Decidual macrophage-mediated ferroptosis in trophoblasts leads to recurrent spontaneous abortion

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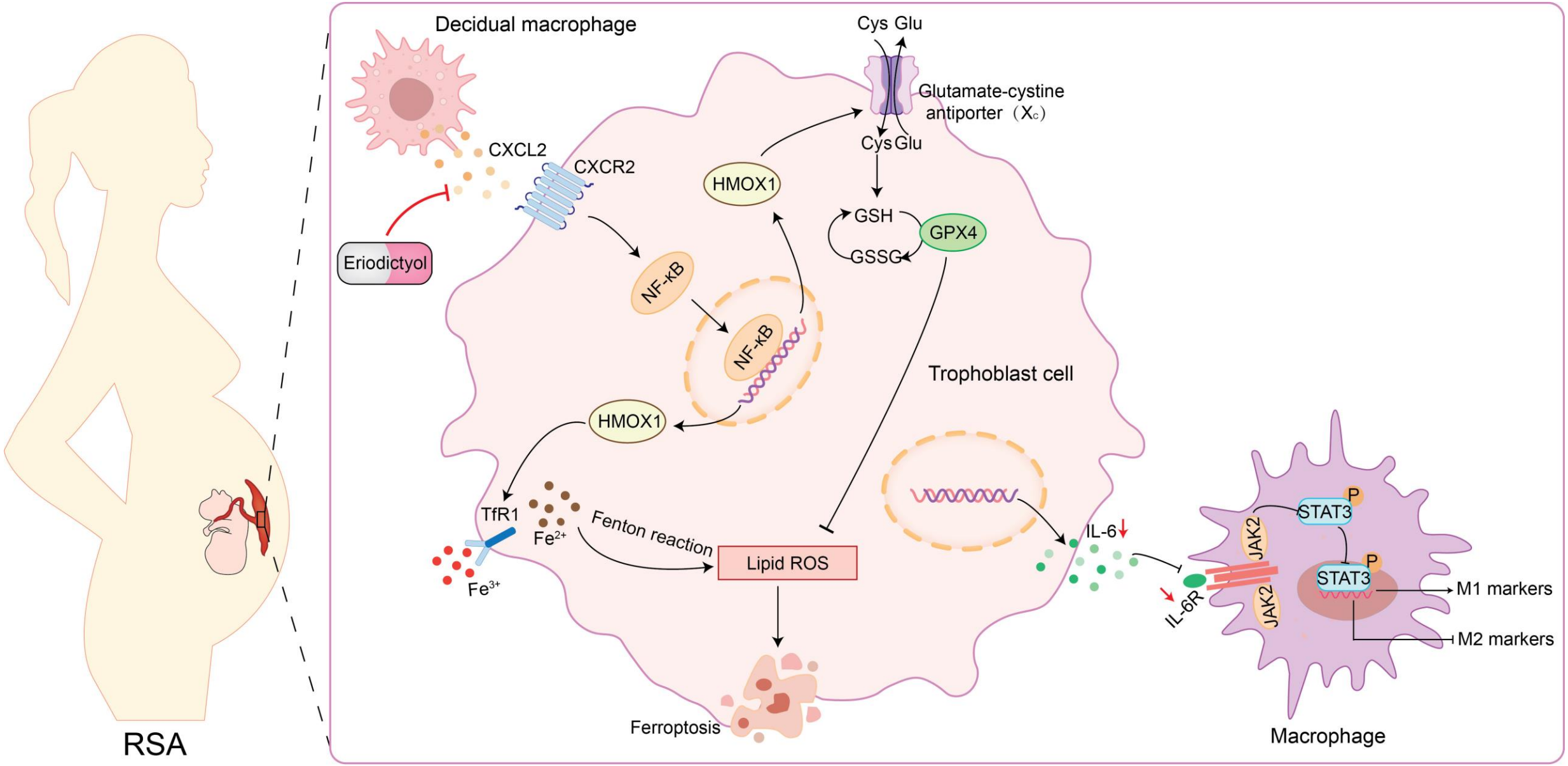
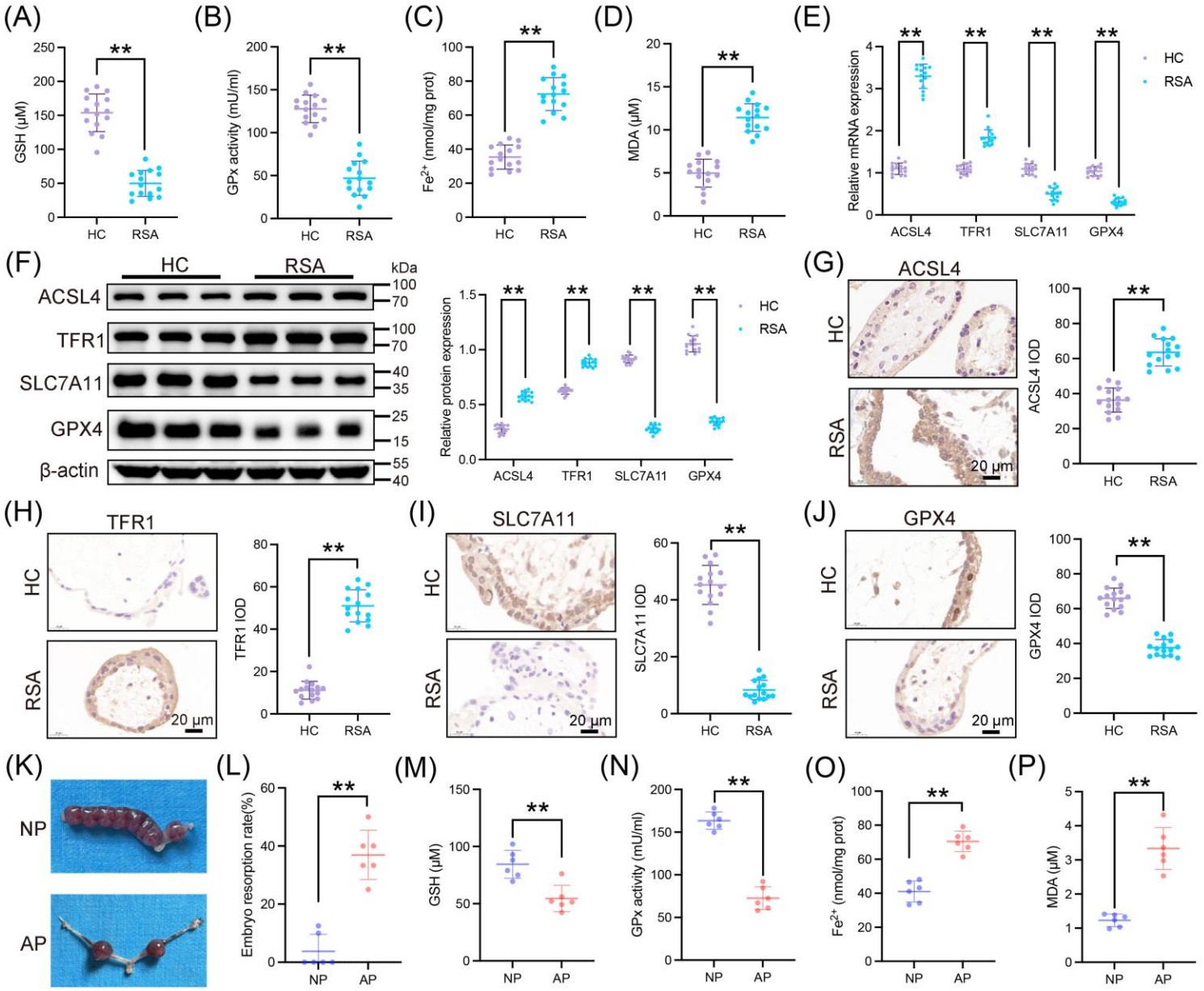
INTRODUCTION



