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**Three dimensional endometrium-like culture system as a model for embryo implantation studies****Tali Tavor Re'em**

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Implantation failure remains an unsolved obstacle in reproductive medicine and is a major cause of infertility. Only about 20% of embryos transferred to the uterus, following in vitro fertilization, lead to the birth of a healthy infant. Due to obvious ethical restrictions, there is an unmet need to establish an in vitro model that mimics the events in the uterine wall during the implantation process. The available 2D models do not fully represent the events taking place at implantation. Endometrial cell lines, RL95-2 or HEC-1A, displaying receptive and non-receptive endometrial properties, respectively, were seeded into alginate macro-porous scaffolds, prepared by a freeze-dry technique. Cell constructs were cultivated in sequential hormonal treatment; one week priming of estrogen, followed by two weeks of progesterone treatment. Cultivation within 3D macro-porous alginate scaffolds enabled long-term cell viability for at least three weeks. E-cadherin mRNA expression levels, were shown to be hormone-dependent in RL95-2 cell constructs, compared to HEC-1A cells, where no hormonal effect was evident. In two weeks old RL95-2 constructs, estrogen treatment significantly increased E-cadherin mRNA expression, compared to other treatments. E-cadherin immuno-staining revealed pronounced protein expression in RL95-2 cell constructs, compared to HEC-1A. JAR spheroid attachment to three weeks old RL95-2 culture was confirmed by H&E staining, whereas no such attachment was evident in HEC-1A. Moreover, transfection of HEC-1A cells with estrogen receptor- indicated restored capability of JAR spheroid adhesion. Our model is useful for studying the regulatory mechanism governing implantation process and evaluation of potential novel therapeutic strategies for regulating implantation failures.

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