Novel therapeutic approaches for EGFR-mediated drug delivery using engineered peptides in anaplastic thyroid cancer

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Anaplastic thyroid carcinoma (ATC) represents the most aggressive and deadliest thyroid cancer in humans, presenting a high proliferative and metastatic potential. Mostly affected signaling pathways in ATC are those of MAP kinase and PIP3/AKT/mTOR. The median survival of patients with ATC is of about 4 months after diagnosis and the mortality rate attains almost 100%. Currently, there is no cure for this cancer, which is highly invasive and resistant to conventional therapies. Accordingly, targeted therapies and delivery, such as those studied in the present work, should be considered to improve the prognosis of patients. Our targeted therapy aims to inhibit the PI3K/AKT/mTOR signaling pathway, thereby inducing apoptosis of target cells with a therapeutic peptide (TP) developed in our laboratory. The epidermal growth factor receptor (EGFR) is commonly studied in oncology as it is overexpressed in cancer cells and is actively investigated in the framework of receptor-mediated drug delivery. Therefore, an EGFR-targeted peptide (vector peptide, VP) was also developed by our group and coupled to TP in a peptide complex (PC) to enable the specific drug delivery to ATC cells. Our results show that EGFR is overexpressed and overactivated in ATC. VP is endocytosed independently of the EGF presence and without activating the EGFR. Within cells, VP is colocalized with EGFR, following its trafficking pathway. Moreover, 10 µM of PC induces cell apoptosis after 1h of incubation. To conclude, our studies confirmed that VP is a good EGFR-targeting candidate to deliver TP to cancer cells. In addition, this VP is able to induce endocytosis of EGFR and thus to deliver TP intracellularly to induce apoptosis.