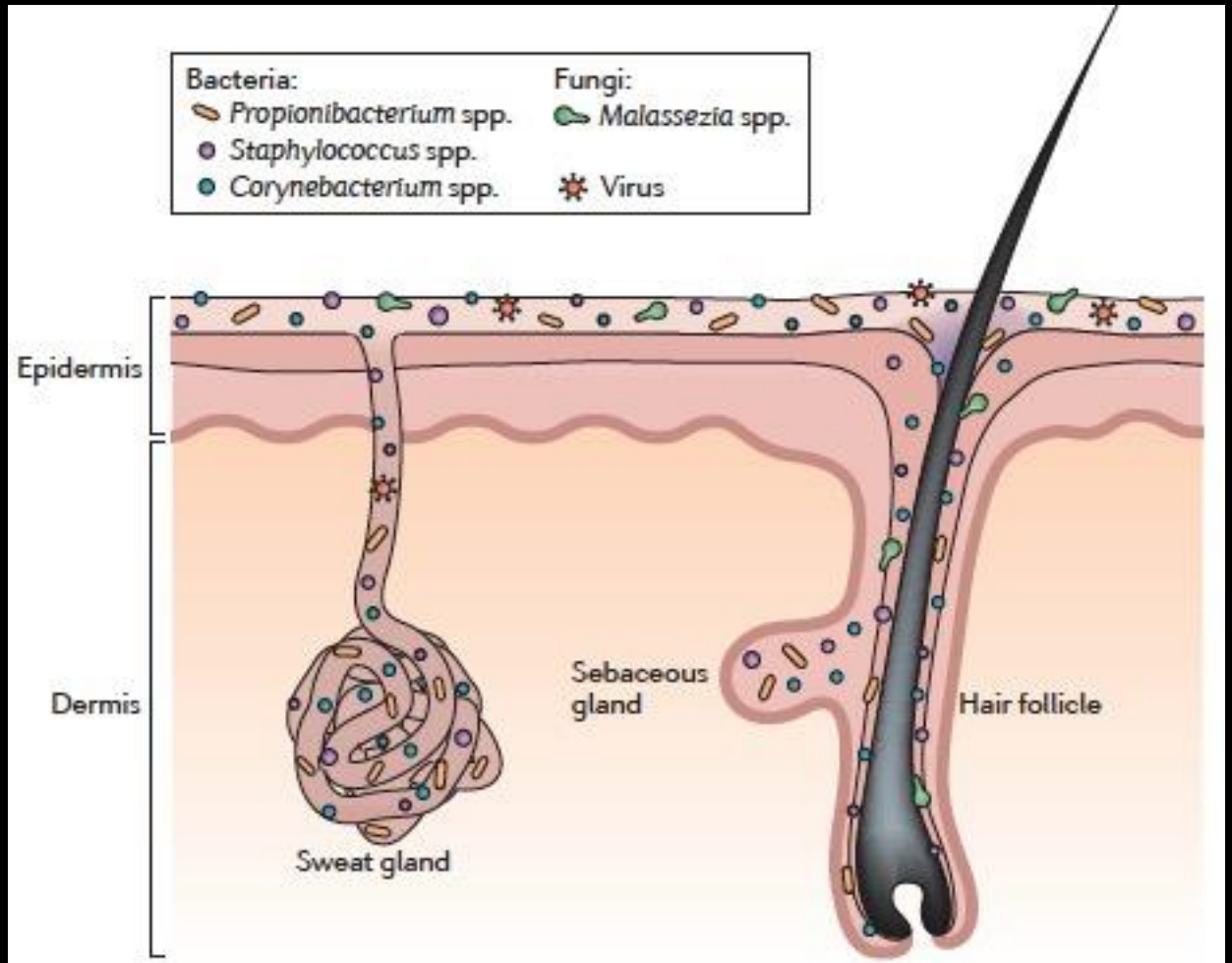


Figure 1. Compositional differences in the microbiome by anatomic site

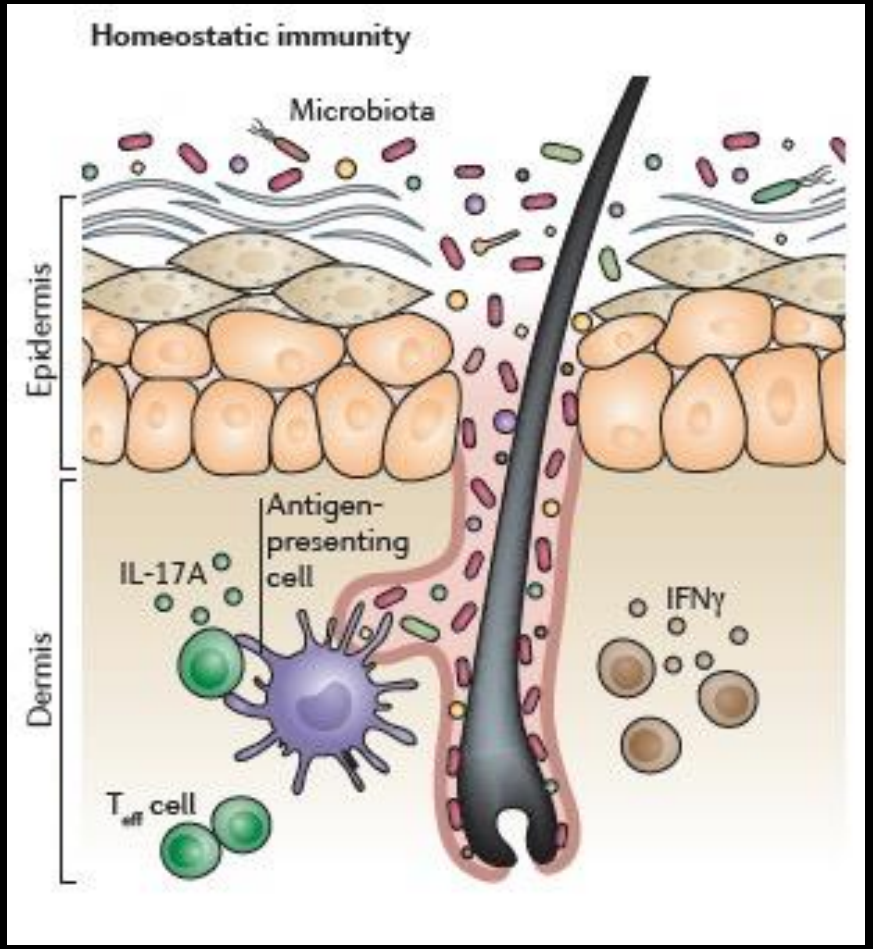
Cho and Blaser Nat Rev Genet. ; 13(4): 260–270.

Human microbiome

1) Stable by site over time
2) Stable in one person over time; differs between people
3) Diet and age affect it
4) Some microbiome types linked to disease but big variation between people with same condition (eg obesity, IBD)



