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Nanobioconjugates for targeted delivery of antigenic and therapeutic peptides at colorectal cancer

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1. Abstract

Colorectal cancer (CRC) presents challenges due to the limited effectiveness and side effects of conventional treatments like chemotherapy and surgery. Nanobioconjugates, such as poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs), offer improved drug delivery alternatives. Peptides bonded to CRC receptors show potential as therapies and vaccines. This study encapsulates the P1 peptide in PLGA-PEG-Mal NPs, functionalized with the G3 peptide for targeted CRC cell delivery to inhibit cell proliferation[1,2], and encapsulates the P2 peptide in PLGA-COOH polymer to inhibit tumor growth via CD8+ T-cell activation, using D-mannosamine for targeting antigen-presenting cells[3,4]. By studying the physicochemical properties of PLGA and peptides, the research aims to enhance stability and controlled release while minimizing side effects and improving CRC therapy from nanobioconjugates and peptide synergies.

2. Methodology

Strategy I

Selected peptide

P1 (100 % hydrophobic)

↓ Metastasis formation
↓ Cell invasiveness[1]

Ligand

G3 peptide

↑ Selectivity to CRC cells
↑ Transmembrane activity [2]

Selected polymers

PLGA-PEG-Mal 25:5 kDa, LA:GA 75:25

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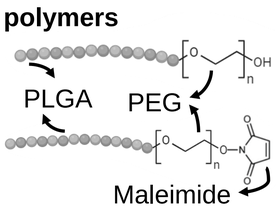
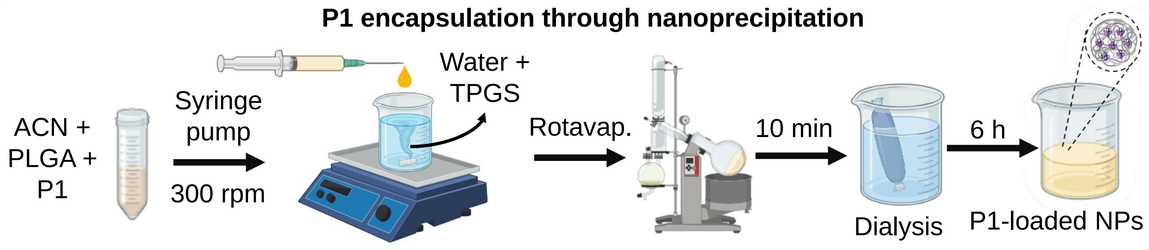
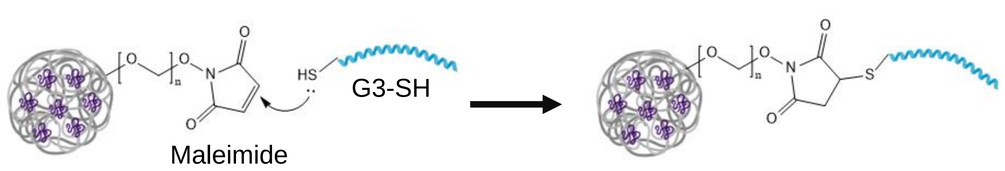


P1 encapsulation through nanoprecipitation



Functionalization of P1-loaded PLGA NPs



Strategy II

Selected peptide

P2 (65 % hydrophobic)

↑ Immune response through CD8⁺ T-cell activation[3]

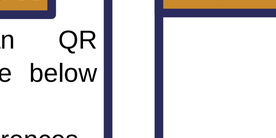
Ligand

$D\text{-manNH}_2$

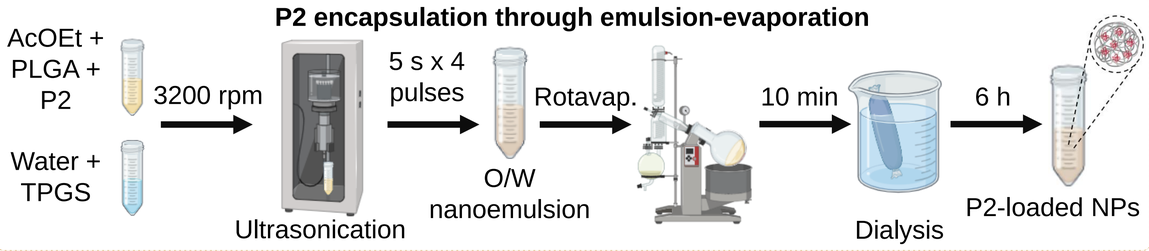
↑ Cellular uptake by antigenic-presenting cells[4]

