Biophysical State-Driven Regulation of Biomimetic Nanoparticles

Implications for Biomedical Applications

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FARMATEC

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Controlled Release Society
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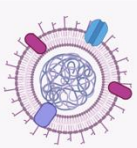
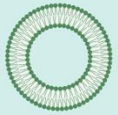
JULY 13-18, 2025

NEXT-GENERATION DELIVERY INNOVATIONS

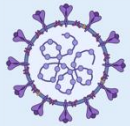


Cell Membrane-Coated Nanoparticles



Lipid-Based Biomimetic Nanoparticles

Artificial Cell-Derived or Inspired Vesicles



Protein-Based Biomimetic-Nanoparticles

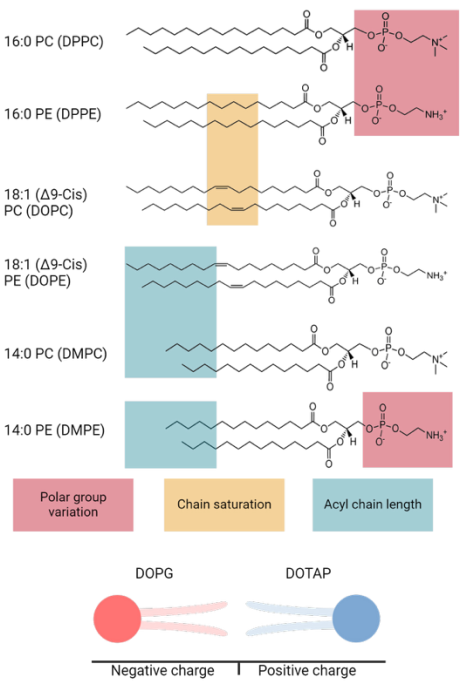
Other Noteworthy Biomimetic Strategies

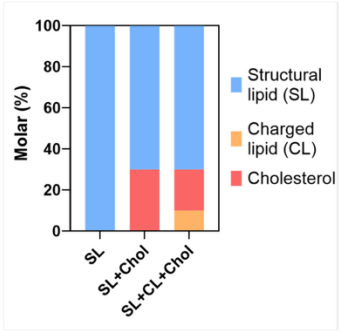
Why membrane organization matters

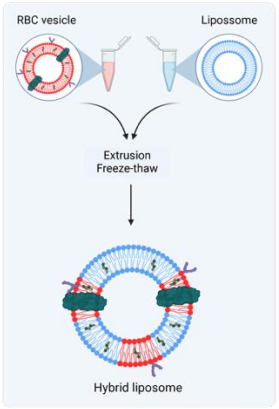
- Membrane organization is a **key determinant of biomimetic nanoparticle function**, shaping how they interact with cells and biological barriers.
- It affects **biocompatibility**, **cellular uptake**, **targeting specificity**, **immune evasion**, and **functional performance**.
- Different biomimetic strategies: **cell membrane coatings**, **lipid-based systems**, protein-based platforms, and hybrid vesicles --- leverage membrane architecture to enhance therapeutic potential.
- Understanding and controlling membrane structure **is essential to optimize nanoparticle design** for drug delivery and diagnostics.