https://www.nature.com/articles/nrmicro.2017.157



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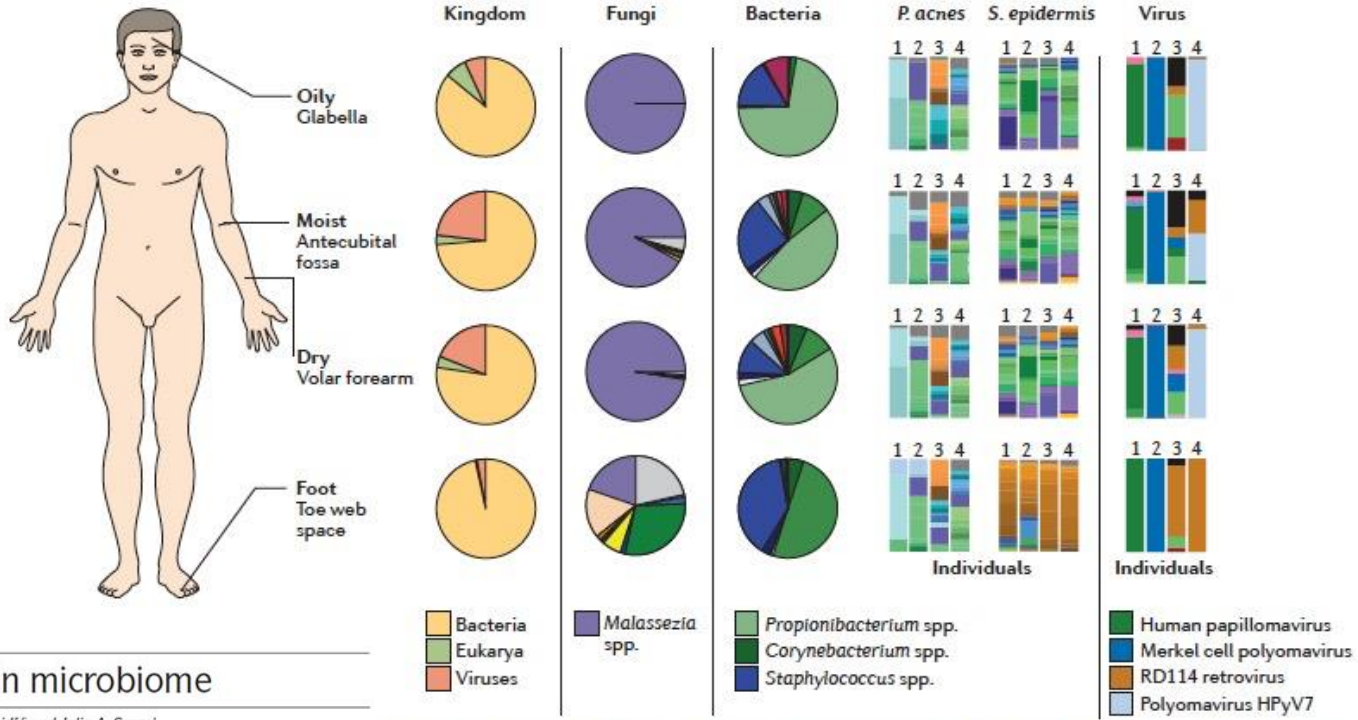

MICROBIOME

The human skin microbiome

Allyson L. Byrd[1–4], Yasmine Belkaid[5,5] and Julia A. Segre[1]

Colonization resistance
A mechanism where commensal microorganisms prevent the colonization of harmful microorganisms.

Figure 2 | **Skin microbial communities are shaped by physiological characteristics and the individual.** Four sites are shown to represent major microenvironments of the skin: glabella (also known as the forehead) sebaceous (oily); antecubital fossa (moist); volar forearm (dry); and toe web space (foot). Pie charts represent consensus relative abundances of the kingdom, fungi and bacteria across healthy adults[2]. The bacterial species *Propionibacterium acnes* and *Staphylococcus epidermidis* and eukaryotic DNA viruses are displayed as bar charts for four representative individuals to highlight how individuality shapes these communities[25]. For kingdom, fungi, bacteria and virus relative abundance plots, major taxa colours are identified in the legend. Unlabelled colours may be grouped as 'Other'. For the *P. acnes* and *S. epidermidis* bar charts, similar colours represent closely related strains.

