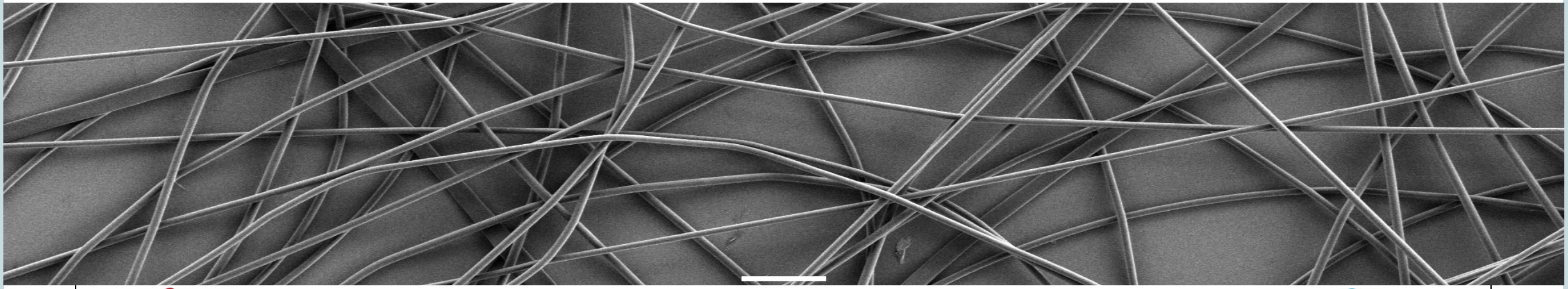
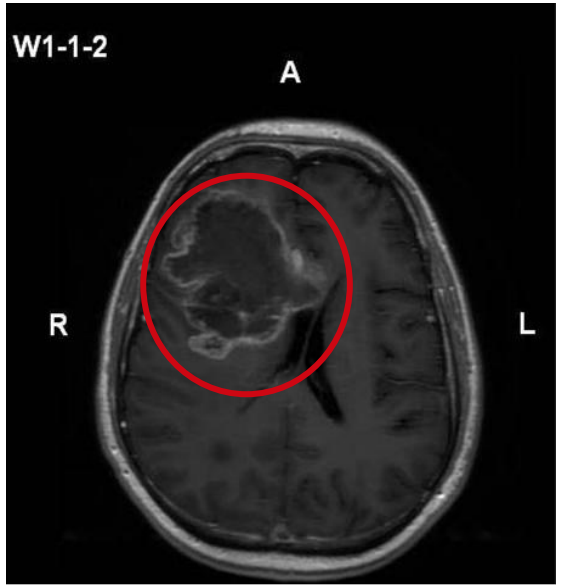


PHOTOACTIVE POLYMERIC BIOMATERIALS FOR LOCAL COMBINED THERAPY AGAINST GLIOBLASTOMA

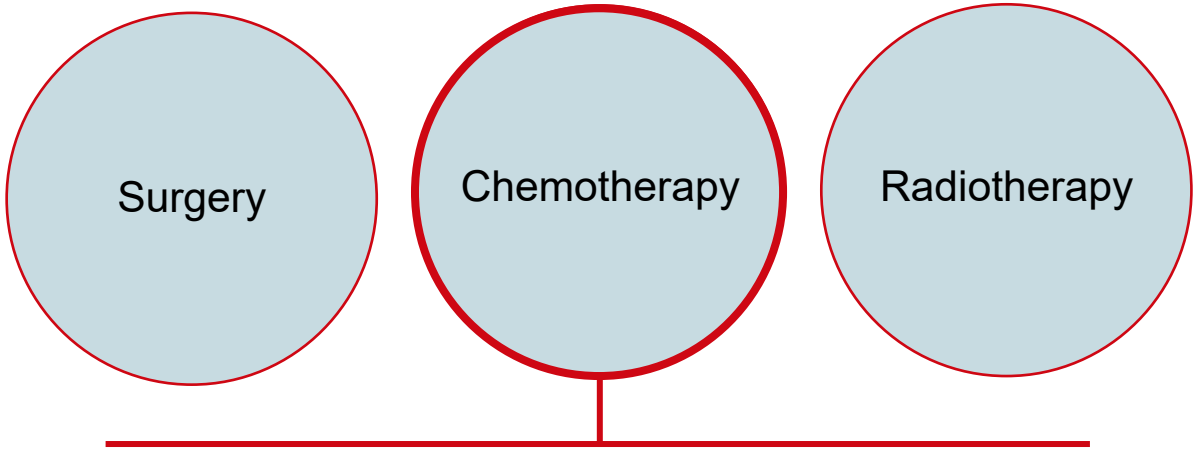
GRUPO DE DISEÑO Y VALIDACIÓN DE NANOBIOMATERIALES

PEDRO VALENTÍN BADÍA HERNÁNDEZ

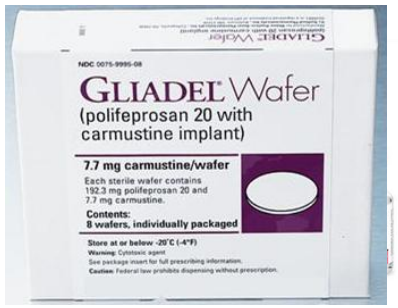
Glioblastoma



80% mortality rate



Temozolomide (TMZ)



Carmustina (BCNU)

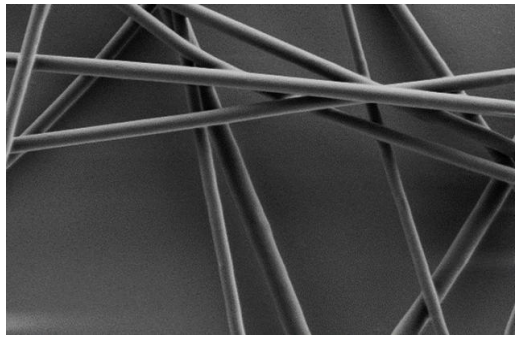
Doxorubicin (DOX)

