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Running title:

Phenotype and antimicrobial activity of Th17 cells induced by *Propionibacterium acnes* strains associated with healthy and acne skin

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Short title: Protective Th17 cells targeting *P. acnes*

Abbreviations: PBMCs, Peripheral blood mononuclear cells; prTh17, Protective Th17 cells; paTh17, Pathogenic Th17 cells; $P_{A,}$ *P. acnes* strains associated with acne; P_H, *P. acnes* strains associated with healthy skin; CFU, Colony forming units

Key words: *P. acnes;* Protective Th17 cells; Ribotypes; Pathogenic Th17 cells; Interleukin 17.

Abstract

Studies of human skin microbiome suggest that *Propionibacterium acnes* strains may contribute differently to skin health and disease. However, the immune phenotype and functions of Th17 cells induced by healthy (P_H) vs. acne (P_A) skin-associated *P. acnes* strains are currently unknown. We stimulated PBMCs from healthy donors and observed that P_A strains induce higher IL-17 levels than P_H strains. We next generated P_H and P_A strain-specific Th17 clones and show that *P. acnes* strains induce Th17 cells of varied phenotype and function that are stable in the presence of IL-2 and IL-23. Although P_H and P_A- specific clones expressed similar levels of LL-37 and DEFB4, only P_H-specific clones secreted molecules sufficient to kill *P. acnes*. Furthermore, electron microscopic studies revealed that supernatants derived from activated P_H and not P_A-specific clones exhibited robust bactericidal activity against *P. acnes*, and complete breaches in the bacterial cell envelope were observed. This antimicrobial activity was independent of IL-26, as both natural IL-26 released by Th17 clones and rhIL-26 lacked antimicrobial potency against *P. acnes.* Overall, our data suggest that *P. acnes* strains may differentially modulate the $CD4^+$ T cell responses, leading to the generation of Th17 cells that may contribute to either homeostasis or acne pathogenesis.