Title: Determination of the effectiveness of polymeric nanoparticles loaded with mRNA encoding TIMP-3 released from a thermosensitive Poloxamer hydrogel matrix for melanoma treatment

Abstract:

Technological advancements are driving a more integrative and precise approach to medicine. Since the success of mRNA-based vaccines, new therapies using mRNA are emerging as a promising strategy for treating diseases that currently lack effective solutions. A relevant example is the use of mRNA encoding TIMP-3, a protein often downregulated in various cancers, including melanoma. The reduction of TIMP-3 expression promotes uncontrolled tumor cell proliferation and metastatic potential.

In this context, IQS has developed advanced polymeric formulations that enable controlled and efficient mRNA delivery, resulting in high transfection rates and therapeutic efficacy. However, tailoring these formulations to each specific pathology is crucial to maximizing their effectiveness.

For melanoma treatment, the use of mRNA-loaded nanoparticles embedded in a thermosensitive polymeric hydrogel, applied locally to the skin, represents an innovative approach. This strategy allows precise and sustained mRNA administration, offering spatial and temporal control over release, potentially improving therapeutic efficacy while minimizing side effects.

Workplan:

Characterization of nanoparticle internalization in target cells using flow cytometry and confocal microscopy

This section focuses on studying the internalization of nanoparticles loaded with mRNA encoding the GFP protein in target cells. The nanoparticles will be administered both in solution and from a pre-characterized Poloxamer hydrogel matrix to allow a thorough comparison of the variation in effectiveness due to encapsulation within the hydrogel. The polymer forming the nanoparticles will be fluorescently labeled to enable detailed characterization of their distribution and behavior within the target cells (melanoma).

Evaluation of the effectiveness of pBAE nanoparticles with mRNA encoding TIMP-3

This part of the project is centered on characterizing the functional efficacy of pBAE polymer nanoparticles loaded with mRNA encoding TIMP-3, a protein known for its metastasis-inhibiting properties. The effect of the nanoparticle system will be

studied both in the absence and presence of a Poloxamer hydrogel to determine how the matrix influences its activity. The main techniques used will be Western Blot, ELISA, and qPCR.

The experiments will be conducted in metastatic melanoma cell lines and control cell lines (epithelial cells and fibroblasts), both in vitro and in three-dimensional Poloxamer matrices.

Transition to in vivo models

Once the efficacy of the nanoparticles is validated in vitro, the project will proceed to in vivo animal models to study the modulation of the proteins of interest in pathological contexts. The effectiveness of the nanoparticle system in inhibiting tumor growth and regulating metastasis will be analyzed in melanoma cancer models.

Organization:

This is a project that will be held in IQS facilities, under the direction of Dr. Cristina Fornaguera and co-direction of Dr. Carles Bofill. Also, this is in collaboration with Dr. Guillaume Bastiat, from the University of Angers, who will also participate in the project.