Biomateriales

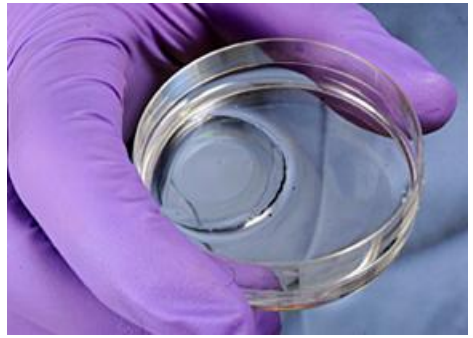
Macrostructured

Nanostructured

Nanofibers



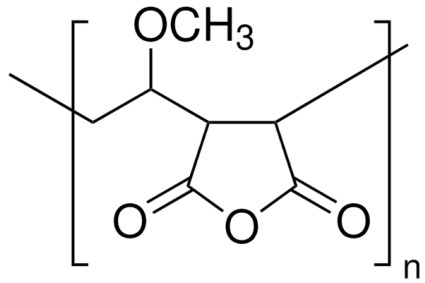
Hydrogels



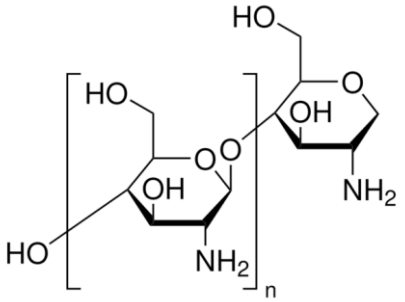
Malleable
Easy to synthesize
Administration: local, oral, or topical
Low storage and transportation costs

Introduction

Synthetics
Poly (methyl vinyl ether-alt-maleic) (PMVEMA)



Natural
Chitosan

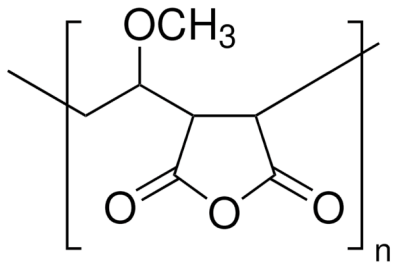


Functionalized polymers for combined therapy

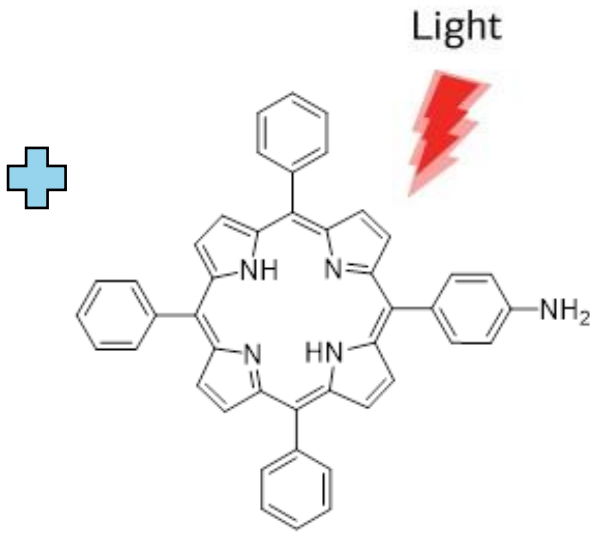
Macrostructured

Nanostructured

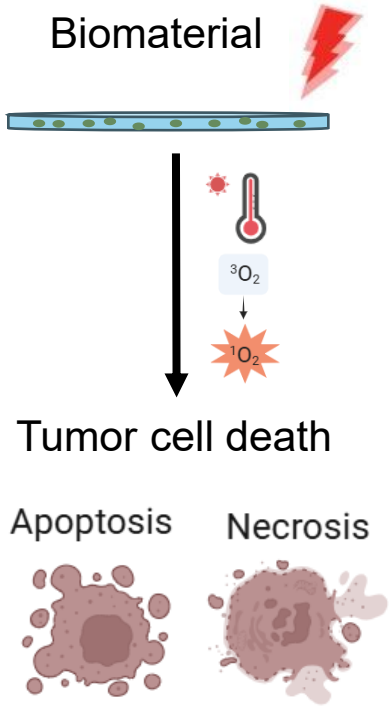
Photosensitizer conjugation	Phototherapy (PDT)



PMVEMA



Aminophenyl-
Tetraphenylporphyrin (TPP-NH2)

