MATERIALS AND METHODS

Docetaxel inhibits proliferation of MCF-7 cells in a dose dependent manner. Melatonin enhances the tumors and enhances the efficacy of cancer chemotherapy. However, little is known about the effects of Melatonin on gene expression of breast cancer cells. In the present study, we demonstrate the modulatory effect of melatonin on the expression of tumor suppressor genes p53 and p21, CDH13, BAX, BAD, BCL-2, MUC1, GATA3 and MYC in MCF-7 cell line treated with docetaxel (1 µM) and/or melatonin (1 nM). Melatonin pretreatment consisted in addition of melatonin (1 nM) 24 hours prior to other treatments. Melatonin pretreatment for 24 hours prior docetaxel also enhanced the pro-apoptotic effect of this chemical agent.

HYPOTHESIS AND OBJECTIVES

Melatonin is an oncostatic agent that reduces the growth and development of hormone-dependent tumors and enhances the efficacy of cancer chemotherapy. However, little is known about the effects of melatonin on gene expression of breast cancer cells. In the present study, we demonstrate the modulatory effect of melatonin on gene expression of breast cancer cells. Therefore, using ER+ MCF-7 breast cancer cells as a model, the objectives of this work were:

1. To establish the changes in gene expression induced by docetaxel.
2. To verify if melatonin is able to modulate those changes.
3. To check if melatonin potentiates the antiproliferative effects of docetaxel.
4. To test the ability of melatonin to further stimulate the apoptosis triggered by docetaxel.

RESULTS AND DISCUSSION

Table 1: Gene expression profiling (RT2 Profiler PCR array). Up and down-regulated genes (more than 2 fold change) when MCF-7 cells were treated with docetaxel (1 µM) and/or melatonin (1 nM).

Figure 2: Effects of docetaxel dose on MCF-7 cell proliferation. Cells were treated with docetaxel at different concentrations for 3 days. Data are expressed as percentage of the control group (mean ± SEM).

Figure 3: Potentiation of docetaxel-induced growth inhibition by melatonin. Effects of docetaxel (1 nM, 0.1 nM) and/or melatonin (1 nM) on MCF-7 cells proliferation after 6 days of culture. Data are expressed as percentage of the control group (mean ± SEM).

Figure 4: Potentiating effect of melatonin on docetaxel-induced apoptosis in MCF-7 cells. A) Representative dot-plots showing viable cells (Annexin-IP+/PI-) and early apoptotic cells (Annexin-IP+/PI+). B) Histograms showing percentages of each population. Values are presented as means ± SEM.

CONCLUSIONS

1. Docetaxel induces changes in gene expression of transcription factors, tumor suppressor, adhesion, proapoptotic and cell cycle related genes in MCF-7 cells. Melatonin seems to modulate those changes according with its previously well established oncostatic and antitumoral actions.
2. Docetaxel inhibits proliferation of MCF-7 cells in a dose dependent manner. Melatonin enhances the antiproliferative effects of subpharmacological doses of this agent.
3. Melatonin enhances the pro-apoptotic effect of docetaxel in MCF-7 cells, improving the tumor killing efficacy of this chemotherapeutic agent.
4. In summary, melatonin may benefit breast cancer patients who are receiving docetaxel and might have a potential to be an excellent adjuvant for chemotherapy treatments currently used in breast cancer.

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