Highlights

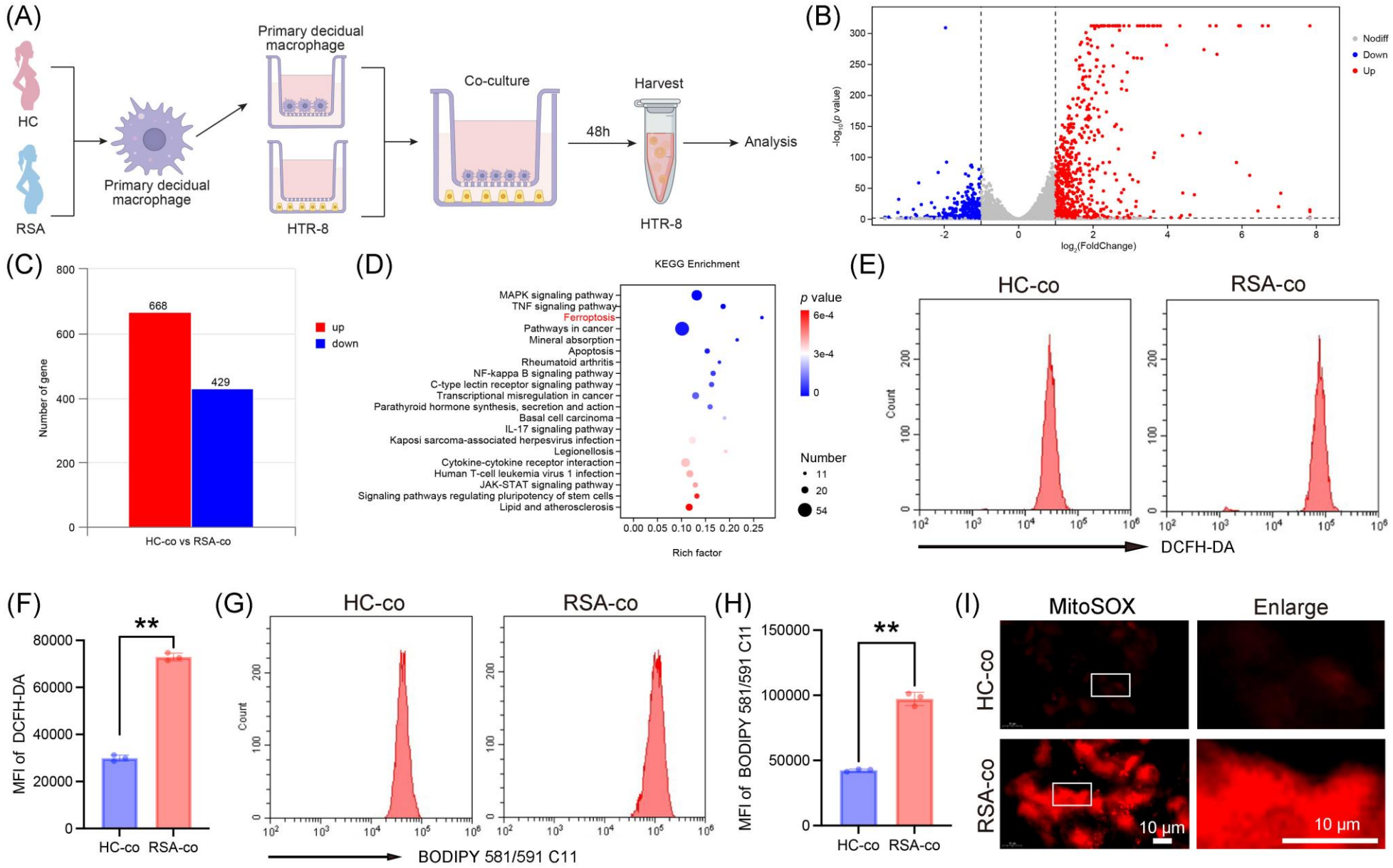
- **Decidual macrophages from RSA patients induce trophoblast ferroptosis and dysfunction the CXCL2/NF-κB/HMOX1 axis**
- **Trophoblasts co-cultured with RSA decidual macrophages promote pro-inflammatory macrophage polarization through IL-6 deficiency-mediated inhibition of JAK2/STAT3 signaling**
- **Eriodictyol shows therapeutic potential against RSA, offering a strategy to restore maternal-fetal tolerance**

