Lipid Nanoparticle-based delivery of peptide-based therapeutic agents to anaplastic thyroid cancer

[1]Rachel Baillif, [1]Zehra-Cagla Kahvecioglu, [1]Juliette Ninane, [1]Nilay Yesilbas, [1]Chloé Millaire, [1]Thomas Vangijzegem, [1]Dimitri Stanicki, [3]Sven Saussez, [1,2]Sophie Laurent, [1]Carmen Burtea

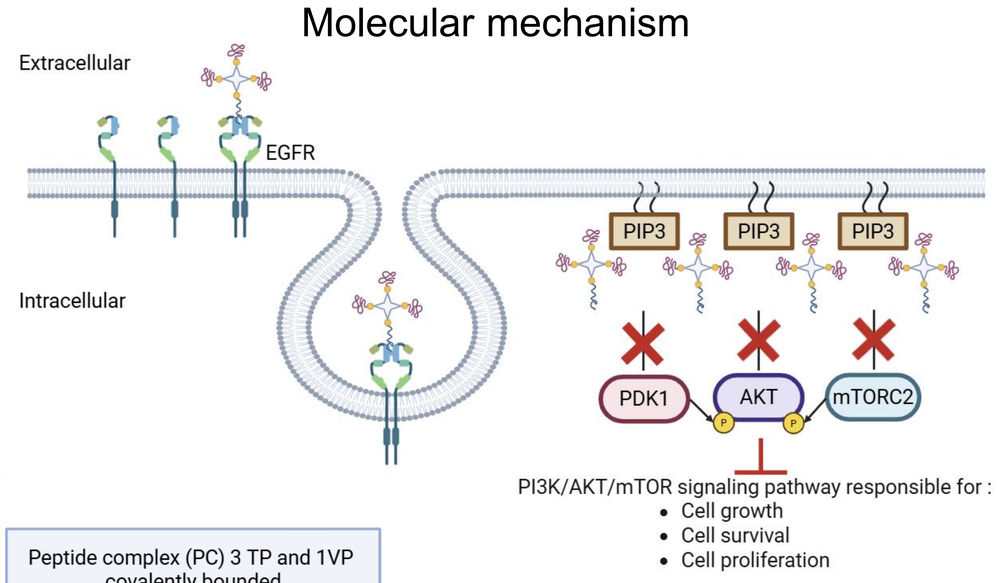
[1] General, Organic and Biomedical Chemistry Unit, NMR and Molecular Imaging Laboratory, Faculty of Medicine, Pharmacy and Biomedical Sciences, University of Mons, B-7000 Mons, Belgium
[2]Center for Microscopy and Molecular Imaging (CMMI), Charleroi, Belgium
[3]Human Anatomy and Experimental Oncology Unit, Faculty of Medicine, Pharmacy and Biomedical Sciences, University of Mons, B-7000 Mons, Belgium

