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# A novel fibrin-based matrix for the creation of an artificial ovary prototype for human application

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Context: The development of an artificial ovary is actually an experimental fertility preservation strategy addressed to women affected by cancer with high risk of ovarian involvement who cannot benefit of the ovarian tissue cryopreservation and transplantation. Essential requirement for the creation of a bio-engineered ovary is the physical support needs to encapsulate isolated ovarian follicles. Ideally, this matrix should mimic the human ovarian tissue as far as possible in terms of microstructure and rigidity. Although fibrin-based matrices appear to be the best choice, identifying the appropriate combination of fibrinogen (F, mg/mL) and thrombin (T, IU/mL), the principal constituents of fibrin, for human ovarian follicle encapsulation and grafting remains a challenge.
Objective: To improve the composition of the fibrin-based artificial ovary prototype by mimicking human ovarian tissue ultrastructure and rigidity.
Methods: Fresh human ovarian cortex from different women (n=3) and four fibrin formulations using different concentrations of F and T (F12.5/T1, F30/T50, F50/T50, F75/T75) were investigated by scanning electron microscopy. Rheology was performed in fibrin matrices to evaluate their stiffness. Fibrin formulations most closely resembling human ovarian tissue were used to embed isolated human follicles, and compared in terms of follicle recovery rate after encapsulation.
Results: Ovarian tissue cortex exhibited a similar ultrastructure, with a mean Â± SD of fiber thickness of 66.4 Â± 8.6 nm. Of the 4 fibrin formulations, only F12.5/T1 and F30/T50 showed significantly thicker fibers (137.5 Â± 45.5 nm 100.8 Â± 13.2 nm respectively), while F50/T50 and F75/T75 had comparable fiber thickness to ovarian tissue (64.5 Â± 2.3 nm and 65.4 Â± 18.4 nm respectively). Interestingly, fibrin stiffness was positively correlated to F and T concentrations, with F50/T50 rigidity similar to human ovarian tissue stiffness (Wood et al., 2015). F50/T50 and F75/T75 were therefore used to encapsulate isolated human preantral follicles, and recovery rates obtained (44% and 47% respectively) were not different between these two fibrin formulations.
Conclusions: We showed, for the first time, that human ovarian cortex exhibits a similar ultrastructure in age-related women. This allowed us to standardize fibrin matrix architecture and select the fibrin formulation that best resembles native tissue in terms of ultrastructure and rigidity.

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