ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

THE INFLAMMATORY DRIVE UNDERPINNING HIDRADENITIS SUPPURATIVA: HISTOLOGICAL ASSESSMENT, CYTOKINE PROFILING AND GLOBAL GENETIC PATTERNS

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Introduction/Background: Hidradenitis Suppurativa (HS) is a chronic inflammatory disease associated with significant morbidity. Genetic studies suggest an immunopathogenic mechanism in HS, particularly a role for the inflammasome. However our understanding of the cellular and molecular mechanisms underlying the inflammation in HS remains limited.

Objective: To assess the molecular mechanisms underpinning inflammation in HS.

Materials and Methods: HS tissue biospecimens sourced from the Dermatology Biobank, Liverpool Hospital, Australia. Lesional and non-lesional skin biospecimens were histologically and morphologically assessed. Multiplex cytokine profiling, imaging cytometry and genetic analyses were also performed.

Results: In situ elevation of several inflammatory cytokines was noted in lesional tissue, particularly the inflammasome-derived cytokines IL-1beta (40-fold change) and IL-18 (5-fold change), as well as IL-6 (25-fold change). TNF-alpha and IL-17 were also detected in HS lesions but were mostly undetectable in non-lesional skin. TNFRI (7-fold), TNFRII (17-fold) were significantly elevated in HS lesions, consistent with the known role for TNF-signaling in this disease. Interestingly, the keratinocyte and endothelial cell-associated cytokine IL-33 was significantly elevated in HS (7-fold change), which may reflect epidermal thickening or vascular remodeling.

Conclusions: Our findings show evidence of in situ inflammation in lesional tissue. The increase of IL-1beta and IL-18 support a role for the inflammasome in the pathogenesis of

HS, and further implicate TNF-alpha and IL-17 pathways.