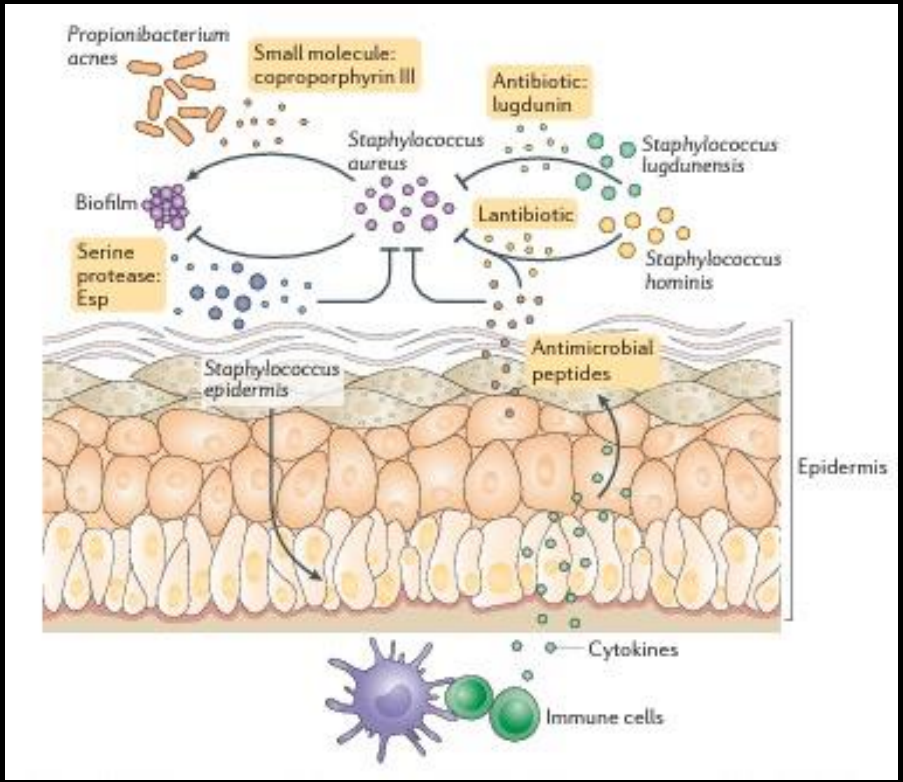

Figure 3 | **Skin commensal interactions with *Staphylococcus aureus*.** Skin microbial communities are shaped by interactions between organisms and with the host. In the skin, many interactions between commensals and *Staphylococcus aureus* have been identified. Antibiotics produced by coagulase-negative Staphylococcus and specifically by *Staphylococcus lugdunensis* prohibit colonization of *S. aureus*. Also, *Staphylococcus epidermidis* can inhibit *S. aureus* biofilm formation with production of the serine protease glutamyl endopeptidase (Esp). Moreover, when Esp-expressing *S. epidermidis* induces keratinocytes to produce antimicrobial peptides via immune cell signalling, *S. aureus* is effectively killed. In addition, *Staphylococcus hominis*-produced lantibiotics synergize with human antimicrobial peptide LL-37 to decrease *S. aureus* colonization. In contrast to inhibiting *S. aureus*, *Propionibacterium acnes* produces a small molecule, coproporphyrin III, that promotes *S. aureus* aggregation and biofilm formation.

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American Journal of Clinical Dermatology (2020) 21 (Suppl 1):S36–S43
https://doi.org/10.1007/s40257-020-00536-w

