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

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Introduction

Anaplastic thyroid cancer (ATC):
- The most aggressive thyroid cancer in humans [1]
- High mortality rate (2-6 months from diagnosis)
- Treatment: conventional therapies
- Need for new molecular targeted therapies

The strategy consists of bringing a PIP3-targeted therapeutic peptide (TP) directly into the thyroid cells thanks to a vector peptide (VP) targeted to EGFR.

Materials and Methods

Phage Display: A phage display library of randomized linear dodecapeptides fused to the pIII proteins of the M13 bacteriophage capsid was screened against EGFR and PIP3.

Immunohistochemistry (IHC): The total and phosphorylated EGFR expression, the presence of PIP3 and phosphorylated AKT and the binding of VP and TP to the target were confirmed on ATC biopsies by immunohistochemistry.

Materials and Methods

Immunohistochemistry validation of EGFR expression and EGFR targeted peptides (PS and P20) on ATC biopsy sections

Results

Immunohistochemistry validation of EGFR expression and EGFR targeted peptides (PS and P20) on ATC biopsy sections

Detection of EGFR by Immunofluorescence in ATC in the absence and presence of peptides P5 and P20

Detection of activated caspase-3 by immunofluorescence in ATC in the presence and absence of peptide EGFR-P5 (VP) coupled to PIP3-P2 (TP) via streptavidin (St-PIP3-P23-EGFR-VP3)

Conclusions & Perspectives

Vector Peptides bind the extracellular domain of EGFR and act as non-competitive inhibitors of EGF (i.e., they are not competitive inhibitors as determined by ELISA; data not shown). This effect suggests their good specificity and affinity.

The coupling of VP to TP 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:

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