Sensitization of tumor cells by gene therapy with cyclophosphamide

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Currently, due to the chemotherapies lack of specificity and efficacy that cause several side effects, new targeted therapies are thus developed. Among these, we study a gene directed enzyme pro-drug therapy which allow the direct CYP2B6 transfer into cancer cells. This enzyme is able to convert cyclophosphamide into cyto-toxic metabolites (phosphoramide mustard) directly in tumor site. Two vectors can be used to target cancer cells, the first one is lentivirus and the second one is mesenchymal stem cells, which are known to be attracted by microenvironment tumor. We have tested this strategy on three cancer cell types and demonstrated that the first strategy with lentivirus is not efficient to kill all cancer cell types. Indeed, breast cancer cell lines are not sensitive to CPA after transduction with lentivirus. In opposite, all tested cancer cell types are sensitive to CPA in presence of MSC. Therefore, our results show that MSC strategy is more efficient than lentivirus. Moreover, first in vivo studies confirm MSC efficiency as a vector for CYP2B6TM-RED transgene and enable to consider it for a new anti-cancer therapy.

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