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The combination Astemizole-Gefitinib as a novel and promising therapy for human lung cancer: *In vitro* studies

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Lung cancer is a major cause of cancer mortality. Thus, novel therapies are urgently needed. Repositioning of old drugs is gaining great interest in cancer treatment. Astemizole is an antihistamine proposed to be repositioned for cancer therapy. This compound targets several molecules involved in cancer including histamine receptors, ABC transporters and the potassium channels Eag1 and HERG. Astemizole inhibits the proliferation of different cancer cells including those from cervix, breast, leukemia and liver. Gefitinib is widely used to treat lung cancer, however, no response or resistance to gefitinib occurs in many cases. Here, we studied the combined effect of astemizole and gefitinib on the proliferation, apoptosis and gene and protein expression of Eag1 channels and aquaporins (AQPs) in the human lung cancer cell lines A549 and H1975. Cell proliferation was assayed by the MTT method and apoptosis by flow cytometry. Gene and protein expression were assessed by real time PCR and immunocytochemistry, respectively. We obtained the IC20 and IC50 for each drug from the cell proliferation experiments. Drug combination at their IC20 reduced cell proliferation in more than 80%. Apoptosis was increased by the combination in comparison to the effect of each drug alone. Eag1 mRNA levels were decreased by the combination in A549 cells while AQP5 mRNA levels were decreased by the combination in both cell lines. Astemizole induced sub-cellular localization changes in A549 cells. These *in vitro* studies suggested that the combination astemizole-gefitinib may be a novel treatment option for lung cancer patients.

Biography

Javier Camacho has studied Ion Channels involved in Cancer for almost 20 years. Several patents have been filed based on the findings of his group. He focuses his research in finding early tumor markers and novel therapeutic targets for cervical, liver and lung cancer. He studies ion channel gene and protein expression in human cell lines, *in vivo* cancer models and human biopsies. His group also investigates the effect of ion channel blockers on the proliferation of human cell lines, primary cultures from human biopsies and the preventive and therapeutic effect of such blockers on tumor development *in vivo.*

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