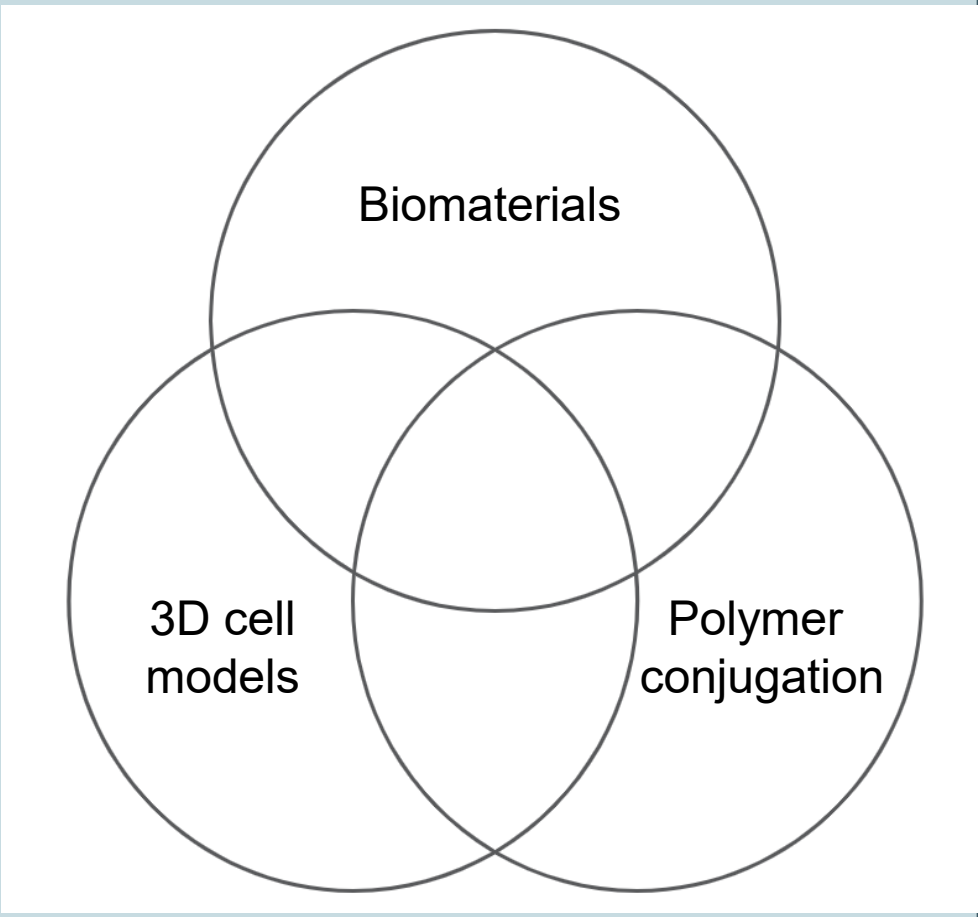


4

Main aim

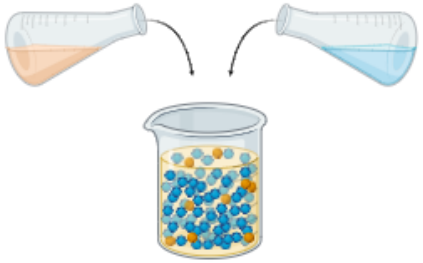
Developing photoactive delivery systems based on biopolymers for the administration of glioblastoma treatments

- Development and characterization of electrospun PMVEMA nanofibers as drug deliver systems for antineoplastic DOX, TMZ and BCNU.
- Evaluation of their effect in cell models.
- Development of 3D cell models of glioblastoma.
- Functionalization of PMVEMA with porphyrins for PDT.

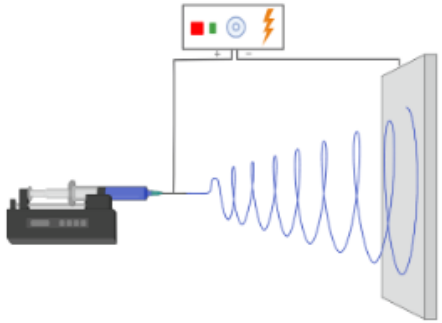


Material and Methods

Doxorubicine (DOX) or Carmustine (BCNU)



PMVEMA disoluttion
Antineoplastic drug (% w/w)



Synthesis by
Electrospinning

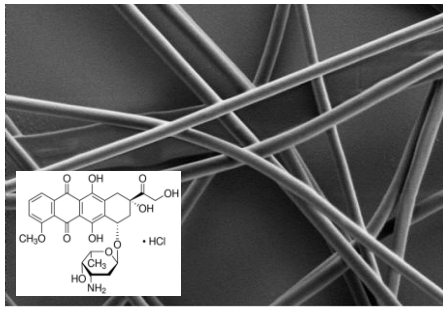
Characterization of nanofibers

- Scanning electron microscopy (FESEM) Confocal mircoscopy
  - Morphology and composition
- Liquid chromatography (HPLC-UV)
  - Encapsulation efficiency and release kinetics
  - Cell viability assay (MTT)
- Effect on gliobastoma patient cell lines from the Hospital General Universitario de Elche (HGUE-GB) and 3D model development

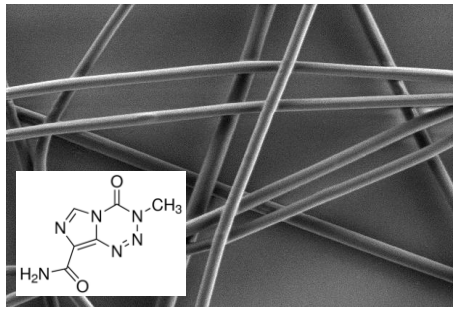
PMVEMA dissolutions (w/w):
- PMVEMA-Ac at 20 % in water
- PMVEMA-Es at 25 % in ethanol

Parameters considered:
- Voltage (kV)
- Distance (cm)
- Flow (mL/h)