REVIEW ARTICLE

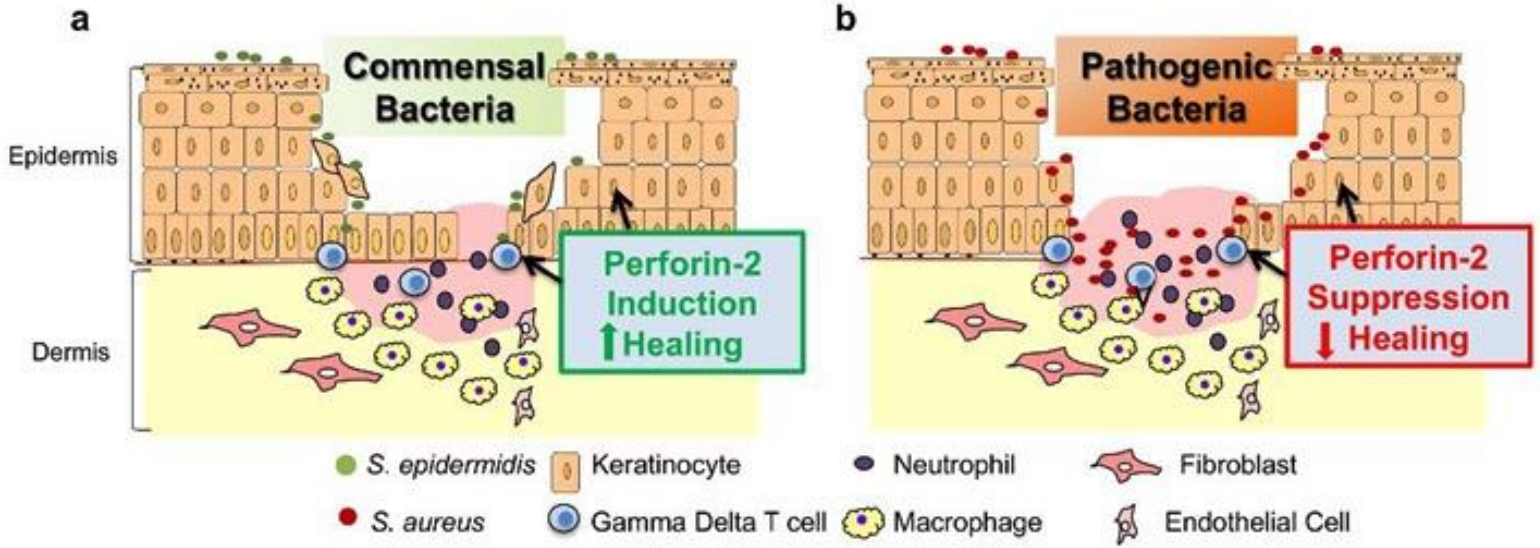


Fig. 2 Cutaneous immunity is differentially regulated by commensal and pathogenic microorganisms through modulation of Perforin-2. **a** Colonization of the wound with commensal bacteria may promote wound healing by inducing antimicrobial proteins such as Perforin-2, thus stimulating a protective immune response against pathogenic bacteria. **b** Wound infection with pathogenic bacteria results in Perforin-2 suppression in both hematopoietic and nonhematopoietic cells and inhibition of healing

Biofilms:

“self-constructed accumulations of microorganisms that produce a matrix of extracellular biopolymers …The collective behaviour of bacteria within biofilms promotes communication and interaction to ensure propagation and survival.”

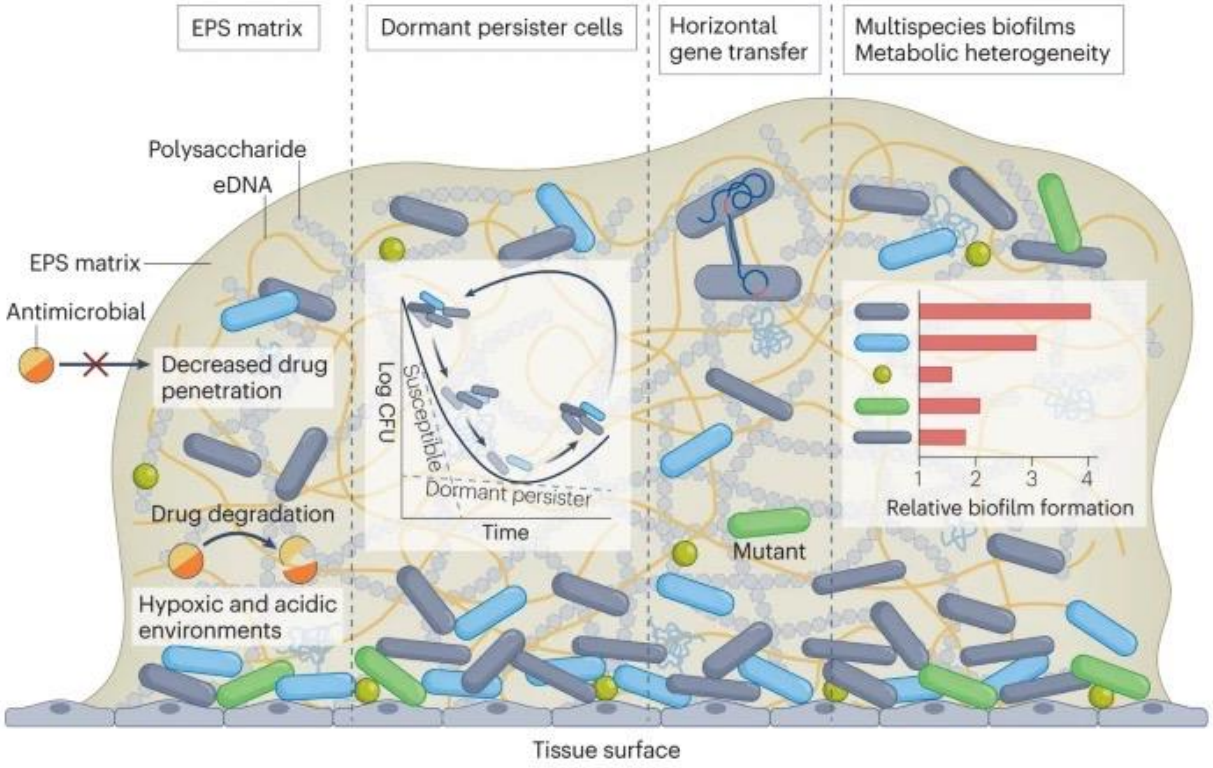
https://www.nature.com/articles/s41579-023-00905-2