1. Ferroptosis is observed in the villous tissue of patients with RSA



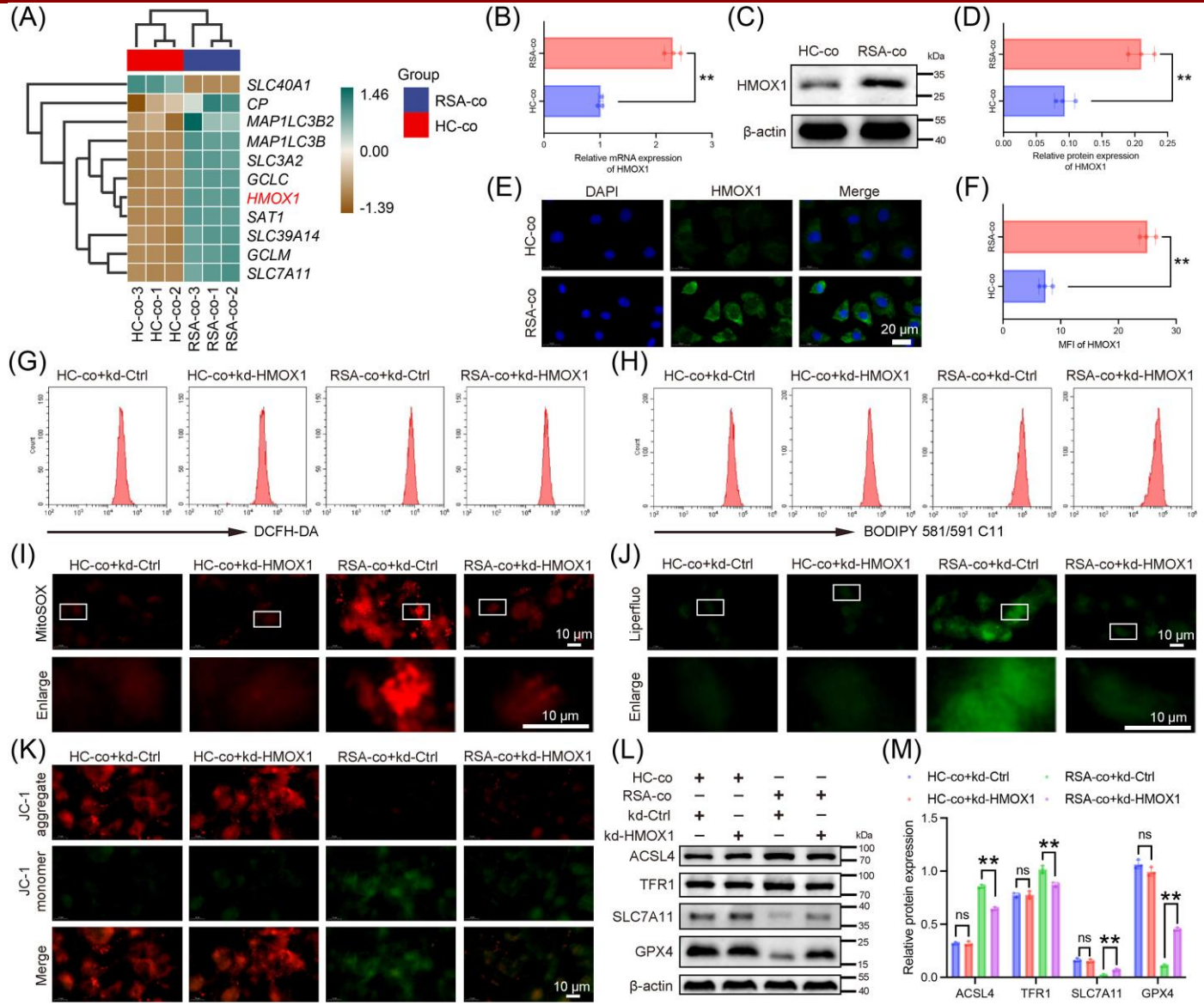
Placental trophoblast ferroptosis may contribute to the pathogenesis of recurrent spontaneous abortion

