The synthetic peptide CIGB-300 inhibits nuclear factor κB (NF-κB) traslocation affecting the survival and chemoresistance of human lung cancer cells.

Cirigliano SM[1], Díaz Bessone MI[1], Flumian C[1], Berardi D[1], Perea S[2], Bal De Kier Joffé E[1], Farina H[3], Todaro L[1], Urtreger A[1]

[1]Institute of Oncology "Ángel H. Roffo", CABA/Argentina. [2]CIGB, Havana / Cuba. [3]UNQ, Bernal / Argentina.

INTRODUÇÃO. The protein-kinase-2 (CK2) is involved in cell proliferation, survival and apoptosis. CIGB-300 is an antitumor peptide that binds CK2 substrates preventing the enzyme activity.
NF-κB activation can reduce chemotherapy efficiency in lung cancer. We have determined that CIGB-300 inhibits NF-κB (p65) nuclear translocation. Also, CIGB-300 alters the ability of lung cancer cells to grow in a three-dimensional spheroid model. **OBJETIVO:** To study the treatment efficiency of cisplatin with CIGB-300 and its effect on p65 nuclear levels. To determine proteasome activity after CIGB-300 treatment, given that NF-κB stability is regulated by proteasome-selective proteolysis. To analyze whether CIGB-300 affects spheroid compact structure, that resembles in vivo avascular tumors. **MATERIAL E METODOS:** A cisplatin resistant cell line (A549-Rcisp) was developed by chronic administration during six months. Proteasome-selective activity was assessed with Proteasome-Glo™ Assay (Promega). Biotin-labeled CIGB-300 was used to treat NCI-H125 spheroids at different time points and detected by immunohistochemistry. **DISCUSSÃO E RESULTADOS**: Nuclear p65 levels were highly increased after treating human NCI-H125 cells with cisplatin (Western blot). Moreover, when cells were treated with cisplatin plus CIGB-300, NF-κB activation was abolished. Remarkably, in a chemoresistant setting, A549-Rcisp cells showed an increase in CIGB-300 sensitivity compared with the parental cell line ($p<0.01$). Moreover, only A549-Rcisp showed increased p65 nuclear levels after cisplatin treatment, suggesting that both cisplatin resistance and CIGB-300 sensitization might be linked to NF-kB.
Surprisingly, we observed increased proteasome activity after 30 minutes of CIGB-300 treatment. Thus, proteasome complex is a newly identified target of CIGB-300.
Finally, we observed effective penetration of CIGB-300 into NCI-H125 spheroids, beginning after 5min of treatment and reaching the spheroid core at 60min. **CONCLUSAO:** Our results show that CIGB-300 negatively modulates malignant progression-related characteristics through different signaling pathways. Moreover, its improved effectiveness in a chemoresistance model associated with NF-κB inhibition indicates that CIGB-300 may become a new strategy for lung cancer treatment.

Palavra chave: CIGB-300, CK2, NF-κB