Ovarian cancer is the 6th most frequent and the most lethal of the gynaecological cancers; it is oestrogen dependent and it is associated with mutations in BRCA1 and BRCA2 genes. Both oestrogens and progesterone, and BRCA1 gene have important roles in the regulation of telomerase and telomeres, key structures in development and in progress in every epithelial cancer.

Ovarian cancer

Ovarian cancer is the most lethal of gynaecological cancers and the 6th most frequent. It normally does not present symptoms and for that there is not any diagnostic. In addition, it usually develops early metastasis, contributing to a high mortality.

It is related to hormones: having no child, an onset menopause or an early menarche favor the development of the disease.

On the contrary, giving birth, taking oral anti-conceptives or having tubal ligations prevent the apparition of this cancer.

Introduction and objectives

Telomeres are key structures in development and in progression in every epithelial cancer.

Genetic factors

10% of the ovarian cancers are hereditary:
- Association with tumour suppressors that act in Knudson model.
- hTERT promoter.

The most important genes are BRCA1 and BRCA2, both of them codifies proteins that repair double strand breaks (DBSs)

- BRCA1: Associated with a probability of 39% of causing ovarian cancer.
- BRCA2: Associated with a probability of 1-17% of causing ovarian cancer.

Methods

Bibliography research in PubMed and summary of all the information collected.

Writing a memory that relates all the items and briefly represent them here.

Ovarian cancer

Ovarian cancer is one of the most frequent and the most lethal of gynaecological cancers, it is hormone dependent and it is associated with mutations in BRCA1 and BRCA2 genes. It is known that oestrogens and BRCA1 have an important paper in the regulation of telomeres and telomerase, a structure and an enzyme that are deregulated in almost every epithelial cancer.

There is not an effective diagnostic, prognostic or treatment for this disease, so, the aim of these reviews is to improve this thanks to the knowledge of the importance, the implication and the regulation of telomeres and telomerase in this cancer.

Figure 1. Relationship of telomeres, telomerase, and BRCA1 or BRCA2.

Different studies suggest that oestrogens and other hormones, as progesterone or androgens, could be involved in the regulation of hTERT transcription

- Oestrogens: Studies in vitro have shown that an increment of oestrogen expression in tumour cells increases hTERT transcription. Specifically, oestrogens directly interact with the hTERT promoter because it has an imperfect oestrogen element response (ERE), it only has one nucleotide of difference with the consensus sequence of oestrogen receptor (ER): GGTCAAGTCATC / GGTCAAN3GTCAC.

- Progesterone: It has an antagonistic effect to oestrogens. It inhibits the expression of hTERT because the hormone upregulates p21, a kinase that inhibits the hTERT transcription. This way progesterone indirectly regulates hTERT expression because other studies have demonstrated that does not exist any imperfect progesterone element response (PRE) in hTERT promoter

Telomerase regulation by BRCA1

hTERT regulates the stability of telomeres, which act as a guardian of genome integrity.

Figure 2. Pubmed logo. Taken from: http://www.ncbi.nlm.nih.gov/pmc/mand

Hormonal regulation

Hormonal therapies consist in using hormones or drugs that block some hormones to heal or treat some types of cancer. In ovarian cancer there are three, but none of them are really effective, so they are not normally used.

1. LHRH antagonists: Remove the oestrogen production in the ovary.
2. Tamsulosin: It is very used in mammary cancer, it acts like an oestrogen.
3. Aromatase inhibitors: Blocks the aromatase enzyme, which can transform diverse hormones into oestrogen.

Hormonal therapy

Conclusions

It can be concluded that both telomerase and telomeres have key roles in the development and the progress in ovarian cancer. In the early stages of the disease it can be supposed that the telomeric dysfunction is fundamental for the formation of tumour cells. Moreover, it can be proved that an activation of telomerase is needed for the maintenance of telomeres that have been shortened as a consequence of multiple divisions.

In addition, it has been proved that both, oestrogens and BRCA1 gene, two factors associated with this cancer, are important regulators of telomere and telomerase, either directly or indirectly. The deregulation of oestrogens levels that occurs in ovarian cancer and mutations in BRCA1 that are associated with the disease promotes the activation of telomerase conducing to immortalization of tumour cells.

The use of techniques that analyse the telomerase activity and the state of telomeres in women with genetic predisposition for ovarian cancer could help to improve her diagnostic and even implant a screening in menopausal women. Furthermore, new studies in hormonal regulation could help to improve the therapies and with everything together decrease the mortality of ovarian cancer.

References