Targeted therapy and delivery of therapeutic agents to anaplastic thyroid cancer

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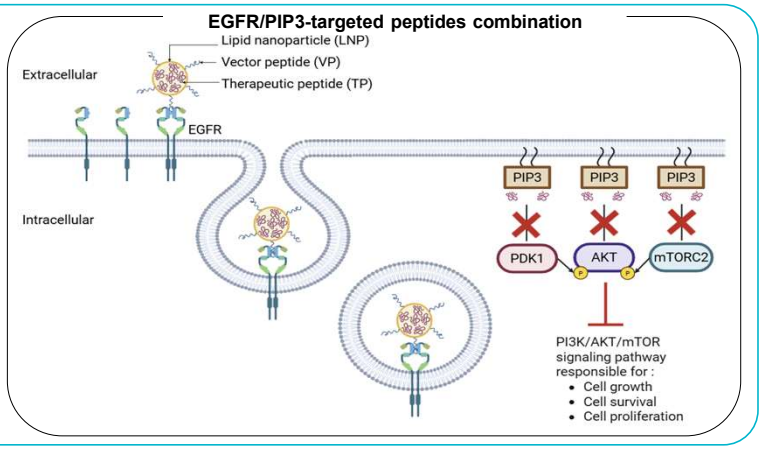
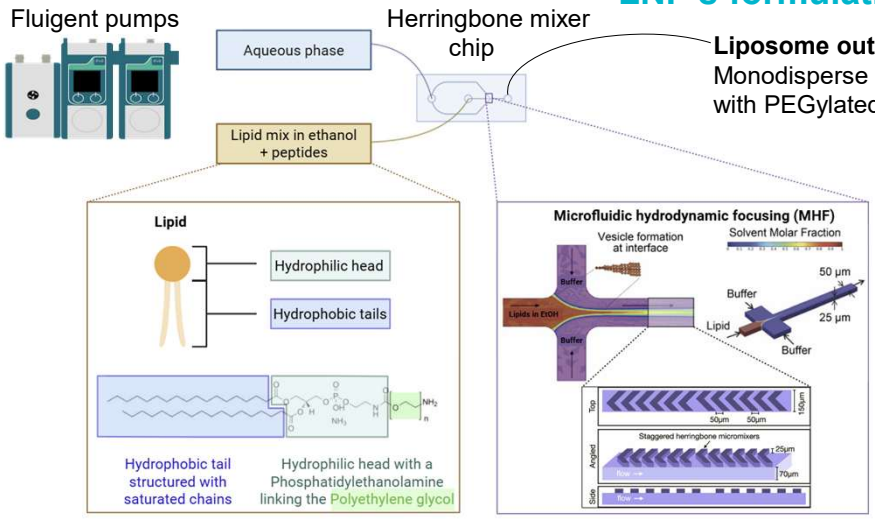
Introduction

Anaplastic thyroid carcinoma (ATC) is the most aggressive and deadliest thyroid cancer. It accounts for 39% of thyroid cancer-related deaths while concerning only 1-2% of all thyroid cancer. The inefficiency of conventional therapy led our team to explore a targeted therapy strategy. A **lipid nanoparticle (LNP)** formulation encapsulating the **therapeutic peptide (TP) targeting PIP3**, thus blocking the PI3K/AKT/mTOR signaling pathway to prevent cancer cells from evading apoptosis. At its surface, the grafted **vector peptide (VP) targets the epidermal growth factor receptor (EGFR),** which is overexpressed in cancer and capable of endocytosis. Thanks to the VP, the TP is specifically delivered to ATC and causes apoptosis.



Methods and Perspectives

LNP's formulation



Inspired by Yu Cheng, et al., Lab Chip,2024,24,4679, DOI: 10.1039/d4lc00380b

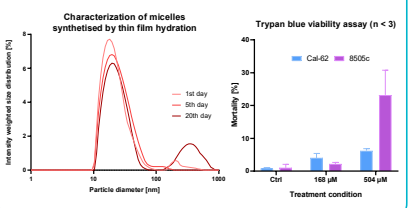
Liposome output
Monodisperse liposome (≈100 nm) collected downstream, lipid bilayer with PEGylated surface

Hydrodynamic Focusing
The lipid stream is narrowed by lateral aqueous flows, creating a controlled ethanol dilution interface

Liposome self-assembly
Lipids reorganize into bilayers during rapid ethanol diffusion, forming vesicles

Preliminary results

Preliminary results:
Monitoring over time of micelle stability and viability of thyroid cancer cell line with empty micelle treatment

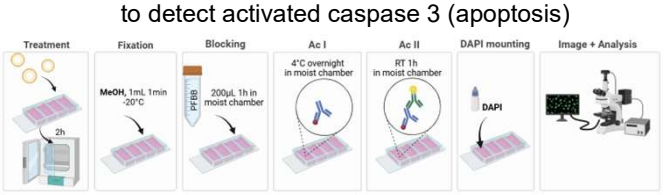


Perspective of stability assessment and *in vitro* assays

① Optimize LNP formulation in distilled water :
- PEGylated phospholipid ratio
- Flow Rate Ratio of aqueous and lipid phase impacts particle size

② Monitoring of the stability over time in a complex medium at 37°C (DLS measurement):
Two thyroid cancer cell lines (8505C and Cal-62) → Two cell culture media to test (RPMI and DMEM)

③ Immunofluorescence after 2h treatment with the formulation to detect activated caspase 3 (apoptosis)



Conclusions

- **EGFR/PIP3-targeted peptides combination** demonstrates **intracellular uptake** in ATC cancer cells and **anti-tumor activity.**
- The prospect of my project is to optimize the formulation of this therapeutic strategy to **concentrate the TP**, **extend bioavailability**, and **reduce side toxicity**.

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