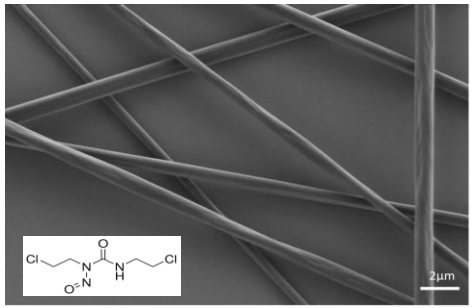
Loaded nanofibers characterization



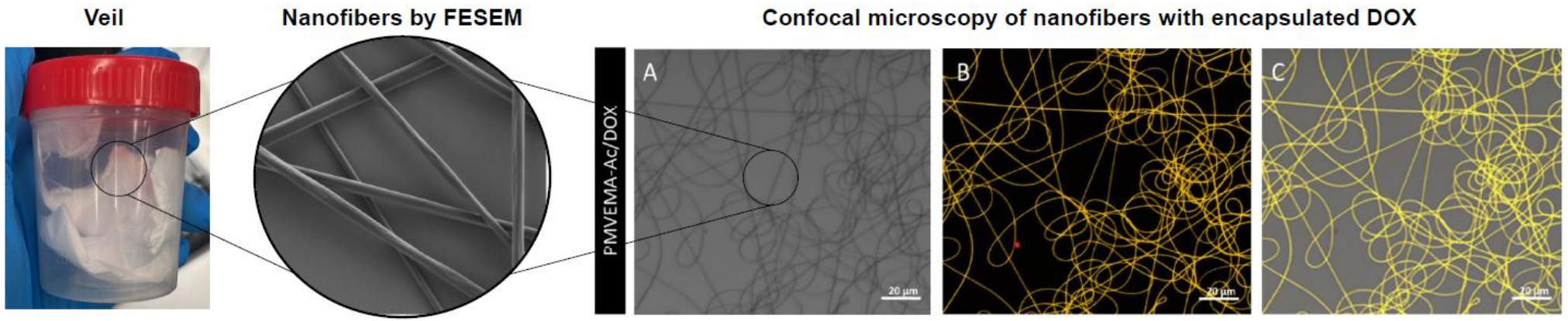
PMVEMA-Ac/DOX 1 %



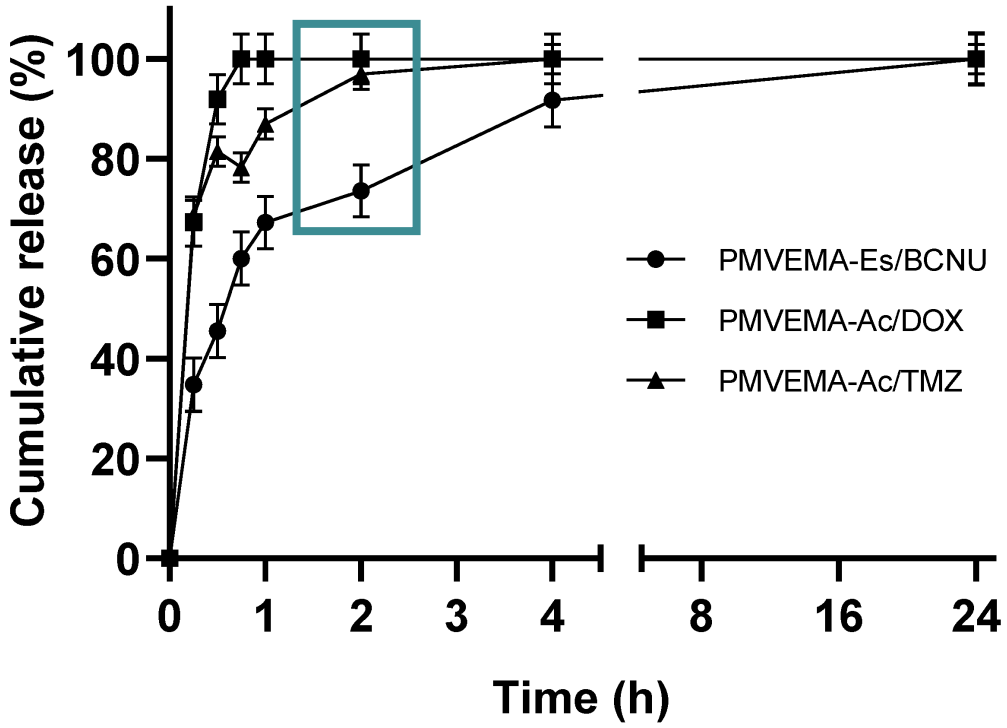
PMVEMA-Ac/TMZ 1 %



PMVEMA-Es/BCNU 8 %

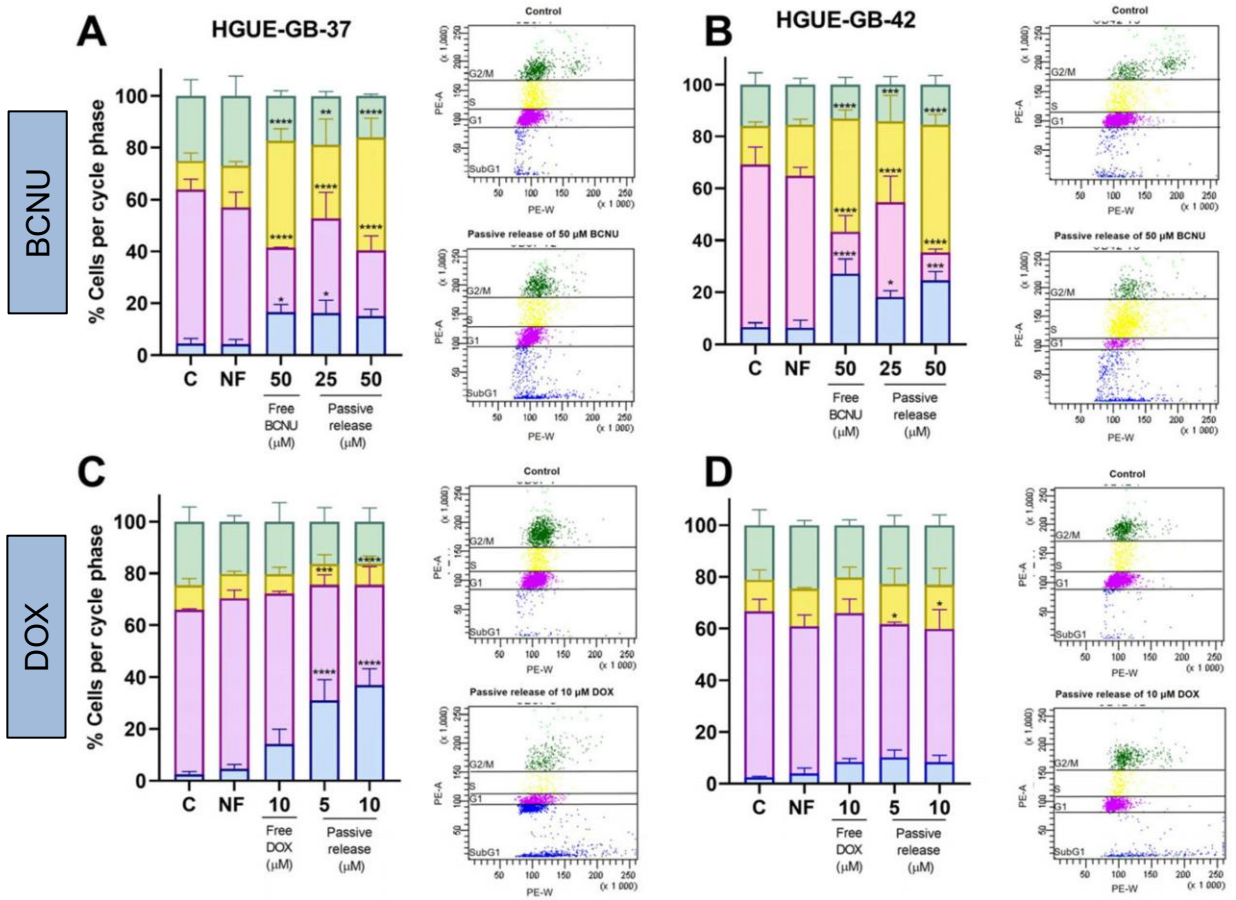


