**Delivery of anticancer peptides combined to mild-photothermal therapy for improved cancer treatment.**

**Context**

Today, cancer is one of the leading causes of death. Current treatments involve mostly chimio- and radiotherapies but they lack specificity and cause damages to healthy tissues. Anticancer peptides (ACPs) are short polycationic peptide sequences, typically produced by microorganisms, that have anticancer properties via membrane disruption, pore formation or metabolisms disfunction. The efficiency of ACPs can be enhanced when combined to mild photothermal therapy (PTT) using plasmonic nanomaterials. Mild PTT (<45°C) is safer for healthy tissues than traditional PTT (>60°C). Combining ACPs delivery and mild PTT could thus be a promising strategy for specific and safe cancer treatments. Cancer cells overexpress various biomolecules such as enzymes. This dysfunction in their metabolism can be used for targeted therapy.

**Objective**

The goal of this project is to use plasmonic nanomaterials (gold nanorods and/or silver nanoplates) decorated with ACPs for cancer treatments. Gold nanorods and silver nanoplates have absorption in the near-infrared region (700 nm-950 nm) and can thus be used as thermal transducer *in vivo*. We have developed specific surface modifications of these nanomaterials that allow precise control over the conjugation with peptides. Also, we want to use ACPs that are enzyme-responsive to increase the specificity of the peptide release.

**Methods**

Functionalized gold nanorods and silver nanoplates will be synthesized and then conjugated to ACPs. Various ACPs will be investigated as well as the modification of the nanomaterials with targeting peptides to enhance their selectivity. For every combination of ACPs and targeting peptides, the materials will be characterized using a wide variety of techniques such as UV-Vis, IR, TEM, DLS, … The capacity to release the ACPs form the material surface in the presence of enzyme will be systematically investigated. Promising materials in term of thermal conversion, peptide delivery and colloidal stability will be used in the cytotoxicity study on colorectal cancer and glioblastoma cell lines.

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**Design of functionalized nanomaterials for biomedical applications.**

**Context**

The EMNS Laboratory is developing various types of nanomaterials for biomedical applications, including:

* Gold nanoparticles for RNA delivery to specific organs
* Gold nanorods for photothermal therapy
* Iron oxide nanoparticles as MRI contrast agents

All these applications benefit from a specialized surface treatment developed in collaboration with the Organic Chemistry Laboratory of ULB (LOC-ULB, Prof. I. Jabin).

**Objective**

The primary goal of these projects is to enhance the effectiveness of each application by leveraging the unique properties provided by calixarene-based coatings. These properties include exceptional stability, precise control over ligand density, and excellent biocompatibility. To tailor the nanoparticles for specific biomedical uses, an additional coating with biomolecules—such as antibodies, peptide aptamers, or nucleic acids—is required.

**Methods**

Nanoparticles will first be synthesized and functionalized with a calixarene-based layer. Various chemical strategies will then be explored to attach therapeutic agents and/or targeting ligands at defined densities. The physicochemical and biological properties of the particles will be evaluated *in vitro*, prior to any *in vivo* testing. Depending on their background, students may also participate in the in vitro testing phase, including evaluating the performance of these nanodevices in cell culture experiments.

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**Development of activable NIR contrast agents for photoacoustic imaging.**

**Context**

Photoacoustic Imaging (PAI), the fastest growing biomedical imaging modality in the last decade, has the potential to significantly impact the field of nanomedicine. It is non-ionizing, non-invasive and uses a nanosecond pulsed laser to generate pressure waves that can be detected by conventional ultrasound transducers. Because PAI uses a light-in-sound-out approach, it has the strengths of ultrasound, i.e. good tissue penetration, real-time monitoring, low cost and high spatial resolution, but also the high contrast, specificity and sensitivity of optical methods. Although endogenous contrast agents such as oxygenated or deoxygenated hemoglobin and melanin can be used, PAI still lacks exogenous contrast agents, which could increase sensitivity and allow targeting of specific cells (such as cancer cells). The EMNS laboratory is involved in the development of such functionalized nanomaterials based on **gold nanorods**, **silver nanoplates** and **copper sulfide** **nanoparticles**.

**Objective**

Development of activable contrast agent for photoacoustic imaging. We want to develop contrast agent that produce higher photoacoustic signal upon enzymatic activity.

**Methods**

Students will synthesize the nanomaterials with various shape, size or surface chemistries and characterize them with several techniques. The nanomaterials will be modified with appropriate peptide sequences to make it enzyme sensitive. The performance in photoacoustic imaging will be systematically investigated both *in vitro* and *in vivo*. The activity of the probe upon enzymatic activity will be first investigated with recombinant proteases or kinases. The biodistribution and body clearance of each type of materials will be investigated on murine model.

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**Nucleotide-peptide complex for the specific delivery of miRNA**

**Context**

MicroRNA have emerged has promising candidates for targeted therapy. They can interact with the cell metabolism and restore (or inhibits) the normal (or abnormal) function at the cellular level. The main challenge to deliver miRNA is the specificity of the distribution and the protection of the nucleotide from degradation by endogenous enzymes. Various strategies have been investigated to carry the nucleotide to the cells such as noble metal nanoparticles or lipidic vesicles, but they have either a poor body clearance or a high toxicity, respectively. Developing new strategies are thus highly necessary.

