EVENT ABSTRACT

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Xenografting of isolated human follicles in fibrin scaffold associated to hyaluronan: preliminary results

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Introduction: Transplantation of cryopreserved ovarian tissue is one of the alternatives to restore fertility in cancer survivors. However, this technique is not advisable for patients with certain types of cancer, since there is a risk of reintroducing malignant cells present in the cryopreserved tissue. For these patients, a safer alternative could be transplantation of isolated preantral follicles back to their natural environment. To encapsulate and protect isolated follicles, a matrix should be created. To this end, we have been testing different polymers to embed murine follicles. Our best results were obtained with a fibrin formulation containing low concentrations of fibrinogen and thrombin[1]. Despite these promising results with mouse follicles, our findings with human isolated preantral follicles were significantly inferior. The goal of this study was therefore to evaluate if a fibrin formulation with higher concentrations of fibrinogen and thrombin could improve survival of human isolated be suitable as a matrix to graft isolated human preantral follicles. Moreover, we would like to test if supplementation of the fibrin matrix with hyaluronan (HA) could also have a positive effect on follicle survival and growth.

Materials and Methods: Around fifty preantral follicles were embedded in fibrin clots (50mg/ml fibrinogen and 10IU/ml thrombin) without (fibrin) or with hyaluronan (fibrin-HA), together with 50,000 ovarian stromal cells for each group, and respectively xenografted to right and left pockets created in the inner wall of the peritoneum of nude mice (n=2 clots per recipient: fibrin and fibrin-HA) for ten minutes (D0) (n=4) or seven days (D7) (n=4). After 10 minutes and 7 days the animals were sacrificed and the matrices were recovered.

Results and Discussion: All 16 fibrin beads were recovered at the end of the xenotransplantation period. Table 1 shows the recovery rate of follicles in fibrin and fibrin-HA at D0 and D7 (Table 1, Fig 3A). Although fibrin-HA matrix was more degradable with a higher cell invasion at D7, no statistical difference was observed in the follicle recovery rate.

	D0	D7	
	Follicles (mean ± SD) encapsulated in the matrix	Number (mean ± SD) of recovered follicles	Recovery rate (%)
Fibrin	29 ± 0	7 ± 5	24
Fibrin-HA	32 ± 1	7 ± 2	22

Figure 1. Follicles in the fibrin and fibrin-HA matrices at D0 and D7.

Ki67 staining confirmed the growth of the grafted follicles as all of them showed Ki67-positive granulosa cells. TUNEL assay revealed that on D7, 100% of the follicles were viable in both groups. Granulosa cell activity, which was a parameter to evaluate follicular health status, was confirmed by inhibin-α immunostaining: at D0, the 93% (13/14) and 100% (9/9) of the follicles were healthy in the fibrin and fibrin-HA groups respectively. At D7, the proportion of healthy follicles did not differ from D0: 88% (14/16) and 100% (11/11) for fibrin and fibrin-HA clots respectively.

Conclusion: Isolated human follicles were able to survive and resume growth after encapsulation in fibrin clots and short-term xenotransplantation. Fibrin-based matrix seems to be a promising material in the creation of an artificial ovary, supporting isolated follicle and ovarian cells after grafting. Although HA supplementation did not seem to have a positive effect on follicle survival and development, more studies are necessary to confirm and understand these findings.

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References:

[1] Luyckx V, Dolmans MM, Vanacker J, Legat C, Fortuño Moya C, Donnez J, Amorim CA. A new step toward the artificial ovary: survival and proliferation of isolated murine follicles after autologous transplantation in a fibrin scaffold. Fertil Steril 2014;101(4):1149-1156

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