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DISRUPTED DECIDUALISATION IN *SOCS3* GENE MUTANT MICE

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Cytokines comprise a large family of secreted glycoproteins that regulate many fundamental biological processes. Cytokine signals are relayed to target cells via binding to cell surface receptors. The receptors signal via members of the Janus kinases (JAKs) and signal transduction and activators of transcription family (STATs). The SOCS proteins negatively regulate cytokine signalling by inhibiting components of the JAK/STAT pathway. Genetically modified mice in which individual SOCS genes are ablated have revealed key biological roles for these proteins. SOCS3 null mice die at mid gestation due to placental insufficiency. By embryonic Day (E) 9.5 there is a marked decrease in the spongiotrophoblast layer and an increase in trophoblast giant cells in *SOCS3* null placentae. With increasing gestational age, there is progressive disorganisation of the *SOCS3* null placental labyrinth. Takahashi *et al.* (1) used tetraploid aggregation to demonstrate that the placental defect was attributable to intrinsic defects in the *SOCS3*-deficient trophoblast cells or yolk sac endoderm. Based on evidence from *in vitro* assays, *SOCS3* has a role in downstream negative regulation of signalling via a large number of cytokines. To identify the cytokine responsible for the placental phenotype, we crossed *SOCS3* null embryos with mice lacking leukaemia inhibitory factor (LIF). This rescued the placental phenotype of the *SOCS3* null mice, thereby demonstrating that alterations in LIF signalling are responsible for profound abnormalities of the murine placenta.

(1) Takahashi *et al.* (2003) *EMBO J.* **22**, 372–384.

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