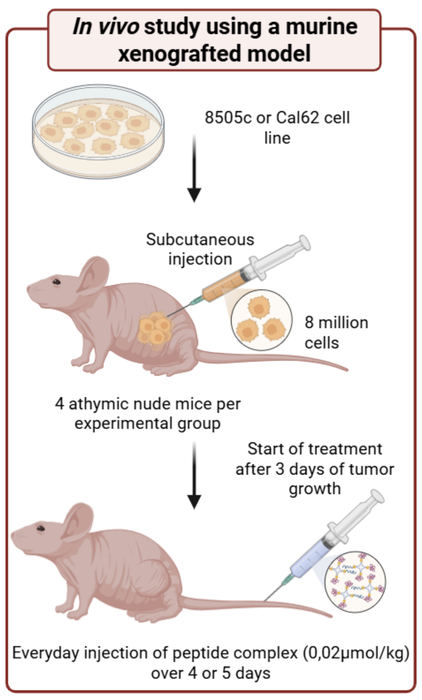
Introduction

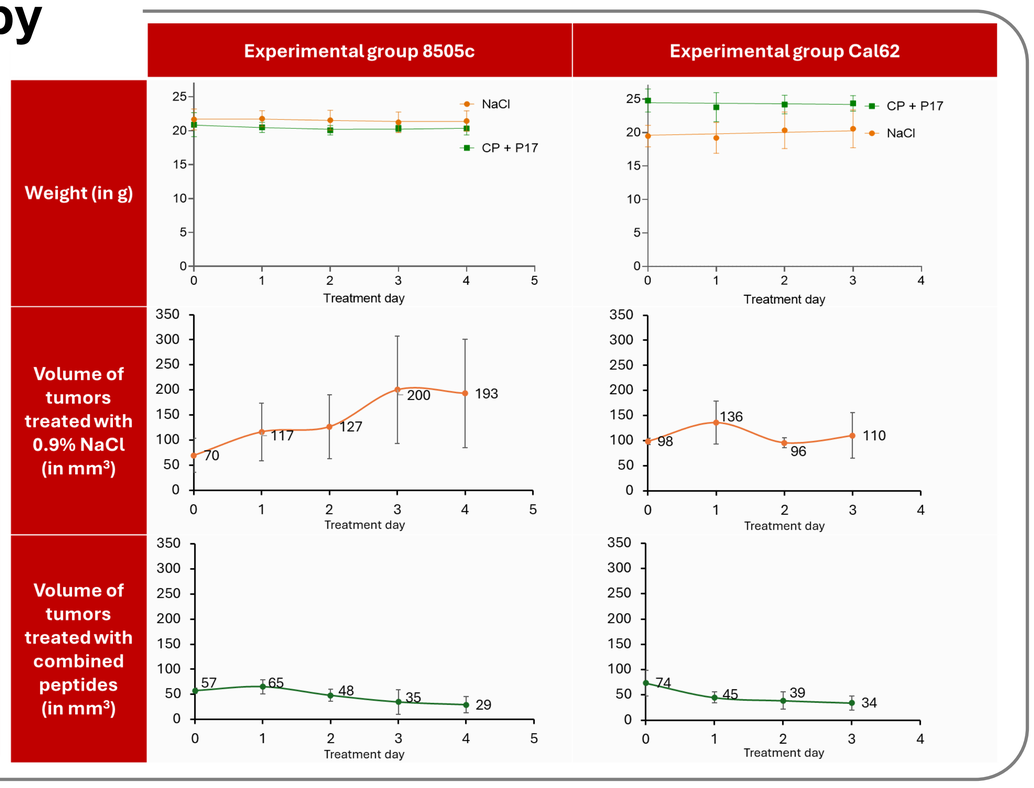
Peptide-based targeted therapeutics show promise but are limited by ***in vivo* instability and low bioavailability**, resulting in a short half-life. **Two peptides** identified in our lab, once combined (peptide complex, PC), display **anti-tumor efficacy in anaplastic thyroid carcinoma (ATC)**, the most aggressive thyroid cancer type. The therapeutic peptide targets PIP3, blocking the **PI3K/AKT/mTOR pathway** to prevent cancer cell resistance to apoptosis. The vector peptide targets EGFR, overexpressed in cancer cells and capable of endocytosis, enabling targeted delivery. This combination showed promising results in ATC cells. To overcome peptide limitations, we are currently optimizing **lipid nanocarrier** formulation by microfluidic or thin film hydration to encapsulate the therapeutic peptide. **Liposomal drug delivery systems** are already used in approved cancer therapy to improve pharmacokinetics and minimize systemic toxicity.

