Introduction

Recent studies have proposed that the adult mammalian ovary’s oocyte-containing follicles is not definite, but rather they possess oogonal stem cells (OSCs) that provide for its renewal. Although their existence is not widely accepted by the scientific community, as it challenges the principle that the number of oocytes in a mammal’s ovaries is fixed at birth, the isolation and development promotion of such cells is specially interesting in infertility treatment procedures in women.

Materials and methods

Databases of citations and abstracts were consulted, such as Pubmed and Scopus, in search of scientific articles relevant to the subject with a high impact factor and recent publication dates in order to avoid out-dated information.

What are OSCs?

These cells were discovered due to the initial suspicion that primordial follicle cells were discordant with the rate of follicle atresia in mice ovaries [1]. Immunohistochemical analysis of mouse Vasa homologue (Mvh, also known as Ddx4), expressed exclusively in germ cells, confirmed the presence of cells in the ovarian surface epithelium. They are mitotically active, as they appear positive for 5-bromodeoxyuridine (BrdU) injection.

OSCs can be isolated from ovary tissue using a fluorescence-activated cell sorting (FACS)-based protocol using immunomagnetic beads targeting surface-expressed domain of Ddx4. It appears OSCs exhibit cell-surface expression of this protein, unlike oocytes [2].

Potential clinical applications

Injection of OSCs engineered to express GFP into mouse ovaries results in ovulation of GFP-positive oocytes

Ovulated GFP-positive oocytes can be fertilized in vitro, reaching the hatching blastocyst stage.

Human OSCs generate oocytes in xenografted human tissue

When GFP-OSCs are re-aggregated with dispersed adult human ovarian cortical tissue, large GFP-positive cells become enclosed by smaller GFP-negative cells in structures resembling follicles. When xenografted into NOD-SCID mice, after 1-2 weeks follicles containing both GFP-negative oocytes and GFP-positive oocytes can be observed.

Conclusions

Much evidence has been provided that mammals do indeed possess OSCs, there is still a long way until they are accepted, and more studies are needed to determine their exact function in the ovary. Several questions need to be answered:

- Under what mechanisms do these cells spontaneously generate oocytes in vitro?
- Why do OSCs, unlike oocytes, exhibit cell surface expression of Ddx4?
- Do these cells contribute actively to do novo neo-oogenesis in vitro to maintain follicle numbers, or are they activated only under certain circumstances?

Regardless, what is truly of interest is whether or not these cells are relevant clinically. Additional work is needed to map the exact relationship between OSC and oocyte numbers in vivo, as well as improve the efficiency of isolation.

Bibliography


Table 1. Current strategies for infertility due to different causes and advantages OSCs could offer [5]

<table>
<thead>
<tr>
<th>Current strategy</th>
<th>Age-related infertility</th>
<th>Isotrophic premature ovarian insufficiency</th>
<th>Non-isotrophic premature ovarian insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oscyte donation</td>
<td>Cryptopreservation of oocytes, embryos of ovarian tissue → involves hormonal medication, delays in treatment, risk of reintroducing malignant cells.</td>
<td>Spontaneously conceive (only 5% of cases) or oocyte donation and IVF.</td>
<td>OSC isolation, culture and use in IVF → can use one's own oocytes.</td>
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<tr>
<td>OSC isolation and proliferation → age-related anepidroblast risk unless?</td>
<td>Oscyte isolation → avoids delay in commencing life-saving treatments. No teratoma formation.</td>
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<tr>
<td>Isolated OSCs could be used in many ways to restore fertility in women [4]</td>
<td>Increase oocyte numbers to restore or enhance natural fertility</td>
<td>Return expanded OSCs to ovaries</td>
<td>5 Identification of OSC activators</td>
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