Plastic Surgery Relevance of Biofilm Infection

- Bacterial biofilm infection not routinely detected using standard microbiologic techniques
- Bacteria in biofilm state are recalcitrant to antimicrobials
- Bacteria in biofilm evade host immune response
- Biofilm infection recurs after debridement
- Bacteria on biofilm state express or induce expression of proteins that degrade soft tissue
- Biofilm infection compromises skin barrier function

Barker JC, Khansa I, Gordillo GM. A Formidable Foe is Sabotaging Your Results: What You Should Know About Biofilms and Wound Healing, *Plastic & Recon Surg* 2017; 139(5): 1184e-1194e

Fig. 2: Challenges associated with treating biofilm-associated infections.



https://www.nature.com/articles/s41579-023-00905-2

Drug delivery strategies for antibiofilm therapy

Victor Choi, Jennifer L. Rohn, Paul Stoodley, Dario Carugo & Eleanor Stride

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doi: 10.1097/PRS.0000000000008142
PMCID: PMC8439557
NIHMSID: NIHMS1686443
PMID: 34398099

Biofilm Management in Wound Care

Chandan K. Sen, PhD,[1,2,3] Sashwati Roy, PhD,[1,2,3] Shomita S. Mathew-Steiner, PhD,[1,2,3] and Gayle M. Gordillo, MD[1,2,3]