2. Decidual macrophages derived from RSA patient cause ferroptosis in trophoblast



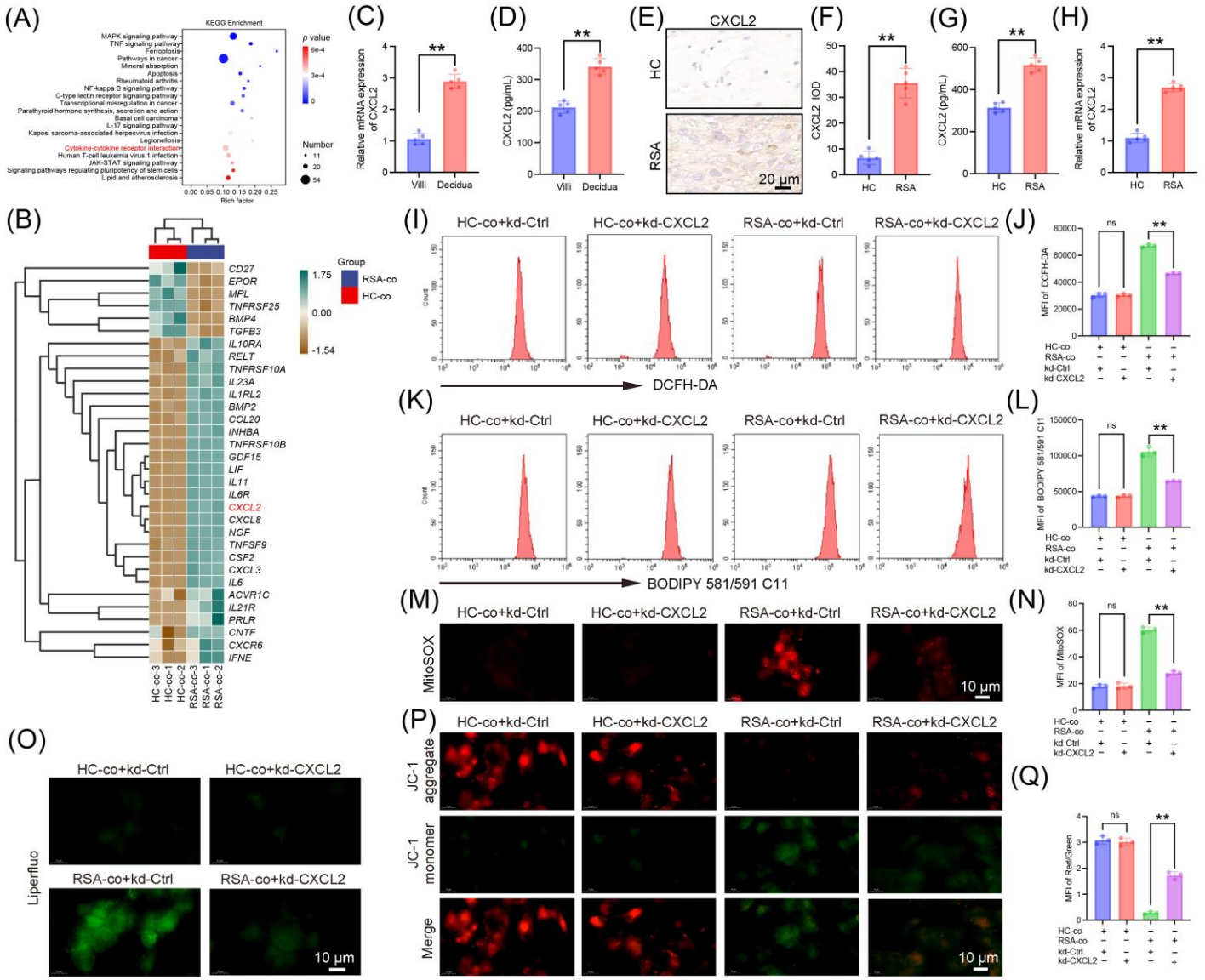
Ferroptosis is a key mechanism underlying cellular injury

3. RSA-derived decidual macrophages