

Description for the general public

Ovarian cancer is the 5th leading cause of cancer-related deaths in Western countries, the second most common malignancy of the female genital tract, and the leading cause of death from gynecological cancers. Although the pathogenesis of ovarian cancer has already been well recognized there are still some issues that hamper full understanding of the complexity of events underlying this process. One of them is senescence of cancer cells, in particular the spontaneous process which is not associated with chemotherapy and/or radiotherapy.

Until recently, cellular senescence was linked exclusively with normal somatic cells, e.g. fibroblasts. Past two decades provided, however, evidence that senescence may also apply to cancer cells, especially those treated with chemotherapeutic drugs (e.g. DNA damaging agents) or radiotherapy. At the same time, the knowledge about the spontaneous form of this process is far more limited.

The aim of this project is to verify our original hypothesis that assumes that spontaneously senescent ovarian cancer cells may contribute to increased progression of the disease and/or increased tumor resistance to chemotherapy. We also hypothesize that the spontaneous senescence may have significantly different outcomes from that induced by certain drugs, which is generally considered as a tumor-inhibiting phenomenon. We believe that opposite consequences of the spontaneous and the drug-induced senescence of ovarian cancer cells may result from different mechanisms and functional phenotypes characterizing cells undergoing both these processes.

The project will consist of experiments on cell cultures (*in vitro*), laboratory animals - mice (*in vivo*) and tumor specimens obtained from patients undergoing cytoreductive surgery. The *in vitro* experiments will be conducted exclusively on a primary material, that is with cells isolated from ovarian tumors. The study will include patients with primary tumors and with peritoneal ovarian cancer metastases (subjected or not to chemotherapy). Patients with four major types of ovarian cancer, i.e. serous, endometrioid, undifferentiated, and clear-cell, will be included.

We believe that our project will improve our knowledge on factors determining the progression of ovarian cancer, in particular the role of the spontaneous and the drug-induced cancer cell senescence. Moreover, it will help to understand whether the spontaneously senescent ovarian cancer cells which as we believe exert cancer-promoting activity may be, at least partly, responsible for chemoresistance of the malignancy. We also plan to identify mediators, mechanisms and signaling pathways underlying senescence of ovarian cancer cells, which may provide targets for new anti-cancer strategies.