

Supervisor(s): Arturo Álvarez-Bautista and Catarina Duarte

Supervisor(s) email address: arturo.alvarez@itqb.unl.pt; cduarte@itqb.unl.pt

Lab/Institution:

TITLE: MULTICORE POLIMERIC-LIPIDIC NANOPARTICLES FOR DRUG RELEASE TO COLON CANCER TREATMENT

BACKGROUND

Colorectal cancer is the third most common type of cancer diagnosed in the world and is the third most common cause of cancer-related death. The majority of cases are sporadic, with hereditary colon cancer contributing up to 15% of all colon cancer diagnoses. Treatment consists of surgery for early-stage disease and the combination of surgery and adjuvant chemotherapy for advanced-stage disease. Management of metastatic disease has evolved from primary chemotherapeutic treatment to include resection of single liver and lung metastases in addition to resection of the primary disease and chemotherapy. The guanylyl cyclase C (GCC) receptor possesses several well-established properties ideal for use as a biomarker in gastrointestinal malignancies. The GCC receptor is constitutively expressed in the apical membranes of the intestine and its expression is universally preserved in primary colorectal tumors and their metastases. Moreover, receptor binding is retained by GCC's cognate ligand, the bacterial enterotoxin ST, even after conjugation to functional moieties. Selective tumor, but not gastrointestinal, uptake of ST in mice bearing GCC-expressing colon cancer xenografts demonstrates the potential of exploiting ST-GCC interaction for diagnostic imaging and targeted therapy of metastatic colorectal cancer. We expect this specific targeting provided by ST-GCC interaction to improve diagnosis, staging and management of colorectal cancer metastases, and ultimately prolong patient survival in this disease. In fact this concept has been demonstrated to be applicable for example for tumor delivery of imaging agents but has never been applied for conjugation with nanoparticulate drug delivery systems.

OBJECTIVES

This Master Plan is part of a major project whose main goal is to develop a novel and efficient delivery system for targeting primary and metastatic colorectal cancer cells in intestinal and extraintestinal tissues. Totally green technology will be applied for the preparation of hybrid multilayered lipid enveloped systems, composed of a hydrophilic shell, a nanosized polymeric core and a lipid layer between the core and shell. The out layer (shell) will be further functionalized with a target which is capable of selectively targeting expressed in primary and metastatic colorectal cancer cells. The Master Student will carry out the synthesis of the nanoparticles with different compositions developed by several techniques. The Master Student will focus as well in the functionalization of these nanoparticles for further analyses.

PROJECT DESCRIPTION

Task 1: Formulation of nanoparticles by different methodologies.

- Formulation of the inner core, composed by biodegradable polymeric, which will be used to entrap de active principles.
- A hydrophilic polymeric shell to enhance the stability of nanoparticles
- A middle lipid layer which serves as template for further modifications.

Task 2: Functionalization of the surface of the nanoparticles with specific target.

Task 3: Solid-state and chemical characterization of the particulate systems prepared.

TIMELINE (use fill tool for the cells)

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10
Task 1										
Task 2										
Task 3										