regulate trophoblast ferroptosis via HMOX1



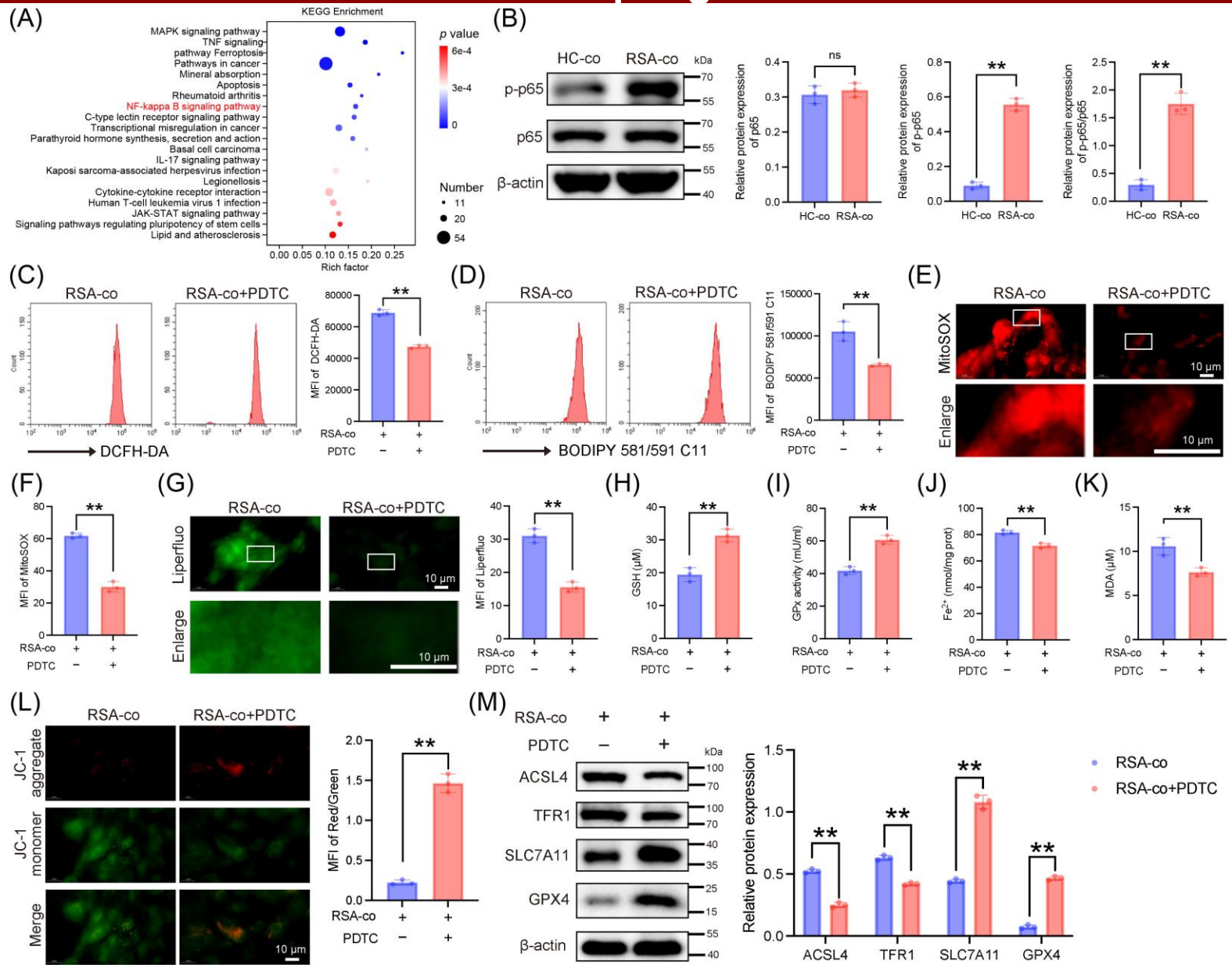
HMOX1 is a key mediator of trophoblast ferroptosis induced by decidual macrophages from patients with recurrent spontaneous abortion

