

EFFECT OF IN VITRO ACTIVATION VS FRAGMENTATION ON HUMAN OVARIAN TISSUE IN CULTURE

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Abstract Body

Women with premature ovarian insufficiency lose their fertility before the age of 40 years and have very limited treatment options. Novel treatments based on activation of PTEN/PI3K pathway in vitro (IVA protocol) has been administrated on refractory POI patients and led to live births. However, some studies suggested that mere fragmentation of ovarian tissue may produce similar effects. Here, our aim was to investigate the impact of fragmentation alone compared to IVA protocol on human ovarian tissue using our xeno-free culture system.

Ovarian tissue collected from consenting caesarean section patients was fragmented and divided to two culture conditions: i) in vitro activation (hOpic+740Yp) and ii) fragmentation only. Follicle survival and growth were evaluated after 24 h and 7 d of culture, gene expression by RNA-sequencing after 24-h culture, and steroid secretion after 7-d culture.

Compared to fragmentation group, significantly higher follicular survival rate, increased number of secondary follicles, and larger secondary follicle diameters were found in IVA group. However, no significant difference was detected on steroidogenesis. When gene expression in cultured groups were compared to the fresh control, in total 3676 and 4223 DEGs were found in the IVA and fragmentation groups (FDR<0.001), respectively. The top enriched gene sets in both groups included several pathways that are known to modulate follicle growth, like PI3K/AKT, MTORC1 and TNF- α . When IVA group was compared to fragmentation group, only 110 DEGs were found (FDR<0.1). IVA affected signaling pathways involving follicle growth but also inflammation and DNA damage.

In summary, our preliminary results indicate that IVA treatment improves follicle survival and promotes the development of larger secondary follicles. However, the mere fragmentation of tissue has far greater impact on gene expression than the IVA protocol in 24 h exposure.