Selected polymers

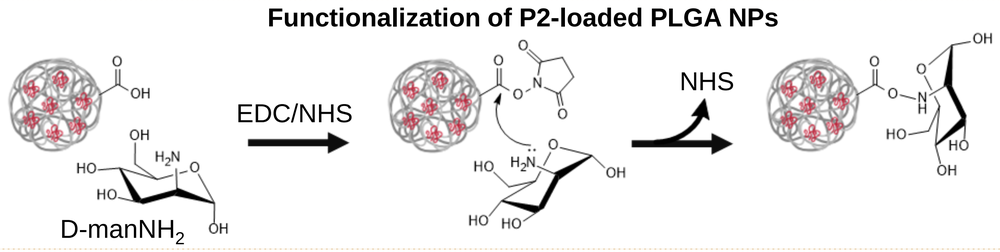
PLGA-COOH 24-38 kDa, LA:GA 50:50



P2 encapsulation through emulsion-evaporation



Functionalization of P2-loaded PLGA NPs



3. Results

Strategy I

Table 1. Chemical profile of P1[5].

Molecular weight (kDa)	0.8
Isoelectric point	6.01
Net charge at pH 7.0	0
Percentage of hydrophobicity	100

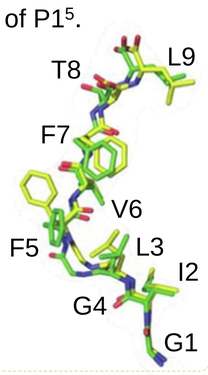


Table 2. DLS results for most relevant nanoprecipitation assays (A#).

Parameter	A1	A2	A3
Size (nm)	71 ± 1	72 ± 1	85 ± 1
PdI	0.13 ± 0.02	0.15 ± 0.01	0.17 ± 0.02
Pζ (mV)	-20.2 ± 0.2	-19.4 ± 1.3	-19.5 ± 0.1

Note. A1 and A2: 27G needle, 0.5 % TPGS; A2: diffusion; A3: 21G needle, 0.25 % TPGS.

Strategy II

Particle size analysis and P2 quantification in PLGA NPs

Table 3. DLS results for empty and P2-loaded PLGA NPs.

Parameter	Empty NPs	P2-loaded NPs
Size (nm)	226 ± 3	256 ± 4
PdI	0.14 ± 0.02	0.21 ± 0.01
Pζ (mV)	-42.8 ± 0.5	-37.8 ± 0.5

Note. Empty NPs were used for surface modification with $D\text{-manNH}_2$.

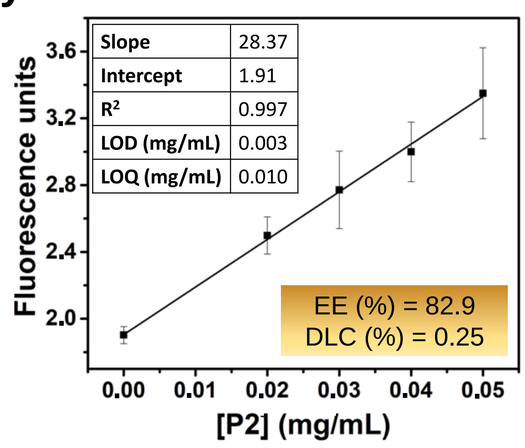
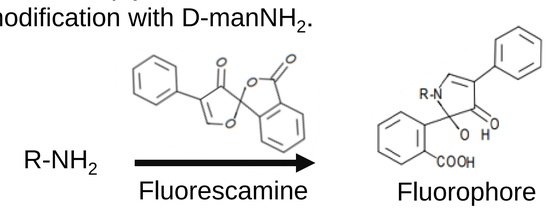
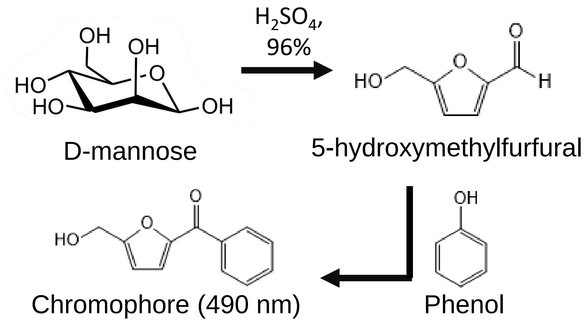


