ABSTRACT BOOK
TXA1.HCl induces autophagy in NCI-H460 cells and reduces the growth of these lung cancer cells xenografted in nude mice

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Modulation of autophagy has been emerging as a potential therapeutic strategy in many diseases, including cancer [1]. Our previous work has identified a hit molecule, named TXA1, from the CEQUIMED-UP library which is a potent inducer of autophagy in a melanoma cell line (submitted for publication). The soluble version of this molecule, TXA1.HCl, was also shown to induce autophagy in other cancer cell lines (work in preparation).

The present work aimed at: i) understanding the mechanism of action of TXA1.HCl in a lung cancer cell line; and ii) investigating its in vivo toxicity and the antitumour activity in xenographs of a human tumour lung cancer cell line in nude mice.

TXA1.HCl decreased NCI-H460 viable cell number and modulated cellular autophagy. Results from gene expression analysis with DNA microarrays of cells treated with of this molecule indicated that the compound induced significant alterations in the expression of genes involved in lipid metabolism. These results are currently being confirmed by qRT-PCR. Interestingly, autophagy has already been associated with the regulation of lipid metabolism in cancer [2, 3]. Importantly, sub-cutaneous injection of this compound into nude mice did not cause toxicity to mice and significantly decreased tumour growth of NCI-H460 cells xenografts.

In conclusion, this ongoing work shows the potential of this hit molecule as a modulator of autophagy, and possibly of lipid metabolism, in tumour cells. Future work will allow confirming the mechanism of action by studying the tumours removed from the treated mice in comparison with the non-treated controls.

REFERENCES:

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