Cancer Research

Poster Session Abstracts

Breast Cancer Patients Receiving Neoadjuvant, Adjuvant and Palliative Chemotherapy Have Different DNA Oxidative Damage and Repair Profiles.

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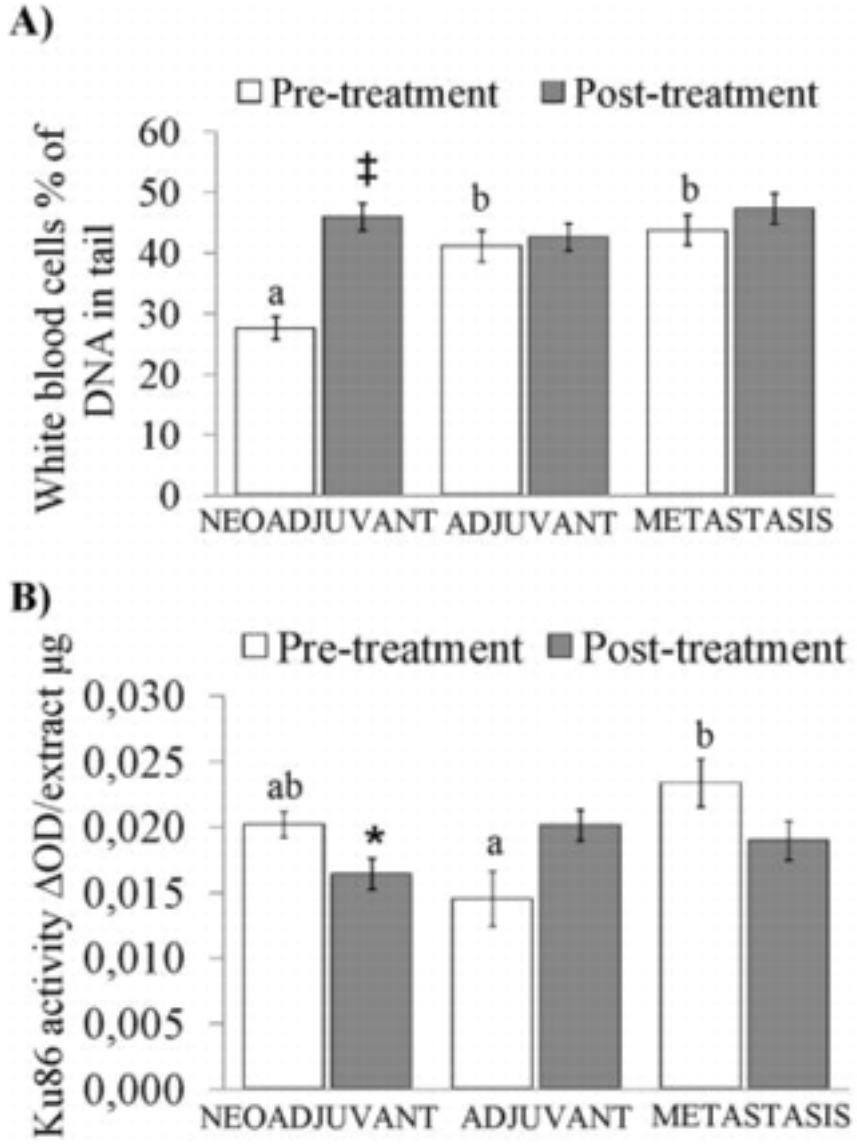
DOI: 10.1158/0008-5472.SABCS-09-1123 Published December 2009