4. RSA-derived decidual macrophages produce CXCL2 as a key regulator in the ferroptosis and other functions of trophoblast



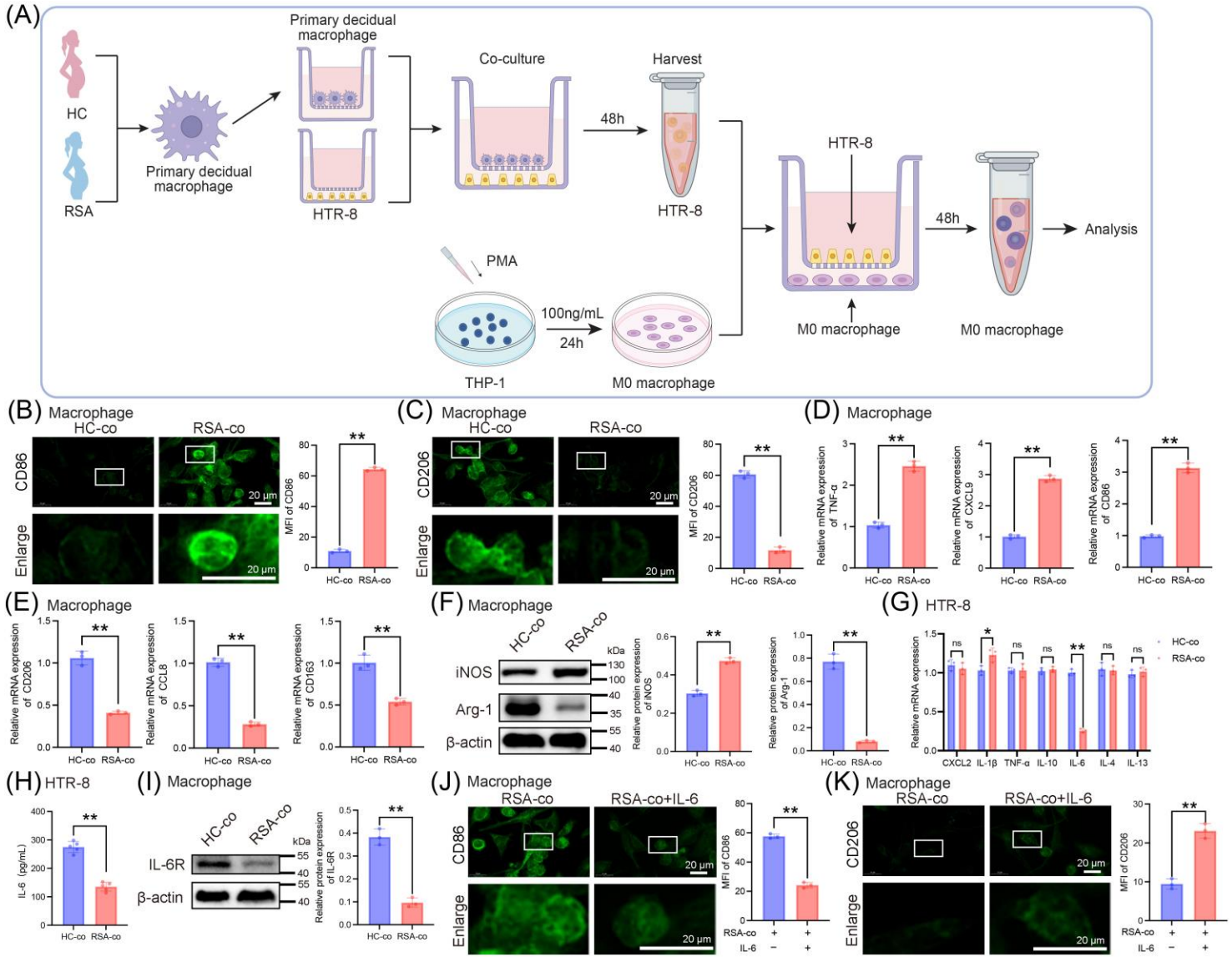
CXCL2 is a key factor mediating trophoblast injury induced by decidual macrophages from patients with recurrent spontaneous abortion

