

## Characterization of the effects of reverse transcriptase and protease inhibitors on ovarian cells

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In Italy, every year new cases of ovarian cancer are approximately 5,000, 3,000 are the deaths; this means that 1 woman out of 70 is destined to fall ill and 1 out of 100 to die for this malignancy. Drugs of choice for the treatment of HIV, able to determine a decrease in viral load, have proven to be effective also against neoplasms (Kaposi sarcoma [1] and non-Hodgkin lymphomas [2]) frequent in subjects with acquired immunodeficiency syndrome (AIDS) that thanks to these drugs, are now in evident decline.

Our research aims to highlight and characterize, therefore, the effects of anti-HIV drug therapy on Skov3 cells (ovarian adenocarcinoma), hoping for a possible role in the control of ovarian cancer, which is not among the cancers specific of HIV infection.

Skov3 cells were cultured and then treated with the chosen drugs: abacavir, tenofovir, efavirenz, etravirine (reverse transcriptase inhibitors) and darunavir (protease inhibitor). At the cytofluorimetric analysis treated cells showed the following results: Abacavir (NRTIs) and Darunavir (PI) do not show any particular modulation of the cell cycle. Tenofovir (NtRTIs) showed an increase amount of cells in the G0/G1 phase of the cell cycle progression. Instead Efavirenz (NNRTIs) and Etravirine (NNRTIs) showed a block in the G0/G1 phase. Between the two drugs of the same class (NNRTIs) the block activity of Etravirine in G0/G1 of cell cycle is higher as compared to Efavirenz; at the same time, Etravirine determines the differentiation of Skov3.

DAPI staining has allowed the identification of DNA damage in cells treated with efavirenz and an increased condensation of DNA in cells treated with etravirine. After treatment with tenofovir, efavirenz and etravirine, in Skov3 cells, we observed through immunoblotting: reduction of cyclin D1 concentration, hypophosphorylation of Rb and increase of p21 concentration. Only Skov3 cells treated with etravirine showed high levels of E-cadherin expression.

Reverse transcriptase, based on these data, can be considered an epigenetic regulator of cell proliferation and differentiation and may represent a new target in cancer therapy. Furthermore, we believe that the drugs used, modulating cell proliferation and differentiation, may represent a new frontier in the development of a therapeutic approach to ovarian cancer.

### References

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### Keywords

Ovarian cancer, anti-HIV drugs.