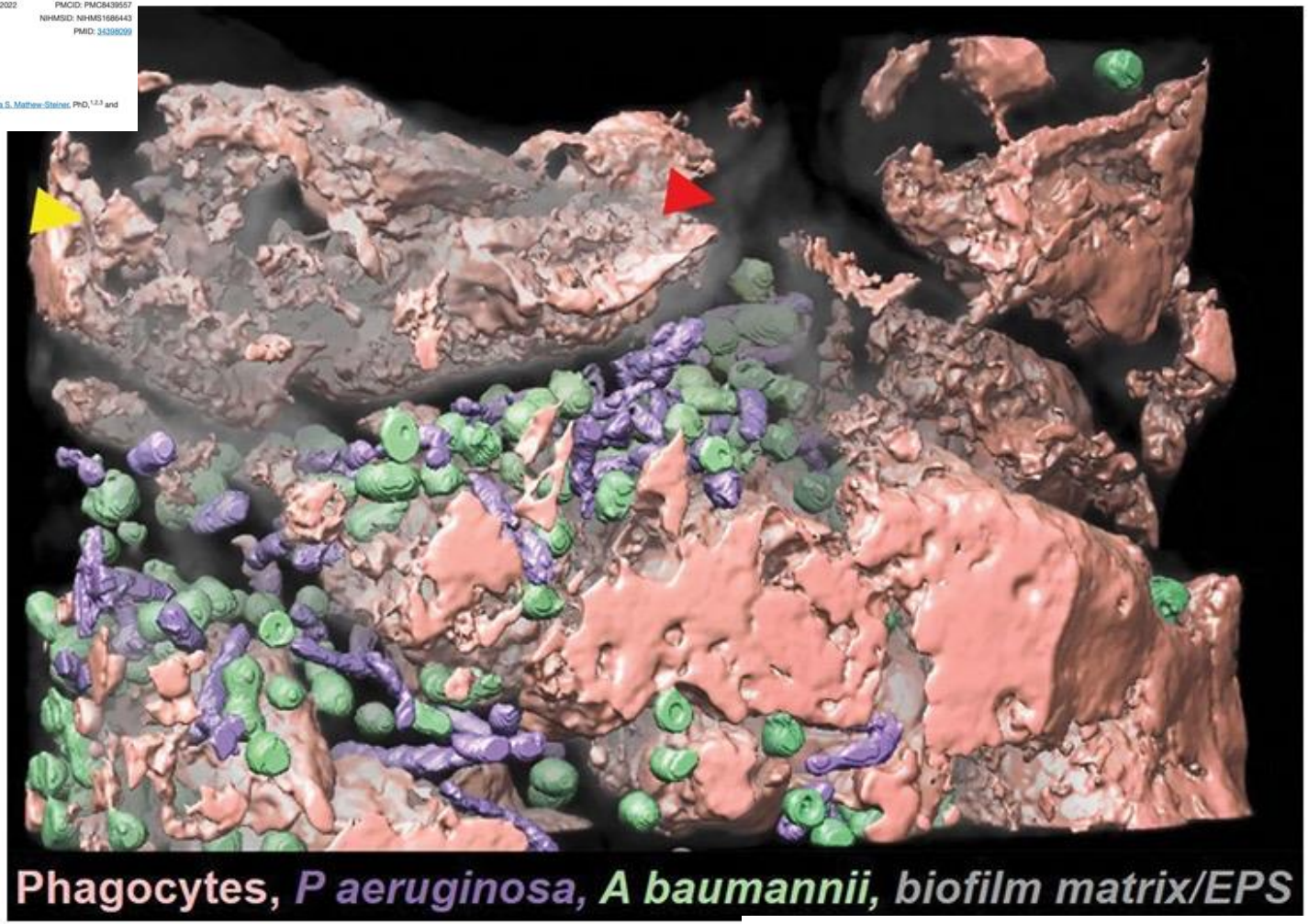
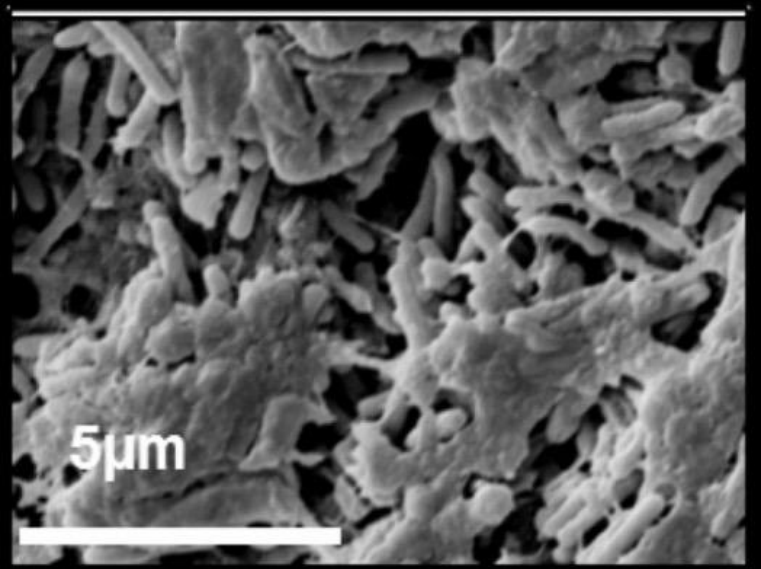