5. The NF-κB signaling pathway mediates trophoblast ferroptosis induced by RSA-derived decidual macrophages



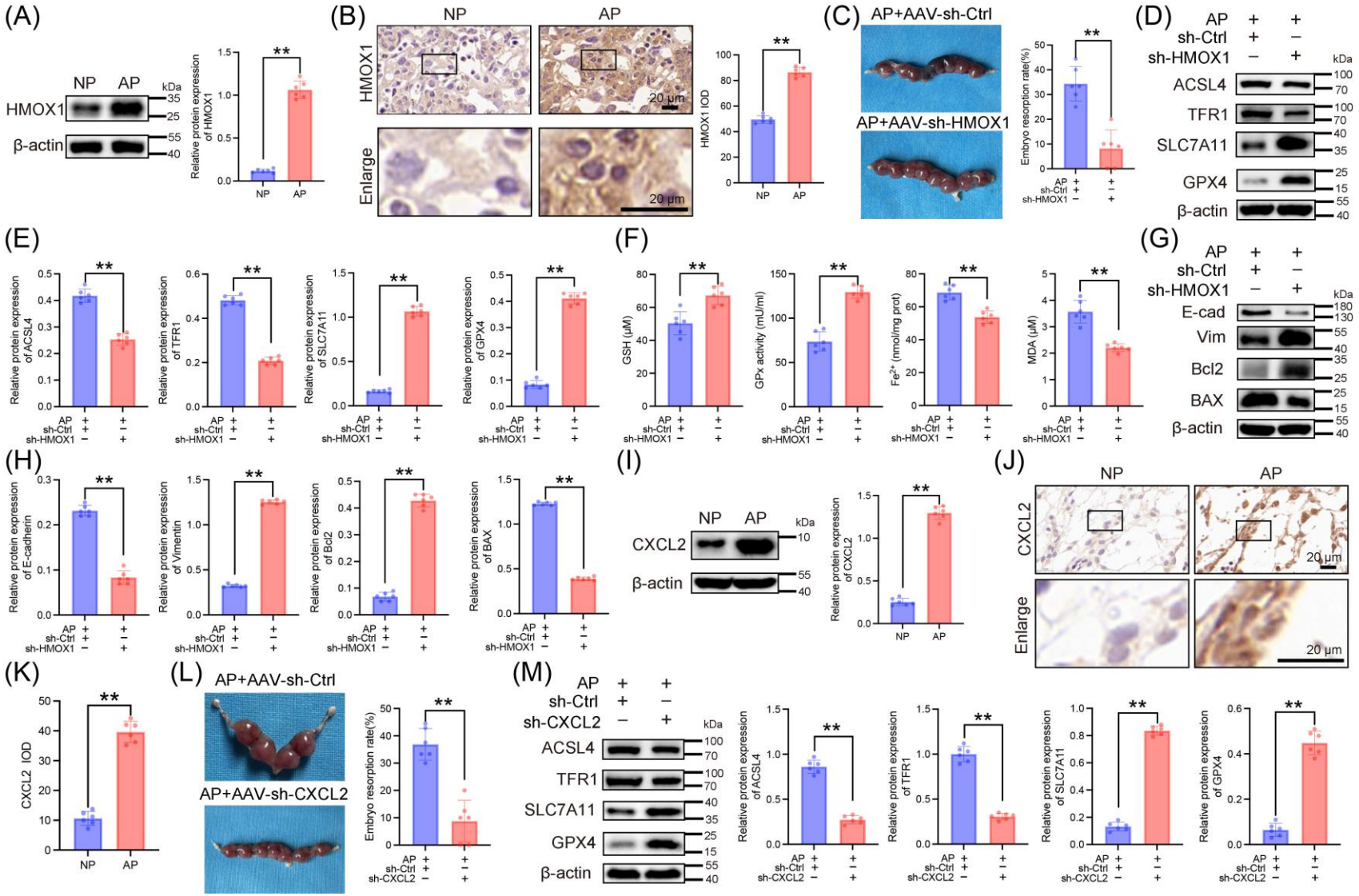
The NF-κB signaling pathway mediates ferroptosis