Fig 1. Calibration curve in DMSO for P2 quantification in PLGA NPs.



Surface modification of PLGA NPs and D-manNH2 quantification



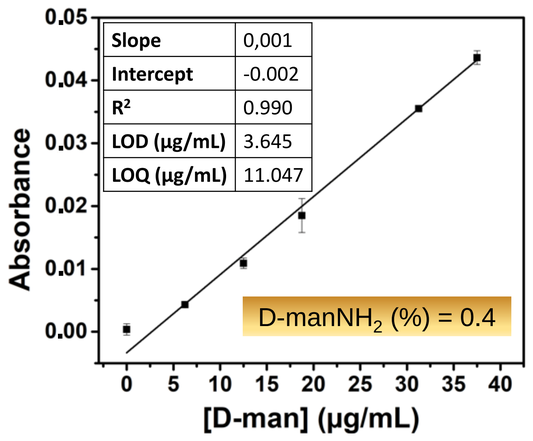


Fig 2. Calibration curve in H_2O for D-$manNH_2$ quantification on PLGA NPs.

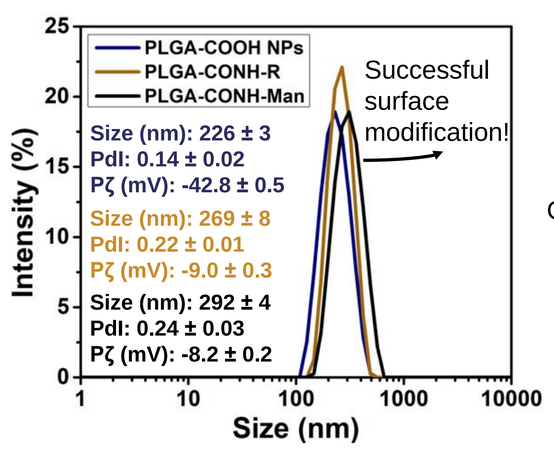


Fig 3. Particle size data of PLGA NPs before (-), in the middle of (-), and after functionalization (-) with D-$manNH_2$.

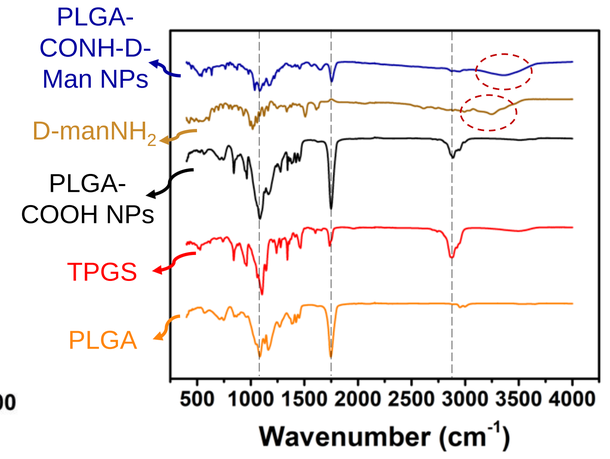


Fig 4. FT-IR spectra for PLGA (-), TPGS (-), PLGA-COOH NPs (-), D-$ManNH_2$ (-), and PLGA-CONH-D-Man NPs (-).

4. Conclusions

The interplay between the physicochemical properties of PLGA and P2 is evident in the particle size, reflecting a balanced influence of molecular weight and the lactic acid:glycolic acid ratio. Changes in ζ-potential values and specific signals from FT-IR confirmed the successful surface modification of PLGA NPs.

Ref.

Scan QR code below for references.

Acknowledgments

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