Kinetic release and effect on cell cycle



Conditions: 37°; PBS; pH 7.4

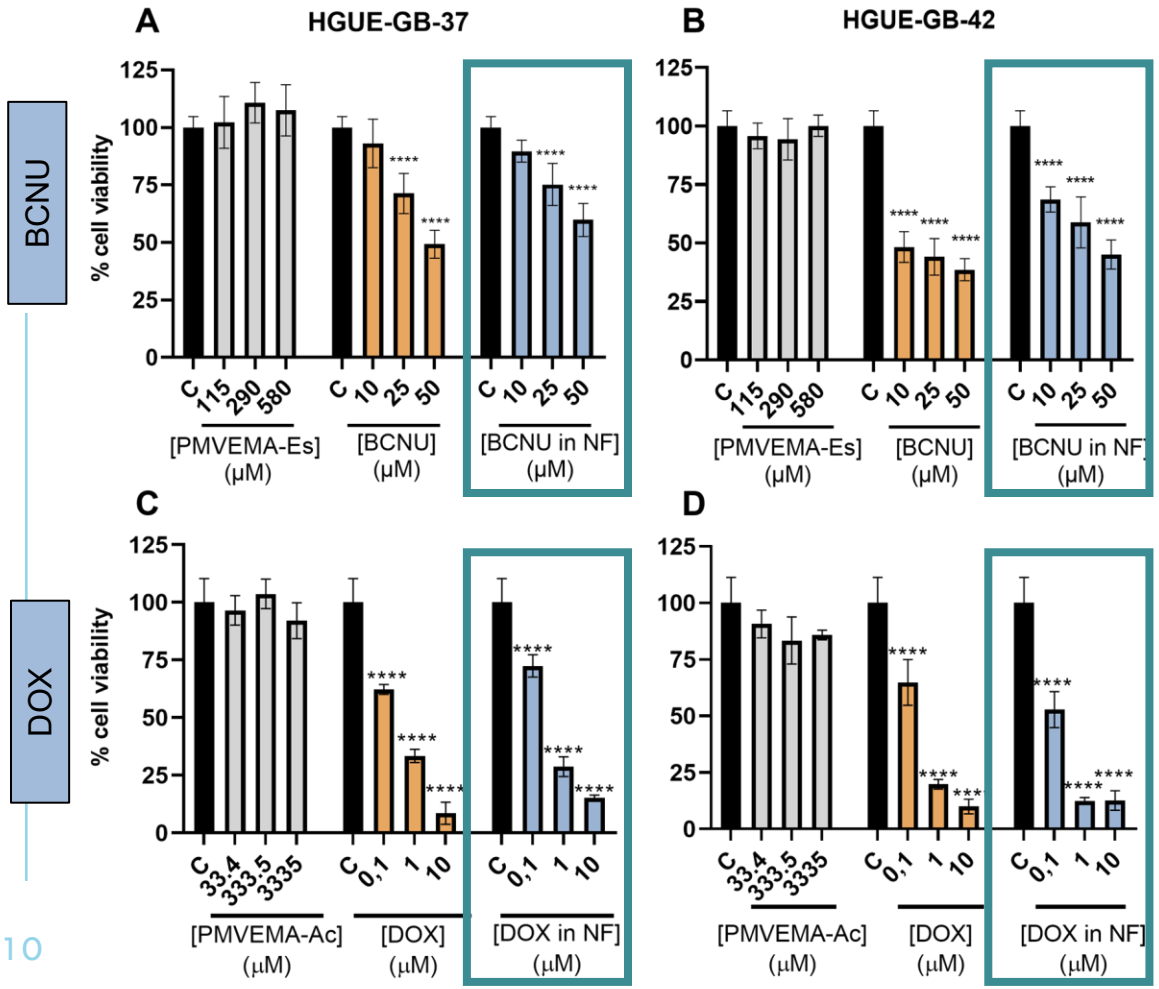
Results

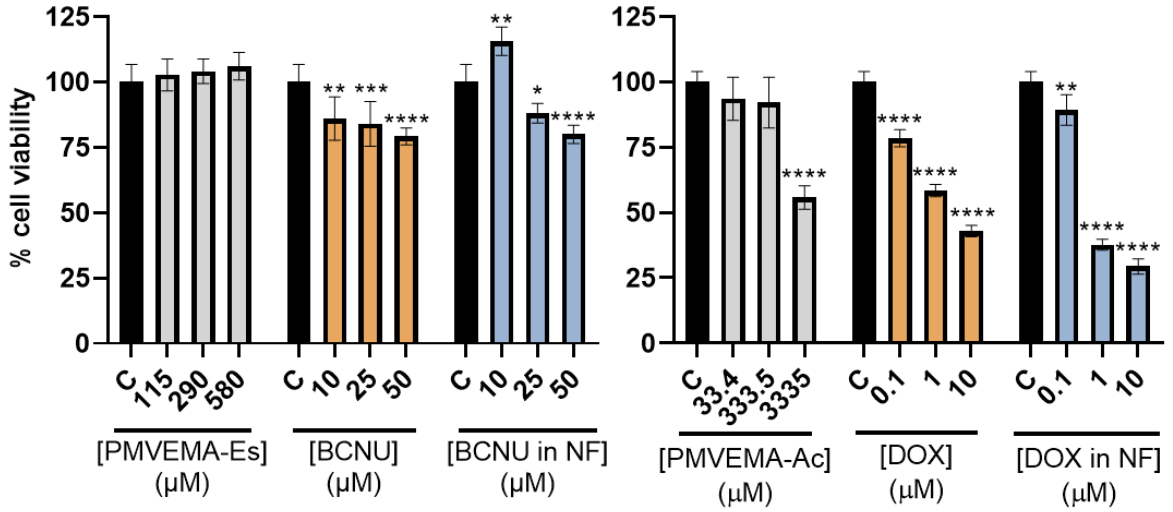


S phase – Cytostasis (yellow)
SubG1 phase – Cytotoxic (blue)