6. RSA decidual macrophages train trophoblasts to modulate M1/M2 macrophages



Decidual macrophages from patients with recurrent spontaneous abortion drive macrophage M1 polarization imbalance via the IL-6/JAK2/STAT3 axis

7. The CXCL2/NF-κB/HMOX1 signaling axis is critical for ferroptosis at the placental interface in aborted mouse



Decidual macrophages from patients with recurrent spontaneous abortion induce trophoblast ferroptosis, suggesting that targeting this process may help restore maternal–fetal immune tolerance

CONCLUSION

In summary, we found that decidual macrophages in RSA patients can induce ferroptosis in trophoblast cells, suggesting that targeting this mechanism may offer new opportunities for reshaping maternal-fetal tolerance. This study provides novel insights into the dysregulation of the maternal-fetal interface immune microenvironment in RSA. Furthermore, it offers crucial theoretical support for developing RSA clinical intervention strategies focused on modulating decidual macrophage-mediated trophoblast ferroptosis

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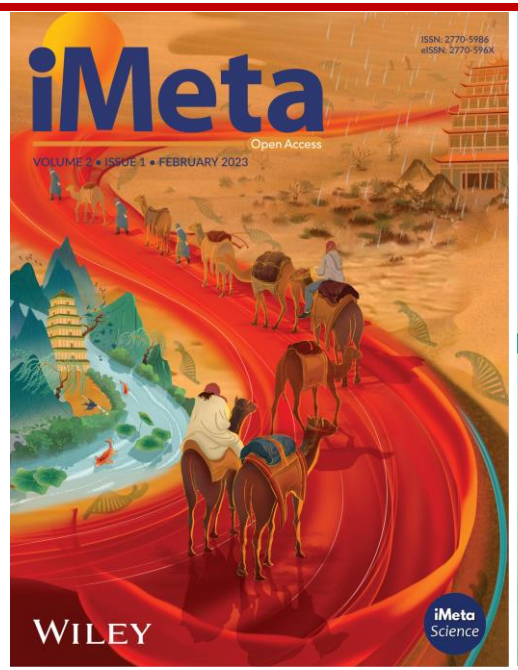

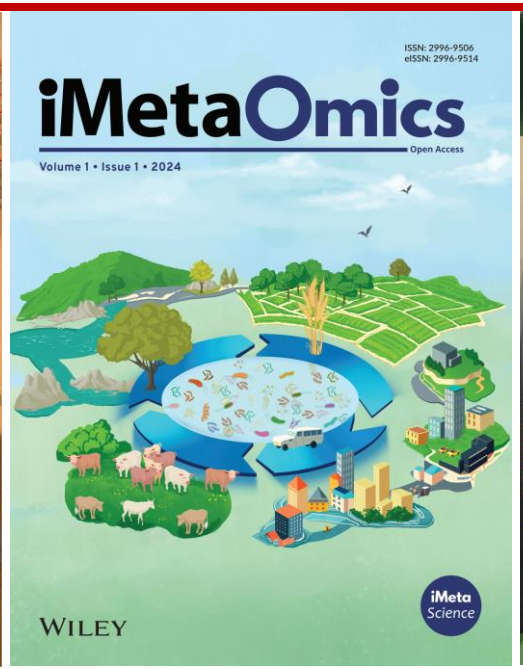

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