The transcriptional repressor Blimp1/PRDM1 regulates the maternal decidual response in mice

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Introduction: Divergent patterns of gene expression underlie the establishment of cell identity. We have been studying the zinc finger protein Blimp1 encoded by the *Prdm1* gene in the context of the early embryo. We previously found that Blimp1 acts as a transcriptional repressor and controls cell fate decisionsin the developing embryo with a loss of function Blimp1 mutant resulting in embryo arrest[1,2]. However, the role of maternal Blimp1, expressed by the uterus, has never been investigated.

Methodology: Initial immunostaining experiments were undertaken to investigate Blimp1 expression within the maternal uterine environment. To explore Blimp1 functional contributions we selectively eliminated Blimp1 expression in the maternal uterine environment using the well-characterised progesterone receptor Cre (PR-Cre) strain. We used immunohistochemistry, immunofluorescence, qPCR and transmission electron microscopy to examine the differences between wildtype and mutant decidua.To further characterise the cellular defects in Blimp1 mutant decidua, RNA-Seq of mutant and wildtype decidua was undertaken followed by ChIP-Seq to investigate Blimp1 functional contributions during decidualisation and identify candidate Blimp1 target genes.

Results: Blimp1 expression is robustly up-regulated at early post-implantation stages in the primary decidual zone (PDZ) surrounding the embryo. Conditional inactivation results in defective formation of the PDZ barrier and abnormal trophectoderm invasion. RNA-Seq analysis demonstrates down-regulated expression of genes involved in cell adhesion and markers of decidualisation. In contrast, genes controlling immune responses are up-regulated. ChIP-Seq experiments identify candidate targets unique to the decidua as well as those shared across diverse cell types including a highly conserved peak at the Csf-1 gene promoter. Interestingly Blimp1 inactivation results in up-regulated Csf-1 expression and macrophage recruitment into maternal decidual tissues.

Discussion and Conclusion: We describe, for the first time, Blimp1 expression and functional requirements within maternal uterine tissues during pregnancy. A loss of maternal Blimp1 function compromises the decidualisation response and results in loss of PDZ barrier formation, ectopic trophoblast expansion, increased macrophage invasion and ultimately, embryonic lethality. These results identify Blimp1 as a critical regulator of tissue remodelling and maternal tolerance during the early stages of pregnancy.

References:

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