Abstract

“Delivery of a drug molecule to thyroid cancer cells via EGFR targeting”

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The anaplastic thyroid carcinoma (ATC) is the most aggressive thyroid cancer and is characterized by a high mortality rate, occurring within 2-6 months from diagnosis. The current systemic treatment is based on conventional therapies. New molecular targeted therapies are explored and are aimed to limit the systemic effects [1,2].

Our strategy consists of bringing a PIP3-targeted therapeutic peptide (TP) (PIP3-P2 and P3 peptides) directly into the thyroid cancer cells thanks to a vector peptide (VP) targeted to EGFR (EGFR-P5 and P20 peptides). The TP and VP peptides were identified using the phage display technology.

The binding of VP to their target was evaluated by immunohistochemistry on biopsies of ATC, subsequent to the validation of total and phosphorylated EGFR expression on the same cases. The staining of these biomarkers is important on all cases, which confirms the receptor overexpression and overactivation in ATC. The staining obtained with peptides is similar, which suggests their good specificity and affinity. Detection of total and phosphorylated EGFR on ATC cells (8505C) by immunofluorescence confirmed that peptides bind the receptor and act as non-competitive antagonists of EGF.

To evaluate the binding of TP to their target, they were detected on several cases of ATC. Before confirming their binding, the presence of PIP3 and phosphorylated AKT was validated by an important staining on all these cases, revealing their overactivation. The labelling observed with peptides is comparable to that of PIP3, suggesting that peptides bind this biomarker with good affinity and specificity. Aiming to evaluate the therapeutic efficacy of these peptides, apoptotic cell death was demonstrated by the immunofluorescent detection
of activated caspase 3 on 8505C cells.

Finally, the most promising TP and VP were coupled via streptavidin and their efficacy was assessed by the detection of activated caspase 3 on 8505C cells. This peptide combination appears as promising since the mortality rate was 100% and the labelling was more localized implying that the VP delivers TP directly into the ATC cells.

REFERENCES