MAIT cells – a novel player in Hidradenitis Suppurativa?

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Graphical Abstract

Introduction

Mucosal Associated Invariant T cells are a population of evolutionarily conserved “innate” T cells, which express the invariant T cell receptor (TCR) α chain Vα7.2-Jα33. MAIT cells have been identified in the gut, liver, adipose tissue, and periphery of humans. Recent research has highlighted a pathogenic role for MAIT cells in numerous inflammatory diseases including rheumatoid arthritis and psoriasis. MAIT cells are capable of robust rapid cytokine secretion, producing a milieu of cytokines including IFNγ, G-CSF and IL-17. Hidradenitis Suppurativa (H.S) is a chronic inflammatory disease of the hair follicles, resulting in painful, scarring lesions. Several inflammatory cytokines have been implicated in the pathogenesis of H.S including IL-1 and IL-17. MAIT cells represent a major IL-17 producing subset in humans, but their role in H.S is currently unknown.

In this study, using patient samples and an in vitro conditioned media model, we show that MAIT cells are altered in the periphery of patients with H.S (reduced frequencies and increased IL-17 production), and actively traffic to the H.S lesion conditioned media via a CCR6-CCL20 axis. Furthermore, conditioned media polarized healthy MAIT cells towards an IL-17 phenotype. Finally, we demonstrate that IL-17 producing MAIT cells accumulate in H.S lesions. Collectively our data reports for the first time a potential role for MAIT cells in the pathogenesis of H.S.

Methodological Approach

Results

Figure 1. MAIT cells are reduced in the peripheral blood of patients with H.S and display increased IL-17. (A) Representative dot plots showing flow cytometry gating strategy for identification of MAIT cells. (B) Scatter plots showing MAIT cell frequencies in control & H.S cohorts. (C) Scatter plots showing IL-17 producing MAIT cell frequencies in control & H.S cohorts (after stimulation with PMA/ionomycin) Data representative of a minimum of 7 independent experiments. Statistical comparisons using student t-test. *p<0.05, **p<0.01, ***p<0.001

Figure 2. MAIT cells migrate via a CCR6-CCL20 axis (A) Schematic outlining the experimental set-up (B) Scatter plot showing frequencies of CCR6 expressing MAIT cells in peripheral blood from control and H.S cohorts. (C) Scatter plot showing relative CCL20 mRNA in control (adjacent) or lesional skin from patients with H.S. (D) Scatter plot showing CCL20 levels in control (adjacent) or lesional conditioned media. (E-F) Scatter plots displaying number of migrated MAIT cells towards control media, media with recombinant CCL20 or lesional conditioned media. Data representative of a minimum of 3 independent experiments Statistical comparisons using student t-test. *p<0.05, **p<0.01.

Figure 3. IL-17 producing MAIT cells accumulate in the lesion of patients with H.S. (A) Scatter plot displaying secreted IL-17 levels from healthy MAIT cells alone, stimulated (antiCD3/28 TCR based) or stimulated in the presence of lesional conditioned media (TCM) for 18 hours. (B) Representative flow cytometry dot plots from different H.S skin biopsies. (C) Scatter plot shewing the frequencies of MAIT cells in adjacent or lesional skin biopsies from patients with H.S. (D) Scatter plot displaying frequencies of IL-17 producing MAIT cells in adjacent or lesional skin biopsies from patients with H.S after stimulation with PMA/ionomycin. Data representative of a minimum of 3 independent experiments. Statistical comparisons using student t-test. *p<0.05, **p<0.01, ***p<0.001

Summary

1. MAIT cells are reduced in the periphery of patients with H.S
2. MAIT cells express CCR6 and migrate towards CCL20, which is abundant in the lesions of patients with H.S
3. The lesion microenvironment polarizes MAIT cells to IL-17 production
4. IL-17 producing MAIT cells accumulate in H.S lesions

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References

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