

THE ATRESIA DURING OOGENESIS IN MAMMALS

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Introduction

Female mammals are born with a finite stock of oocytes. During the last half of gestations at least two-thirds of the germ cells are lost, leaving a reserve of 1 to 2 million of oocytes at birth, at least in humans. This massive germ cell loss before birth is called attrition and it continues after birth and until puberty when 75% of the oocytes have been lost.

In addition, from puberty to menopause more follicles are eliminated by a process called atresia. This means that from the 400 000 follicles left only 400 are ever going to ovulate, the rest will suffer atresia.

Objective

Explain which are the most important possible molecules and mechanisms involved in the attrition and the atresia that have been find out until recently and what reasons could unravel the dramatic loss of so many cells.

Materials and methods

Research

This bibliographic research was realized thanks to several and extensive researches of articles and reviews in different scientific websites such as Pubmed and web of knowledge. The selected references were found by searching "mechanisms atresia/attrition", "atresia mammals", "attrition mammals"... Afterwards, all the papers were read and only the more interesting and relevant ones were used. The program Mendeley was used in order to create a bibliography.

Articles' materials and methods

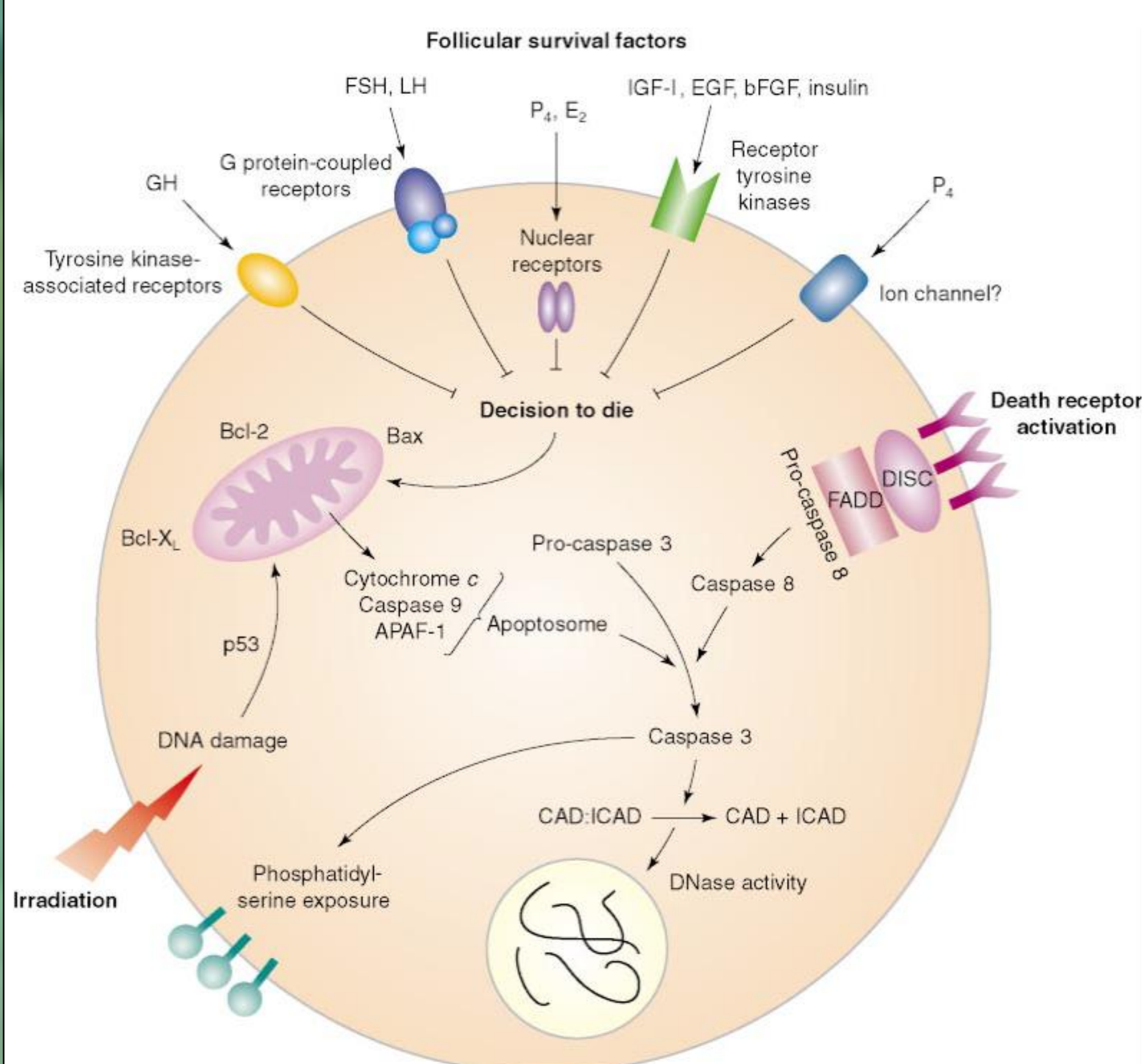
- Dissection of rat ovaries, human fetal ovaries, ovaries of healthy women...
- Detection of different proteins and nuclear markers by using techniques such as immunohistochemical and immunofluorescence staining.