Proof of concept and preliminary results

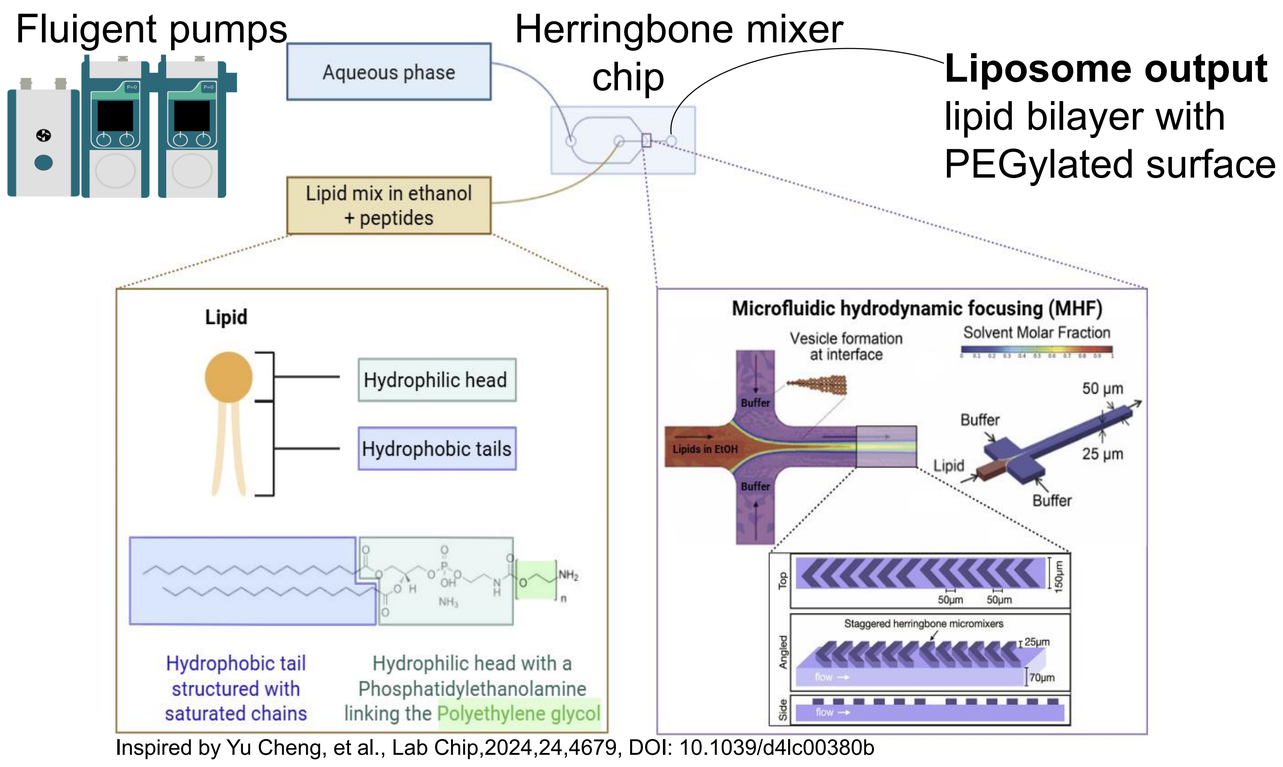
Peptide for targeted therapy







Lipid nanoparticles



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

Lipid mixture in the organic phase

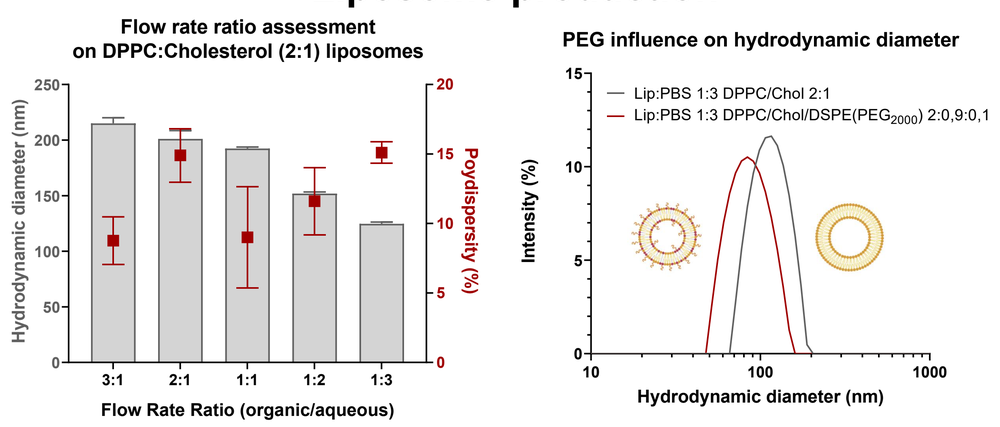
Lipid	Ratio
DPPC*	2
Cholesterol	0.9
DSPE-PEG$_{2000}$**	0.1

*DPPC: Dipalmitoylphosphatidylcholine
**DSPE-PEG: Distearoylphosphatidylethanolamine-polyethylene glycol

Microfluidic parameter

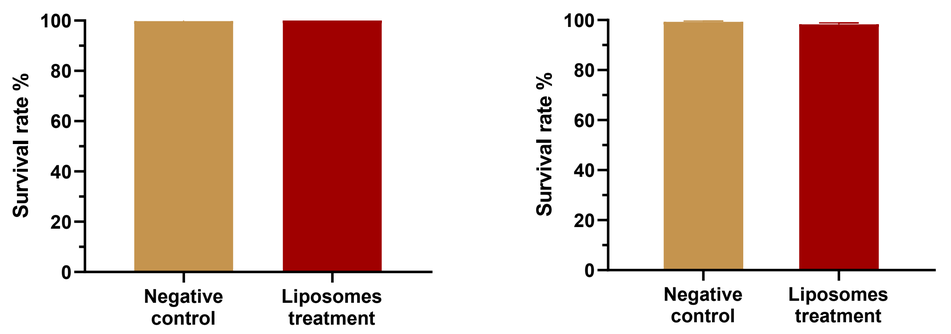
Flow Rate Ratio	1:3 (organic/aqueous)
Total flow rate	1 ml/min
Aqueous phase	PBS
Organic phase	Lipids in ethanol

Liposome production



- Microfluidic parameters validated on DPPC/cholesterol liposomes
- PEGylated liposomes synthesis carried out with a 1:3 flow rate ratio

In vitro viability tests



Conclusions

- The complex combining **EGFR/PIP3-targeted peptides** demonstrates **anti-tumor activity** assessed *in vivo*.
- The prospect of my project is to optimize the formulation of this therapeutic strategy to **concentrate the TP**, **extend bioavailability**, and **reduce side toxicity** with a **lipid-based nanocarrier** strategy.

Acknowledgment: This work was performed with the financial support of the Actions de Recherche Concertées of the University of Mons