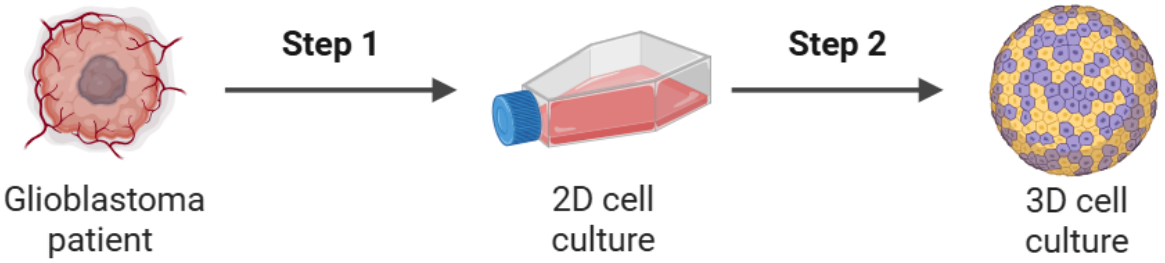
Cell models testing and developing

Results

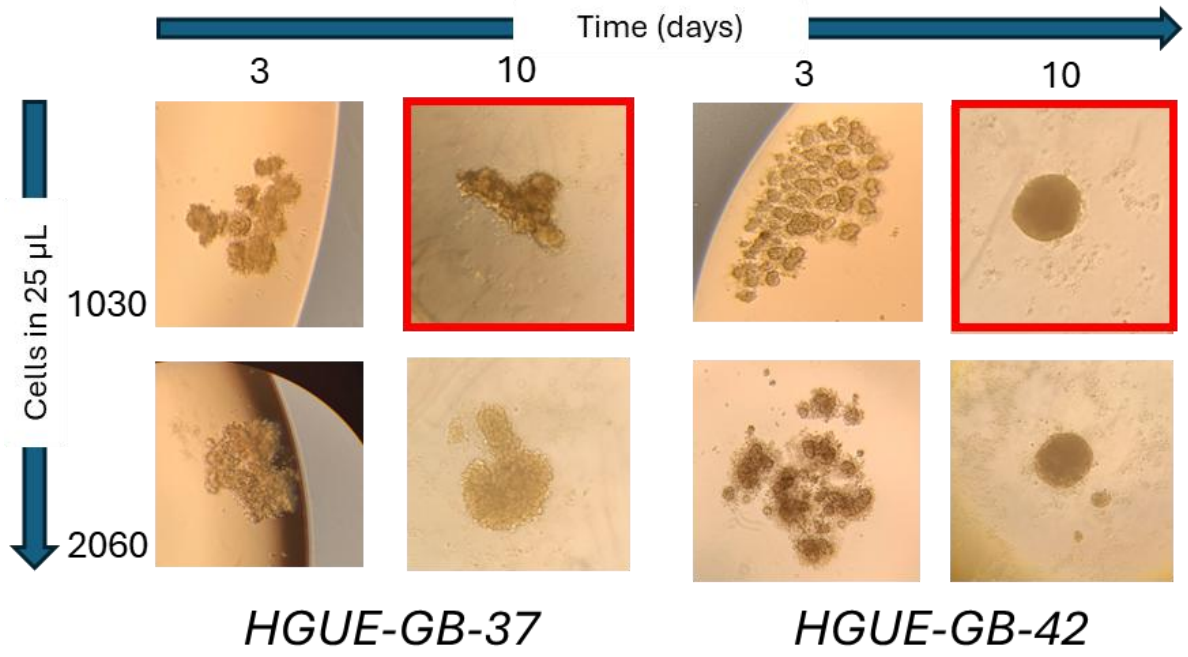




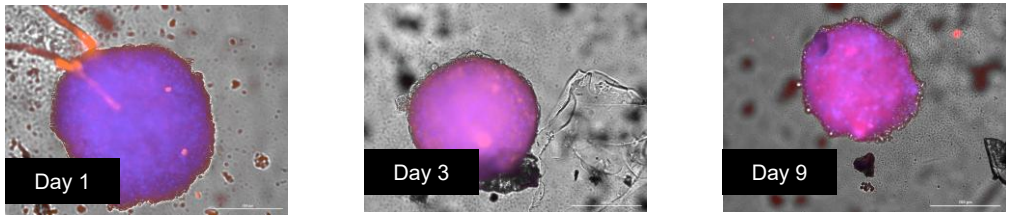
In vitro cancer models



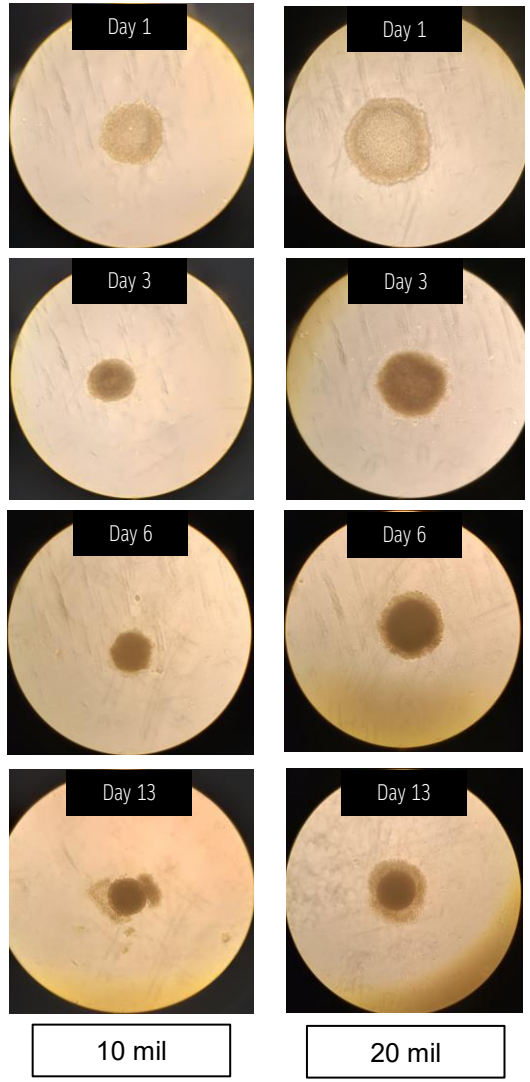
Development of 3D cell models of glioblastoma



