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SLST D1 strains may contribute to skin health

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Dear McDowell and Colleagues,

We thank you for the insightful commentary highlighting the likely contributions of *C. acnes* SLST D1 strains to promote a healthy skin microenvironment in acne patients with a successful response to isotretinoin.[1] As background, *C. acnes* is a polyphyletic species that has been classified into six phylotypes (IA1, IA2, IB, IC, II and III). Single locus sequence typing (SLST) also classifies *C. acnes* into ten classes (A to L). SLST classes A to E correspond to phylotype IA1 strains, whereas SLST classes F, G, H, K and L correspond to phylotypes IA2, IC, IB, II and III, respectively.[2,3] SLST classes A and C (IA1) and F (IA2) are associated with acne, whereas healthy skin is associated with SLST classes H (IB) and K (II).

Isotretinoin selectively alters *C. acnes* strain diversity of SLST A and D classes in the pilosebaceous follicle.[4] Similarly, recent findings by Ahle et al. highlight that antimicrobial active staphylococci (AAS) can target acne-associated (Class A strains) and to a lesser extent the healthy skin-associated strains of *C. acnes* (Class K and L), but co-exist with other SLST classes, including D.[3] In our study, we did not identify changes in the relative abundance of staphylococci within the follicle related to isotretinoin treatment. However, isotretinoin treatment increased the relative abundance of *Staphylococci* on the skin's surface.[5] Continued research into the mechanisms that govern the subsequent effect of isotretinoin on AAS strain diversity on the skin's surface will be an important avenue for further study moving forward. Nonetheless, acne therapies such as probiotics or drugs that selectively target acne-associated *C. acnes* strains, while leaving the rest of the skin microbial community intact, may be beneficial alternatives to antibiotics.

As highlighted by McDowell and colleagues,[1] the *C. acnes* type IA1 SLST D1 strain, HL025PA1—originally associated with moderate-to-severe acne skin— produces fewer inflammatory porphyrins and virulence factors such as oleate-degrading lipases compared to other acne-associated strains. Coupled with the fact that SLST D class strains are present on

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AUTHOR CONTRIBUTIONS

GWA and AMN wrote initial drafts; manuscript editing; reviewing; ALZ and DMT: manuscript editing; reviewing; All authors have read and approved the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

sebaceous skin sites and are dominant on the back of healthy individuals, these data would support the notion of reclassifying SLST D strains as beneficial to healthy skin, and not directly involved in acne inflammatory symptoms. Therefore, investigating the contributions of *C. acnes* strains, like SLST D1, to skin health is warranted to augment therapeutic approaches to treat skin disease.

Overall, your commentary combined with our original article highlight important knowledge gaps in our understanding of how acne therapies, like isotretinoin, modulate skin health and host microbiome interactions.

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The authors have nothing to report.

DATA AVAILABILITY STATEMENT

Data Availability Statement: Sequencing data related to the original publication (Nolan et al., 2023) is available at Sequence Read Archive (SRA): PRJNA935688.

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