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Title: Elucidate the Immune Mechanisms in Endometriosis through Analysis of Retrograde Menstrual Blood

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Endometriosis, affecting up to 10% of reproductive-age women, is marked by the presence of endometrial-like tissue outside the uterus and is linked to retrograde menstruation. This ectopic tissue triggers chronic inflammation, leading to pain, adhesions, and scarring. Immune dysregulation is thought to contribute to disease progression, but the precise cellular and molecular mechanisms remain unclear..

In an effort to elucidate these mechanisms, we analyzed retrograde menstrual blood from endometriosis patients, focusing on immune cell dynamics. Our study utilized single-cell RNA sequencing (scRNA-seq) to uncover key cellular interactions that may contribute to disease progression. Three groups were defined: control (CTL), endometriosis (EMS), and early-stage endometriosis (early_EMS). Retrograde menstrual blood was surgically collected and subjected to scRNA-seq. We analyzed gene expression and cell-cell interactions.

A significant increase in CD8+ MAIT cells was observed in the EMS group. Unlike the CTL group, the EMS group exhibited a lack of FASLG signaling between NK and MAIT cells, suggesting impaired NK cell-mediated apoptosis of abnormal MAIT cells. Furthermore, TNF signaling from MAIT cells to macrophages amplified inflammatory responses, while PARs signaling promoted abnormal epithelial-like cell formation, a hallmark of endometriosis.

Our findings suggest that dysregulated MAIT cells, due to defective NK cell activity, exacerbate endometriosis by driving inflammation and inducing abnormal tissue formation. These insights highlight the crucial role of MAIT cells in the pathogenesis of endometriosis and suggest their potential as therapeutic targets. Additionally, the observed increase in MAIT cells and their involvement in inflammatory and tissue-forming processes suggest that MAIT cells could serve as valuable diagnostic biomarkers, offering new avenues for early detection and targeted treatment strategies for endometriosis.