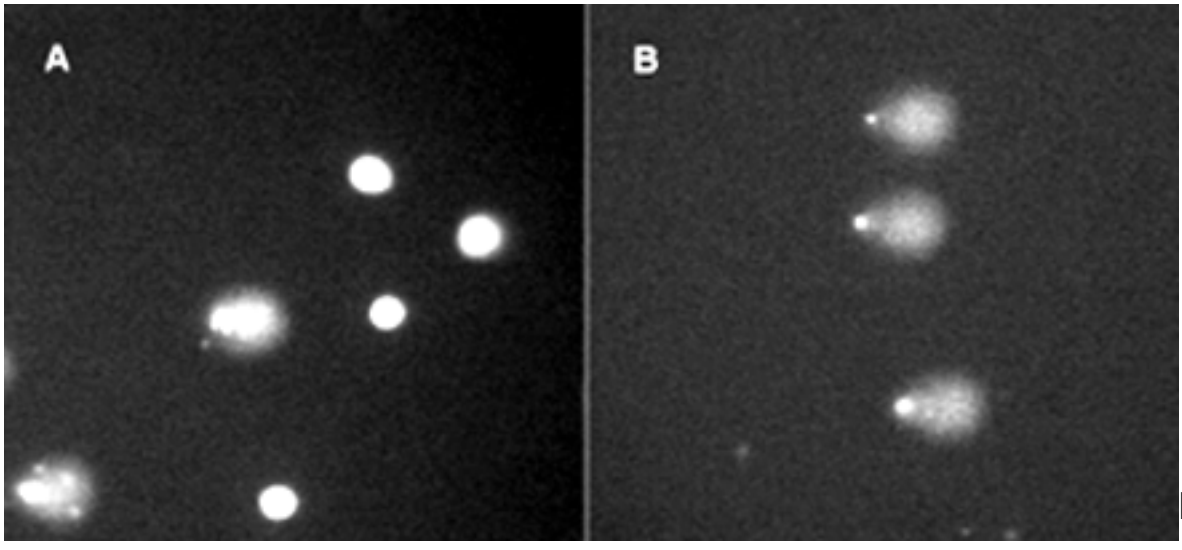
Abstracts: Thirty-Second Annual CTRC-AACR San Antonio Breast Cancer Symposium-- Dec 10-13, 2009; San Antonio, TX

Abstract

Background: Antineoplastic agents induce oxidative stress in biological systems leading to lipid, carbohydrate, protein and DNA damage and affecting cell structure and function. These adverse effects may fuel up the acquisition of new mutations and the development of treatment resistances and secondary malignancies.Methods: We selected 90 breast cancer patients receiving neoadjuvant, adjuvant or palliative chemotherapy, to test the effect of this treatment on the systemic oxidative stress. The patients were distributed in equal groups and paired blood samples, before and after chemotherapy, were extracted. DNA oxidative damage was assessed by alkaline comet assay and a specific inmnoenzymoassay was employed to determine RPA and Ku86

DNA repair activity.Results: We found that neoadjuvant patients presented a marked raise in DNA damage after chemotherapy (Figure 1A). DNA repair activity of KU86 was significantly higher in the adjuvant setting and significantly lower in the neoadjuvant and metastatic settings after chemotherapy. Before chemotherapy administration, KU86 activity was higher in the metastatic and neoadjuvant groups compared to the adjuvant group (Figure 1B).





Discussion: Our results show that chemotherapy induces the production of free radicals to an extent that causes a severe DNA damage. High levels of DNA damage are maintained along

successive clinical interventions, due to continued production of free radicals during breast cancer treatment, despite the activation of the repair mechanisms that are not sufficient to overcome the effects of the oxidative stress at this level. Our work shows that breast cancer treatment affects the redox status of the patients and, because of its effects into cellular signaling pathways and gene expression, it must be considered as a potential therapeutic target to improve breast cancer treatment and minimize the associated toxicity.Figure legend 1.- Oxidative DNA damage and DNA repair markers in neoadjuvant, adjuvant and metastatic patients, before and after chemotherapy. (A) Percentage of DNA in the tail of lymphocytes, as measured by comet assay. (B) DNA repair activity of KU86. Intragroup statistical differences owed to chemotherapy are indicated as ‡ (*P<0.*001) or * (P<0.05). Intergroup statistical differences for each period (before and after chemotherapy) (P<0.05) are indicated by the letters a and b, in such a way that the measures with different superscript letters, are statistically different.Figure legend 2.- Fluorescent microscope images of damaged lymphocytes from a neoadjuvant patient before (A) and after (B) chemotherapy.

Citation Information: Cancer Res 2009;69(24 Suppl):Abstract nr 1123.

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Volume 69, Issue 24 Supplement
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