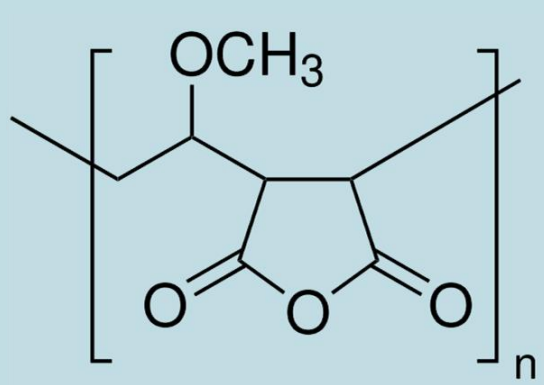
E-cadherin
Hoetch



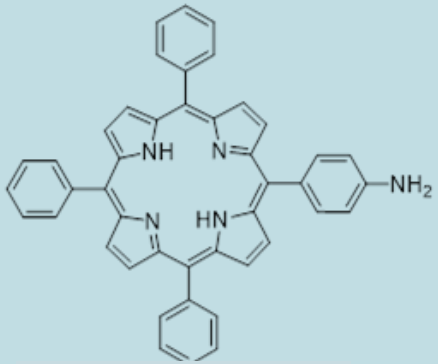
Results



Conjugation of PMVEMA-TPP/NH2



PMVEMA



TPP-NH2

Synthesis:

Microwave reaction

- Ratio 1:0,25 mMol (in 4mL of DMF).

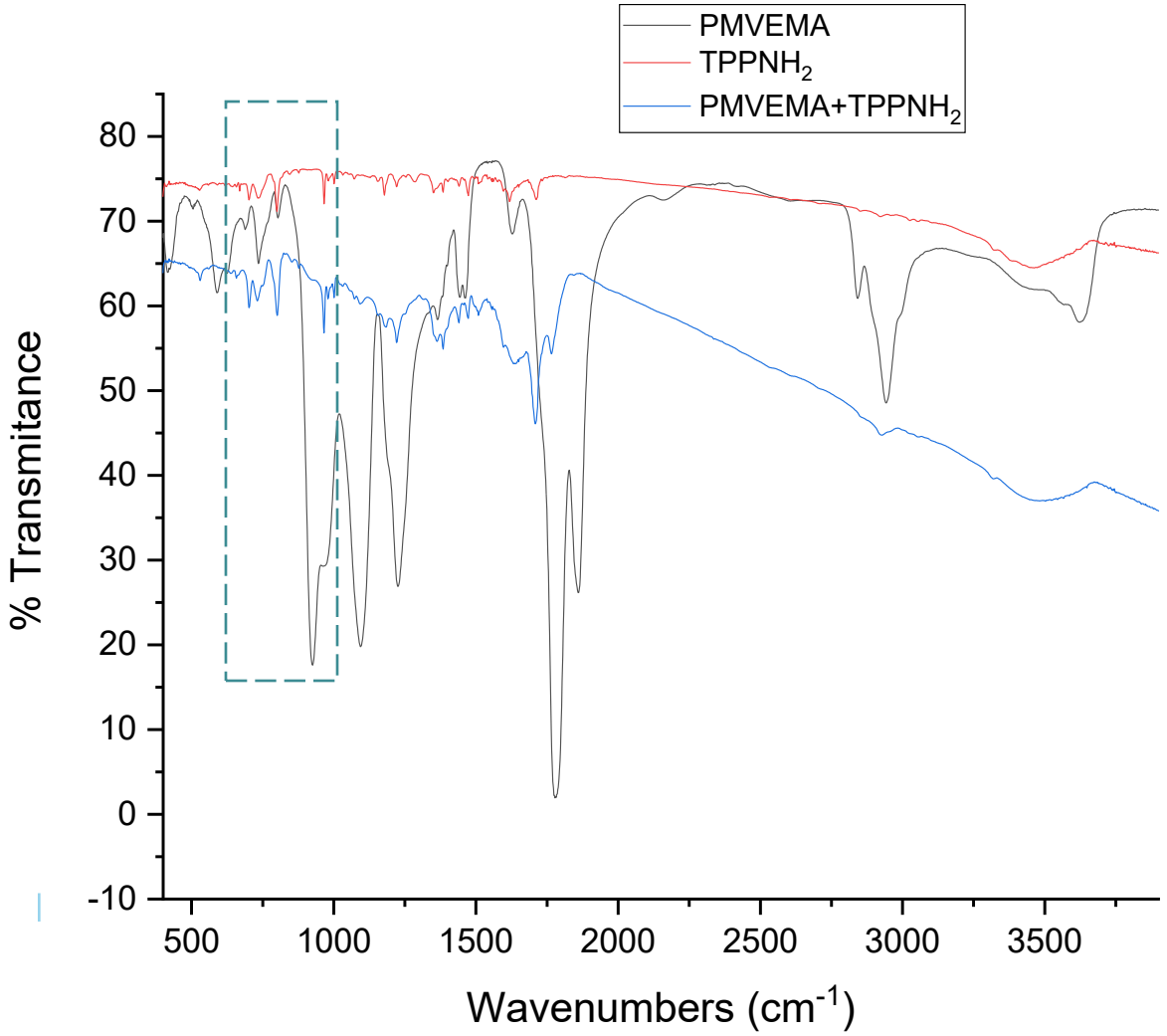
-Conditions: 175°,10p, 20 mins.

