**Systemic Chemotherapy induces Genomic Instability in the Blood Cells of Breast Cancer Patients and the Development of *in vitro* Model to Asses the Genomic Instability in Human Cell Lines**

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Systemic chemotherapy is an important part of breast cancer treatment. This present study was conducted to evaluate whether systemic chemotherapy could produce microsatellite instability (MSI) in the peripheral blood mononuclear cell fraction of breast cancer patients and also aimed creating an in vitro model to evaluate the induction of MSI by alkylating agents on lymphocytes (Lyn). We studied 119 sequential blood samples from 30 previously untreated breast cancer patients before, during and after chemotherapy. For comparison, we also evaluated 20 healthy women (control group). The in vitro model consisted of exposure Lyn and MCF-7 for 30 minutes with two treatments (melphalan and melphalan+amifostine-cytoprotectant agent). We evaluated the commitment of mismatch repair system (MMR) and MSI. We observed MSI in at least one sample. We found a significant correlation between the number of MSI events per sample and chemotherapy with alkylating agents ($P < 0.0001$). In culture cells (Lyn), the treatment with melphalan decreased the expression of hMSH2 protein and MSI was also verified. but not when treated with amifostine. Conclusions: 1) Systemic chemotherapy may induce genomic instability in peripheral blood mononuclear cells from breast cancer patients receiving alkylating agents, possibly mediated by a decrease in hMSH2 expression induced by chemotherapy. 2) Findings in the in vitro model may help to explain the generation of genomic instability and chemioresistance during the treatment and furthermore, contributes to indicate the addition of cytoprotectants agents to prevent such genomic instability.

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