Compositional aspects

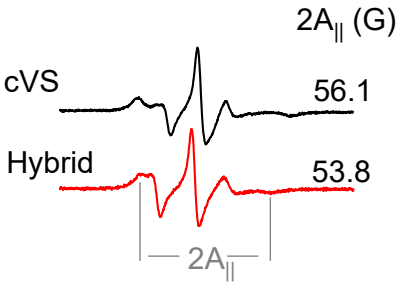
Fine-tunning liposome composition



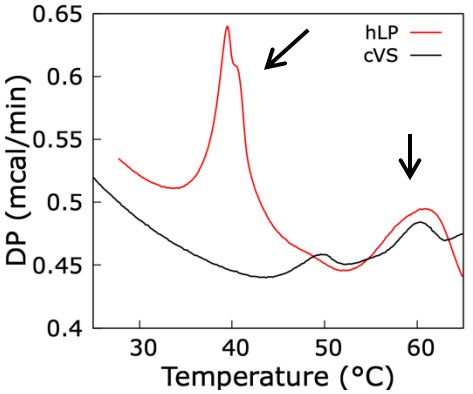




ESR analysis



DSC analysis



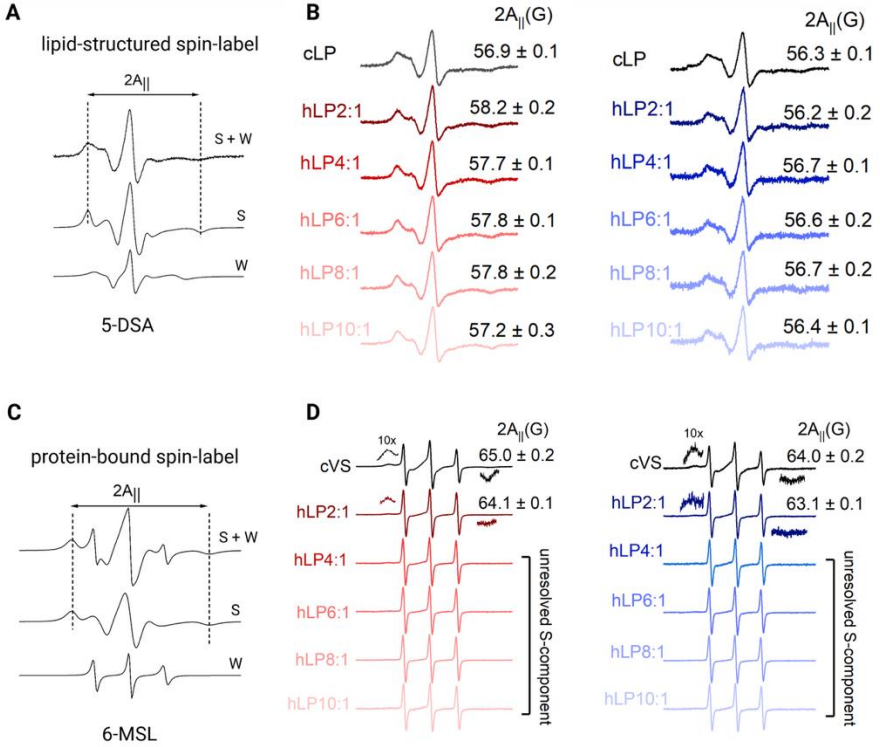
- hLP shows the thermal signatures of its respective synthetic and cell-derived parts.
- hLP and cVS showed different membrane dynamics and thermal fingerprints.

Biophysical outcome

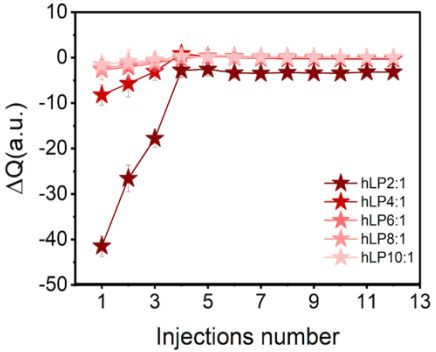
Hybridization modulates membrane dynamics and thermal behavior

Stability aspects

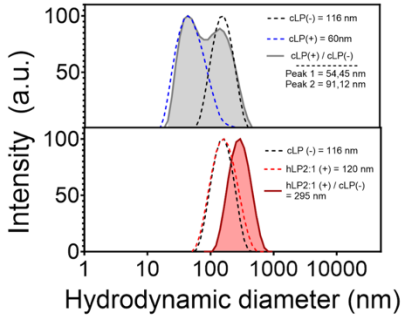
ESR analysis



ITC analysis



DLS analysis



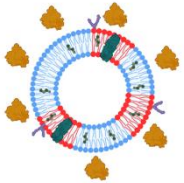
- hybridization ratio modulates TX-100 destabilization of both lipid and protein components.
- Positively charged hLPs showed improved fusogenicity compared to cLPs.

Biophysical outcome

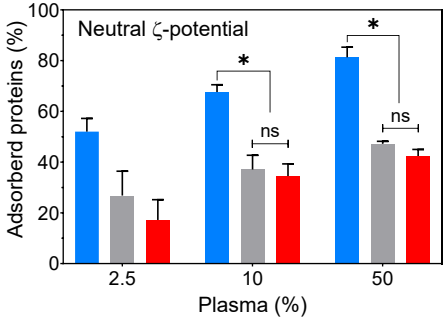
Hybridization increases membrane stability and fusogenicity