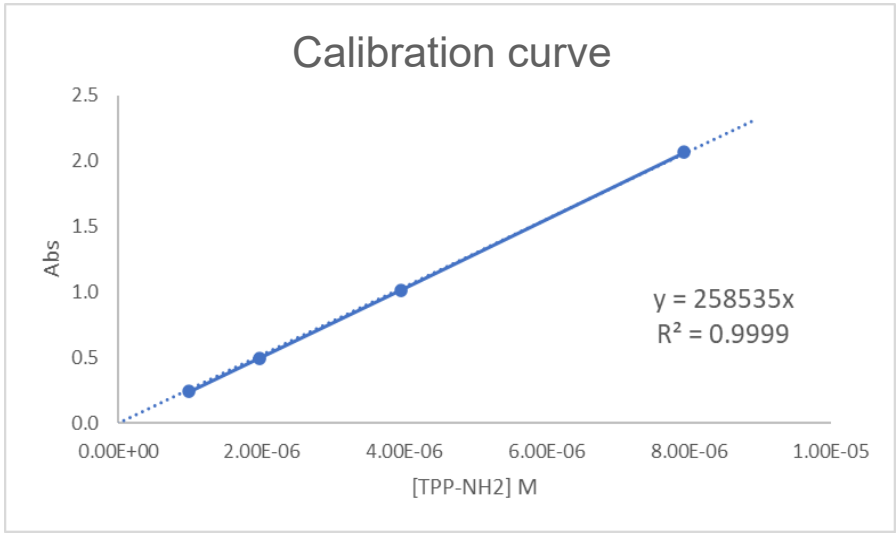
Characterization:

- UV
- FTIR
- NMR
- Cell viability

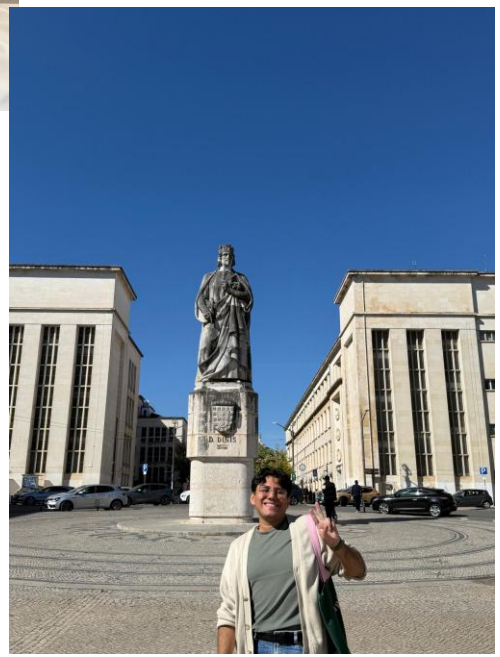
Characterization of PMVEMA-TPP/NH2

Results





PMVEMA_TPP/NH2		
Abs 420	0.556	u.a.
[PM-TPP]	0.0025	mg/mL
Ratio Porf/Polym	541.7	mgPorf/1g Polym
w/w	54.2	%



CONCLUTIONS

BIOMATERIALS

Electrospun PMVEMA-derivate nanofibers were able to encapsulate DOX and BCNU with a loading efficiency comparable to clinically approved versions of drug delivery systems.

IN VITRO CANCER MODELS

The loaded drugs keep their antitumor activity and reduces glioblastoma cell viability with minimum effects in human astrocytes.

HGUE-GB-42 cell line at a cell density of 20,000, it is proposed to establish a glioblastoma mixed cell model.

POLYMER CONJUGATION

PMVEMA-TPP it has been successfully functionalized., further characterization should be performed to use it as a copolymer in nanofibers synthesis, for PDT.

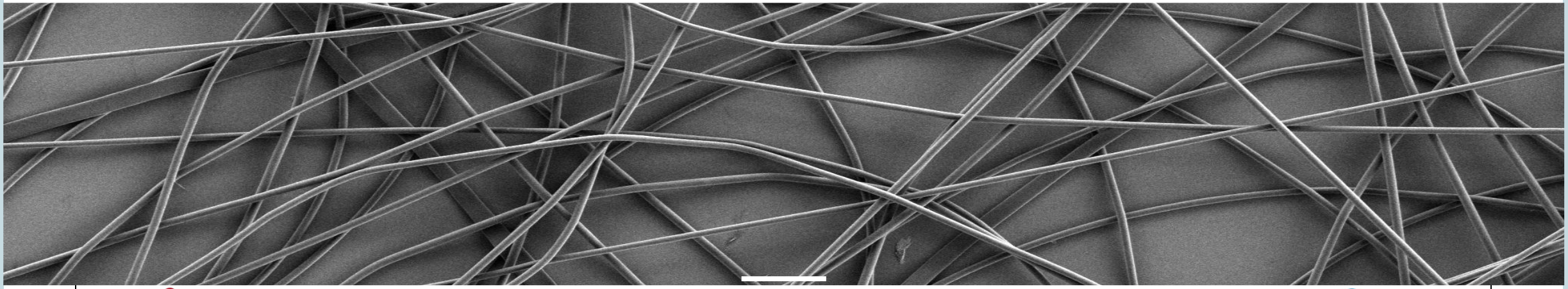
ACKNOWLEDGEMENTS

MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES

DISEÑO Y VALIDACIÓN DE NANOBIOMATERIALES
DVN

Coimbra chemistry centre

UNIVERSITAS Miguel Hernández



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“UnaformadehacerEuropa”