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Alice Poitrinal, Dollet Sandra, Bruno Pereira, Cécily Lucas, Mathis Lepage, Anne Sophie Gremeau, Gaëlle Marteil, Florence Brugnon

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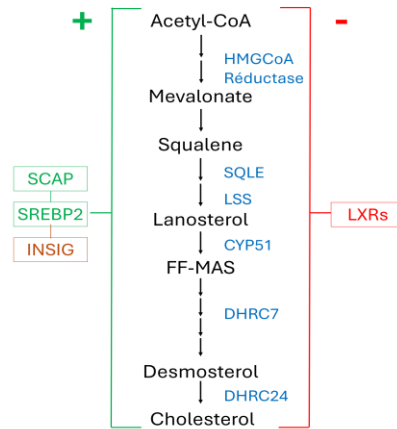
Fertility preservation for patients with breast cancer:

Altered response to ovarian stimulation and loss of cholesterol homeostasis in ovarian follicles

A. Poitral¹, S. Carlet-Dollet², B. Pereira³, C. Rodrigues¹, M. Lepage⁴, A.S. Gremeau¹, G. Marteil², F. Brugnon¹

1. Background

Breast cancer (BC) is the most common cancer among women of childbearing age. **Anticancer treatments and the cancer itself exert a deleterious impact on ovarian function.**¹ To our knowledge, no study has evaluated the impact of breast cancer on the cholesterol biosynthesis pathway in human cumulus cells, a pathway essential for **oocyte maturation and activation.**^{2,3}



Cholesterol biosynthesis pathway and its regulators

Aim of the study: To evaluate the impact of breast cancer on ovarian response to stimulation and on the cholesterol biosynthesis pathway

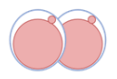
2. Materials and Methods

Since 2019, patients and oocyte donors addressed to the ART unit of Clermont Ferrand University Hospital for fertility preservation or oocyte donation have been included in this study:

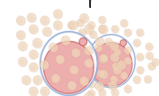
30 oocyte donors (OD, control group) < 38 yo

25 BC patients divided into subgroups according to the tumor's molecular subtype: 10 triple-negative (TN), 8 hormone receptor-positive (HR+), 7 HER2-positive (HER2+) ; < 38 yo

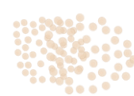
Ovarian stimulation with an antagonist protocol



Mature oocytes



Cumulo-oocyte complexes puncture



Cumulus cells

Cryopreservation for fertility preservation or oocyte donation

Expression of enzymes and regulators of the cholesterol biosynthesis pathway by RT-qPCR. Expression levels were normalized to TBP housekeeping gene

3. Results

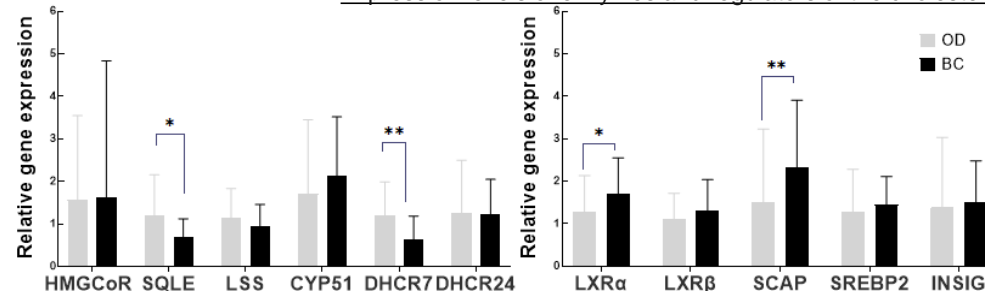
Clinical characteristics and ovarian stimulation according to the molecular subtypes of breast cancer

	OD (n= 30)	BC (n=25)	TN (n=10)	HR+ (n=8)	HER2+ (n=7)	p-value
Patient's characteristics						
Age (years)	32.1±3.8	31.9±3.7	31.6±4.1	31.9±4.1	32.2±3.2	NS
BMI (kg/m ²)	22.3±3.6	22.9±4.0	23.9±3.9	20.1±1.5	24.4±4.8	NS
Ovarian stimulation						
Total dose of FSH (IU)	1870±537	2117±798	2482±881	2241±686	1454±284	0.026 0.041
Ovarian response						
Harvested oocytes	13.7±6.6	9.6±5.3	8.9±5.9	12.0±5.6	7.9±3.3	0.004 0.028 0.009
Mature oocytes ratio (%)	82.2±16.4	73.2±27.6	70.3±31.1	79.7±24.3	70.1±28.9	NS

Data are presented as average ± standard deviation. The groups: BC, TN, HR+, HER2+; are compared to the oocyte donor group. Data that are significantly different from the OD group are presented in red and bold.

- Lower number of harvested oocytes in breast cancer patients compared to oocyte donors
- TN subgroup: lowest number of harvested oocytes despite the highest total FSH dose administered

Expression levels of enzymes and regulators of the cholesterol biosynthesis pathway



- Lower transcripts levels of *sqle* and *dhcr7* genes in breast cancer group compared to oocyte donors
- Higher transcripts levels of *scap* and *lxra* genes in breast cancer group compared to oocyte donors

4. Conclusions and perspectives

- A poorer ovarian response to hormonal stimulation is observed in breast cancer patients. The lowest ovarian response to stimulation is seen in TN patients compared to oocyte donors.
- A **dysregulation of the cholesterol biosynthesis pathway is observed in cumulus cells of breast cancer patients compared to oocyte donors** → **Might account for the deleterious impact of breast cancer on ovarian functions**
- **In perspective, a better understanding of the biological signaling pathways underlying the deleterious impact of breast cancer on ovarian function would permit to optimize fertility preservation strategies for patients according to the molecular subtype of cancer**