**Objective**

We have recently developed self-assembled peptide-nucleotide complexes. By using specific peptide sequence, we could produce stable RNA-peptide assembly with interesting optical properties. We want now to demonstrate its potential for miRNA delivery associated to optical imaging modalities. We want to engineer the peptide sequences to ensure appropriate targeting of the RNA delivery, and two applications are currently under investigation: cancer and Alzheimer’s disease.

**Methods**

Students will investigate the assembly between peptides and nucleotides with various methods such as UV-Vis, emission, DLS, TEM, … Various sequences will be studied to understand the mechanism controlling the assembly. Particularly, isothermal calorimetry, that is an original technique for which the EMNS has a top-notch expertise, will be used to determine the affinity constants and the stoichiometry of the RNA-peptide assembly. When the optimal peptide sequence will be determined, studies on cells and animals will be carried out. The student will use an RNA carrying an infrared fluorophore for the tracking of the RNA delivery. The cell internalization will be investigated with confocal microscopy on cell cultures and the biodistribution will be studied by fluorescence imaging on murine model.

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**Elaboration of micellar nanocatalysts for biomass conversion in water.**

**Context**

There is currently great interest in development of environmental-friendly synthetic processes and, in this context, the replacement of commonly used volatile organic solvents by water is of prime interest. Water is a solvent with little environmental impact but its use has been limited because organic substrates are often poorly soluble in water. Micellar systems represent one of the simplest methods to achieve organic transformation in an aqueous environment. In collaboration with the University of Padova, we are investigating the potential of vanadium-based catalysts in aqueous micellar media for the hydrolysis of lignin.

**Objective**

The work will consist in monitoring the conversion using model substrates in order to identify the key parameters to control for optimum conversion.

**Methods**

This will entail work in the wet-lab and the set-up of HPLC and NMR protocols to characterize the systems and reactions.

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**Study of Copper ionophores with anticancer and antibacterial purposes.**

**Context**

Copper(I) ions are important for living organisms, especially when incorporated in the active catalytic site of enzymes. Cu+ cannot diffuse through cell membranes spontaneously, but several membrane proteins take care of its transmembrane transport, a process that can be mimicked by small synthetic molecules. We have developed synthetic transporters for Cu+ and demonstrated these to be able to transport Cu+ into liposomes as model membranes, as monitored by the quenching of a fluorescent probe. The transport of Cu across cell membranes was then studied in yeast cell, where lead compound “*Cuphoralix*” restored the growth of cells that were modified by deleting their copper transport protein CTR1. Furthermore, *Cuphoralix* and closely related analogues were found to have very potent anti-cancer properties by our collaborators at the Université Grenoble Alpes.[[1]](#footnote-1)

**Objective**

The aim of this project is to study the ability of different organic compounds as copper transporters in liposomes and in yeast cells. These studies in model systems will contribute to the understanding of the function of these compounds as potential copper transporter and correlate these results to their potential anti-cancer activity.

**Methods**

This project will start with the preparation of liposomes with fluorescent probes encapsulated and their use in transport studies by fluorescence spectroscopy. Furthermore, yeast growth assays will be developed on yeasts with various proteins deleted to study the biological impact of copper transport in more detail. These studies will be performed with Dr. Anna Maria Marini and Dr. Mélanie Boeckstaens in Gosselies.

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**Improving the transport of negatively charged drugs across lipid membranes.**

**Context**

Transport of ions across membranes is an important process in biology. Specialized proteins embedded within the cellular membranes take care of this. In our laboratory, we seek to mimic the action of these proteins with synthetic molecules that can transport anions across membranes.

**Objective**

Many important molecules in biology have anionic phosphate or carboxylate groups. The aim of this project is to study how different anionic molecules, especially drugs or models for drugs, can cross the membrane and how this process can be enhanced using synthetic anion receptors.

**Methods**

This will involve the preparation of liposomes, spherical assemblies of lipids, as models for cell membranes. You will use fluorescence spectroscopy and other ion sensing methods to study if different carboxylates and phosphates can diffuse spontaneously across the membrane. Then, synthetic transporters will be added to the membranes, to study the rate at which these transport the different anions. You will analyse how the rate of diffusion and transport of the anions depends on their structure.

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**Preparation of Giant Unilamellar Vesicles using microfluidics and their application for transmembrane transport.**

**Context**

In the EMNS laboratory, vesicles prepared from natural lipids (liposomes) are used as models for cell membranes to study processes like transmembrane transport and cell targeting. With standard procedures, vesicles with diameters of up to 200 nm are easily made, but the preparation of giant unilamellar vesicles (GUVs, ~10 µm) is still a challenge. The TIPS laboratory is specialized in microfluidics, which can be used to prepare droplets and vesicles.

**Objective**

The aim of this collaborative project is to develop a method to prepare GUVs as membrane model system by microfluidics and to study the transport of ions across the lipid membranes of these GUVs

**Methods**

You will use a home-made 3D-printed micro-emulsion generator to produce double emulsions and screen the conditions (fluid viscosities, lipid solutions and concentration, flow rates, geometry) to identify the optimal regime for generating stable GUVs, with minimal organic solvent present. You will then characterise these GUVs by fluorescence microscopy, using encapsulated (water-soluble) fluorescent probes, and by using fluorescent compounds in the membrane. Changes in the fluorescence will then be used to monitor the transmembrane transport of ions.

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1. Calix[4]arenes with high anticancer activity, *Patent EP23305100.2*;

   Preprint : <https://doi.org/10.26434/chemrxiv-2025-2z3pd> [↑](#footnote-ref-1)