The Ubiquitous Colonizer *Staphylococcus hominis* Protects Host Skin from Opportunistic Staphylococcal Pathogens by Blocking Quorum Sensing. M Brown (PhD, GS)[1], A Shahbandi[2], D Todd[2], N Cech[2], and A Horswill[1,],[1]Dept. of Immunology & Microbiology, University of Colorado Anschutz Medical Campus, Aurora, CO, [2]Dept. of Chemistry and Biochemistry, University of North Carolina at Greensboro, NC.

Commensal coagulase-negative staphylococci (CoNS) actively shape the skin barrier to resist colonization or infection by opportunistic pathogens, including *Staphylococcus aureus*, in a variety of mechanisms known as colonization resistance. The best characterized CoNS is *Staphylococcus epidermidis*, yet *S. epidermidis* is a frequent opportunistic pathogen that can actively degrade the skin barrier. We hypothesize that other commensal CoNS may have a greater protective role on the skin than previously appreciated, including the second most frequently isolated CoNS, *Staphylococcus hominis*. A potential *S. hominis* colonization resistance mechanism is the Accessory Gene Regulator (*agr*) quorum sensing system, which is ubiquitous among staphylococci. This two component system senses and responds to its auto-inducing peptide (AIP) signal. In *S. aureus*, *agr* regulates virulence factor expression and inhibiting *S. aureus agr* has been proposed as an antibiotic alternative. We found that spent media from any *S. hominis* skin isolate was sufficient to inhibit *S. aureus agr*. We sequenced a hypervariable region of the *agr* locus and found that *S. hominis* makes at least six AIP variants. Using mass spectrometry, we identified and validated the structures of 5 of these AIPs. We found that synthetic *S. hominis* AIPs inhibit *S. aureus* and *S. epidermidis agr* signaling with varying degrees of potency, but the majority with nanomolar IC_{50}s. Together, these data suggest that *S. hominis agr* cross-talk with opportunistic staphylococcal pathogens may be one mechanism to protect the cutaneous barrier from damage.

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