Results

Mechanisms responsible of the attrition and the atresia

The following mechanisms affect both attrition and atresia:

- Bcl2/Bax rheostat: \nearrow Bax: greater numbers of oogonia, oocytes and follicles lost, \nearrow Bcl2: death susceptibility reduced.
- Availability of grow factors.



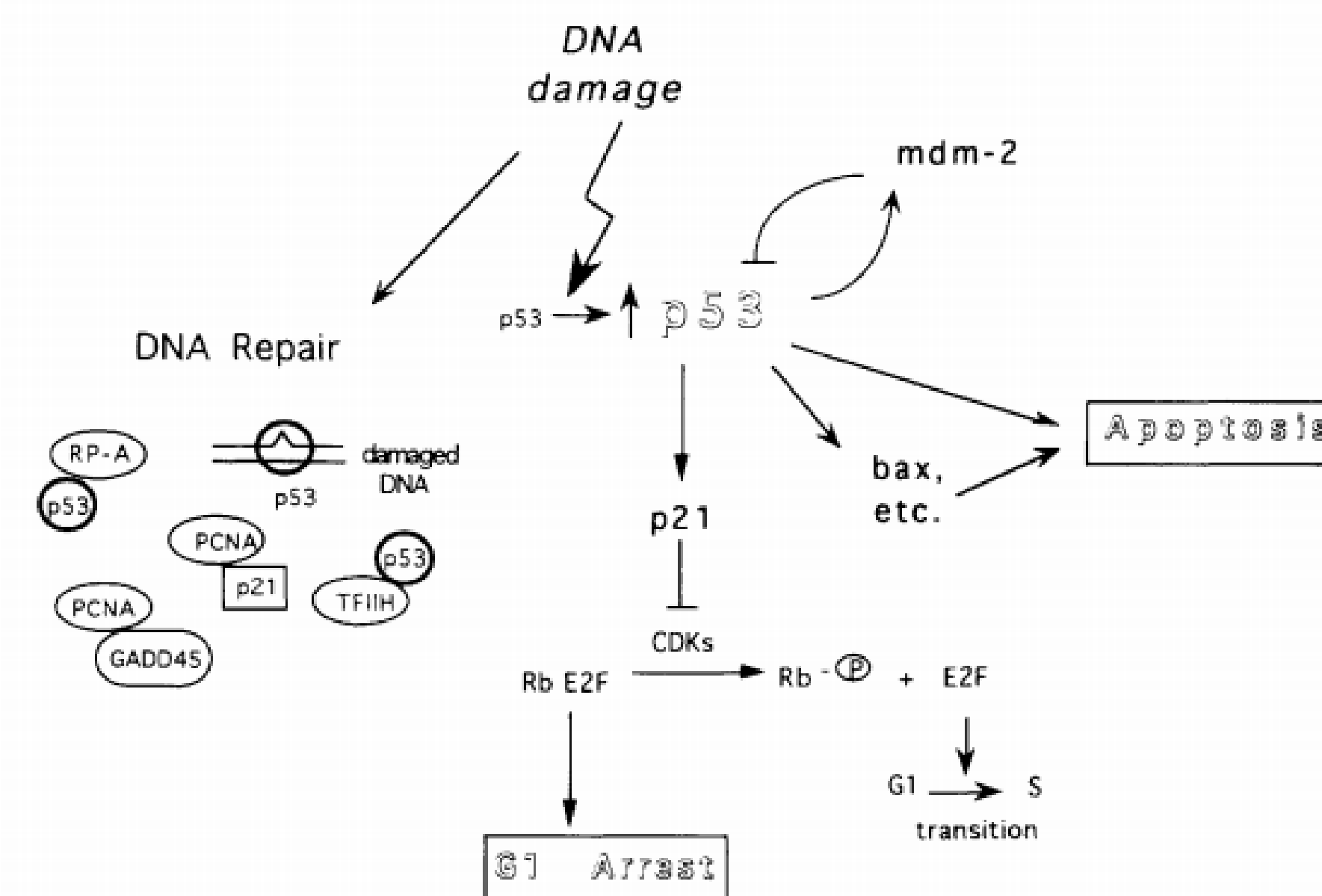
The next pathways concern only atresia:

- The anti-oxidant defense: Bcl2 inhibits and protects granulosa cells in developing follicles from apoptosis.
- Factors and hormones: if \nearrow FSH, LH, P4, E2, GH, IGF-1, EGF, bFGF and insulin: survival, if these molecules \searrow and \nearrow p53: death.
- Meiotic checkpoints: no meiotic progression when defects in chromosome recombination and/or synapsis occur.

Involved molecules

TNF family: group of cytokines whose family can cause apoptosis. The members that specifically cause atresia and are believed to have a critical role include TNF- α , Fas/Fas-Ligand (FasL) and TRAIL.

p53: anti-proliferative transcription factor that regulates the rate of transcription of various genes involved in mitosis and apoptosis. It can cause the detention of the cellular cycle in G1.



Bcl2 family: Some members of this family (Bcl2, Mcl-1 and Bcl-XL) act as inhibitors of the activation of caspases and of the apoptosis. However, others (Bax, Bcl-2-associated X protein) promote the programmed cell death.

Caspases: main effector molecules in ovarian apoptosis. They are activated in the granulosa cells by cell surface receptors and by members of the Bcl-2 family proteins.

Hypothesis of the function of the attrition

- - To guarantee that the number of oocytes matches the proper number of follicle cells as the highest rate of attrition corresponds to the entry into meiosis and primordial follicle formation.
- - Solution to the accumulation of mutation in the mitochondria.

Hypothesis of the function of the atresia

- - Atretic follicles maintain steroidogenic activity by which it would have an endocrine function in the ovary.
 - Failure of germ cells to accumulate adequate energy supplies and cytoplasmic organelles may mark them for elimination.
 - Survival of the follicles enclosing oocytes with the highest developmental potential.
 - Protective function: elimination of the follicles containing a defective oocyte with tumorigenic potential.

Conclusions

- Many mechanisms are involved in the death of the germ cells and they all seem to converge in the fragmentation of the DNA.
- Characteristics of autophagy and necrosis have been observed.
- No cell death pathway determined yet; it is not even know what stimulus exactly activates them.
- Atresia and attrition are influenced by the genetic background, extrinsic and intrinsic factors.
- The oocyte loss acts as a "quality control mechanism" which assures the selection, survival and ovulation of healthy oocytes at the expense of the unhealthy ones.

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