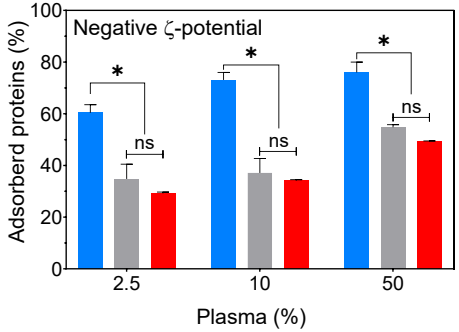
Nanoparticle-protein interactions

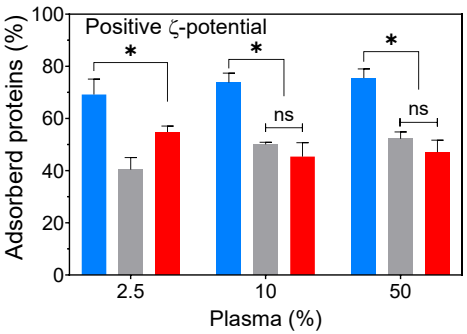
BCA analysis

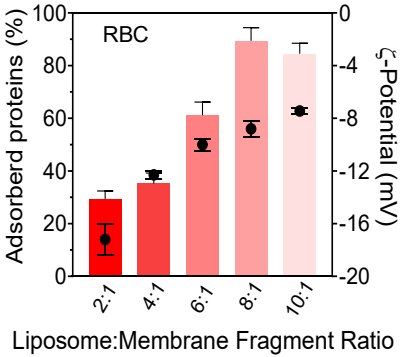


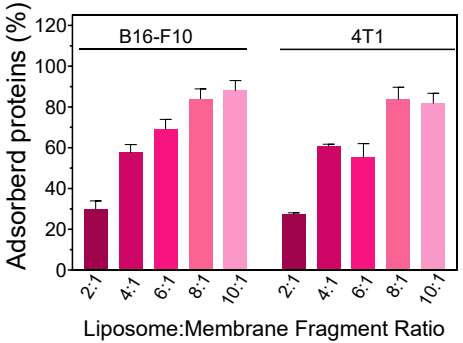
Hybrid











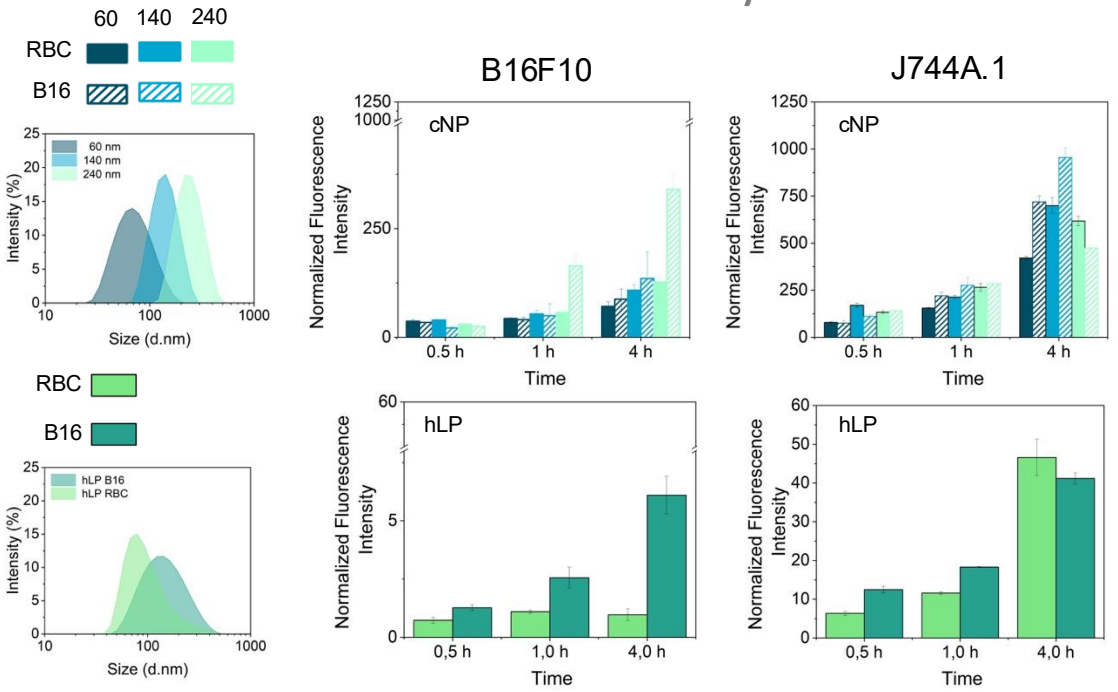
cLP Pegylated Hybridized

- hLPs minimized protein adsorption to levels similar to PEGylated cLPs.
- Hybridization ratio dictates protein corona formation, regardless of membrane source.

