IN VITRO MODELING OF THE HUMAN EMBRYO IMPLANTATION NICHE

Matteo Molè, Peter Rugg-Gunn, Andrea Palomar, Francisco Dominguez

Human embryo implantation is a critical stage whereby the embryo attaches to the maternal endometrium to establish a pregnancy and support foetal intrauterine gestation until birth. This stage of development is commonly referred to as a 'black box' because of the lack of suitable model systems and because of its inaccessibility, as it occurs inside the uterus. Yet, the incidence of implantation failures in fertility clinics is significantly high leading to early miscarriages, and limiting the efficiency of IVF procedures resulting in successful pregnancies. To gain insight into this process, we developed a three-dimensional cell-engineered system which closely recapitulates the cytoarchitecture of the human endometrium, opening the opportunity to study the process of human implantation in vitro for the very first time. Upon hormonal stimulation, the endometrial system adopts key features of tissue receptivity reminiscent of the mid-secretory phase of the menstrual cycle and supports implantation of human embryos and stem cell-based embryo models in vitro. Our findings highlight the key requirement of the receptive maternal tissue for physiological embryo development, provide insights into early stages of human embryo implantation and explore key molecular interactions established between embryo and maternal uterine tissue. This system opens the unprecedented opportunity to investigate the molecular networks underlying human embryo implantation for the first time and could serve as a platform for therapeutics development to address the high incidence of implantation failures.