STROMAL-DERIVED FACTOR 1 SLOWS DOWN THE ACTIVATION OF HUMAN PRIMORDIAL FOLLICLES DURING IN-VITRO CULTURE

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Abstract Body

The development of an in-vitro culture system from preantral follicles up to mature oocytes is promising to recover safely the full reproductive potential of ovarian tissue. Until now, only in the mouse this approach has led to live offspring. Removal of ovarian tissue from its in-vivo environment induces uncontrolled and accelerated growth of primordial follicles. This may be one of the reasons for the lack of developmental competence of mammalian oocytes derived from in-vitro cultured primordial follicles. Stromal derived factor-1 (SDF1) is a chemokine already successfully used as a primordial follicle activation inhibitor in the mouse. We investigated the effect of SDF1 on preantral follicle growth in human ovarian cortex culture.

Ovarian cortex tissue of 7 patients (5 oncological patients and 2 transgenders) was placed into culture for 10 days with and without addition of 100 ng/ml SDF1 to the culture medium. At days 0, 5 and 10, follicle development was assessed after haematoxylin-eosin staining. Differential proteomic analysis on SDF-treated and control tissue of 2 patients was assessed through Liquid Chromatography with tandem mass spectrometry.

SDF1-treatment for 10 days resulted in significant more primordial and fewer secondary/tertiary follicles (37.5% and 16.7%, resp.) compared to the control culture (21.2% and 35.4% resp.) The proportion of primary follicles was not different (43.4% and 45.8%).

Proteomic analysis indicates that in SDF1-treated tissue PI3K-Akt pathway-specific LAMTOR2, LAMTOR3 and mTOR, and Hippo pathway-specific MST1 and YAP1 were downregulated, together with tight-junction related cell communication. MAPK activity was upregulated.

In conclusion, the study revealed for the first time in the human that it is possible to slow down in- vitro primordial follicle activation with SDF1 after 10 days of culture. SDF1 action involves PI3K-Akt, Hippo and MAPK pathways.