Figure 1. 3D imaging of biofilm and host immune cells.

https://pubmed.ncbi.nlm.nih.gov/34398099/

SEM is the way to prove biofilm, not clinically available; biofilms not detectable visually



Day 14

Summary

- Biofilm infection is extremely common in chronic wounds
- Scanning electron microscopy is the gold standard to diagnose biofilm infection
- There are multiple approaches to treat biofilm infection
  - none have been rigorously tested in clinical trials
  - Debridement and topical +/- systemic antimicrobials are the gold standard
- Studies to evaluate therapeutic efficacy of biofilm inhibitors must be done in live animals/human subjects to include host vs. pathogen immune responses

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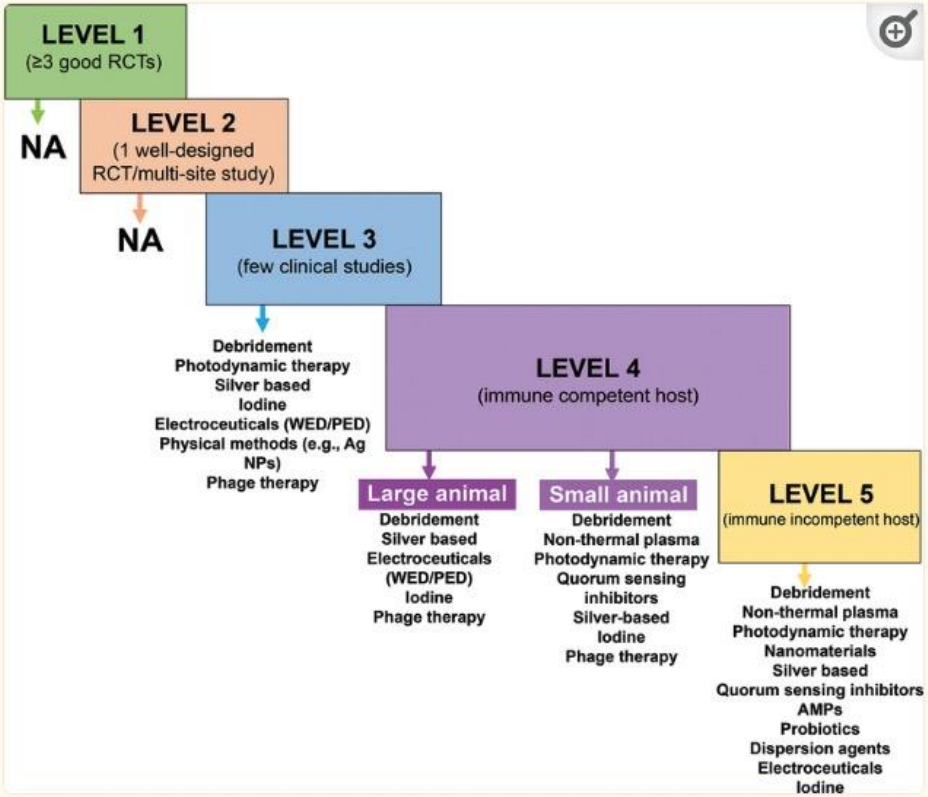

Figure 4.

Levels of Evidence modified for Anti-biofilm strategies.

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Summary

- Microbiome, “life-long (mostly) friendly tenants” discoverable because of major advances in culture independent methods
  - Masses of data, not much knowledge (yet) applicable to chronic wounds, clinical microbiome tests not yet available, …
- Biofilm – “defended, organized enemy camp”.
  - Likely present in most chronic wounds but hard to detect, likely prolongs time/completeness of healing, hard to remove…