The Ministry for Science and Medical Research Plenary Lecture

" Programming adult health in the pre-implantation embryo: the importance of sex and cytokines"

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Human fertility is low by comparison with other species and is declining at an alarming rate, with now one in six couples seeking clinical assistance to achieve pregnancy, and one in thirty babies conceived by IVF. Clues to the underlying basis of infertility and pathologies of pregnancy lie in unravelling the mechanisms by which the genetically foreign conceptus interacts with the mother's immune response, particularly during early pregnancy when the immune dialogue between the mother and conceptus is first established. We have discovered that male factors delivered to the female tissues in semen have a central role in establishing an optimal maternal tract environment. Seminal factors act in the female tissues to activate a cascade of cytokines that 'condition' female immune tolerance of the conceptus, and organise molecular and cellular changes in the endometrium to facilitate embryo development and implantation. Moreover, the survival and development of the pre-implantation embryo directly benefits through trophic responses to the cytokines induced by semen. Our findings indicate that the female cytokine response to semen impacts placental development and function, and is a major determinant of the growth trajectory of the fetus in utero and after birth. A better understanding of the immune and cytokine networks of early pregnancy has applications in improving clinical management of unexplained infertility and recurrent miscarriage, and placental pathologies leading to fetal growth restriction and pre-eclampsia. The imperative to understand these events is growing as we become increasingly aware of the importance of early embryonic environment in programming health in adult life, particularly in regard to the consequences for children born after IVF procedures.

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