Biophysical outcome

Hybridization modulates the hard protein corona formation

Uptake modulation



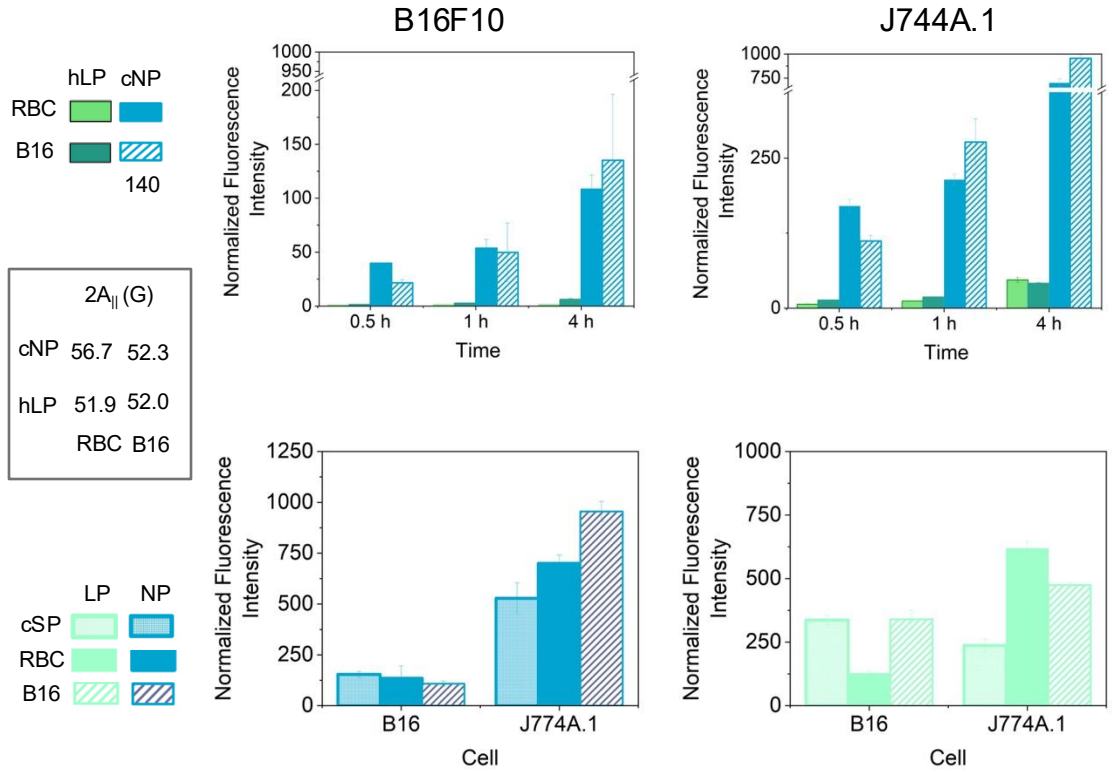
- Uptake of both cNPs and hLPs is influenced by the membrane source, with B16-derived coatings leading to higher internalization in B16 cells compared to RBC-derived membranes.
- This effect is consistent across all tested nanoparticle sizes and becomes more pronounced at 1 h and 4 h, particularly for cNPs.
- In macrophages, uptake differences between B16- and RBC-derived nanoparticles are modest, suggesting limited selectivity in non-target cells.

Biophysical outcome

Membrane identity enhances cell-specific recognition and uptake

Uptake modulation

FC analysis



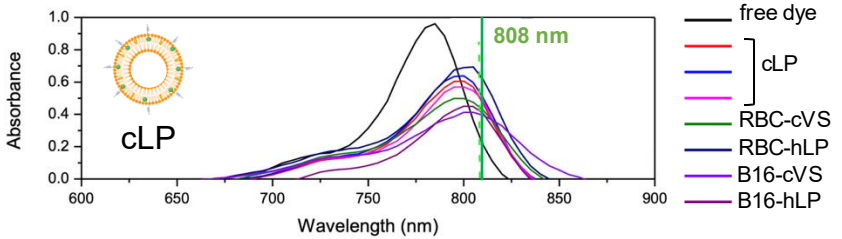
- At 4 hours, cNPs show higher uptake than hLPs, independent of membrane source.
- More rigid nanoparticles display greater uptake in both B16F10 and J774A.1 cells, suggesting membrane rigidity, rather than membrane origin alone, is a dominant factor in uptake efficiency.
- At this time point, membrane coating improves uptake over non-biomimetic particles only in macrophages.

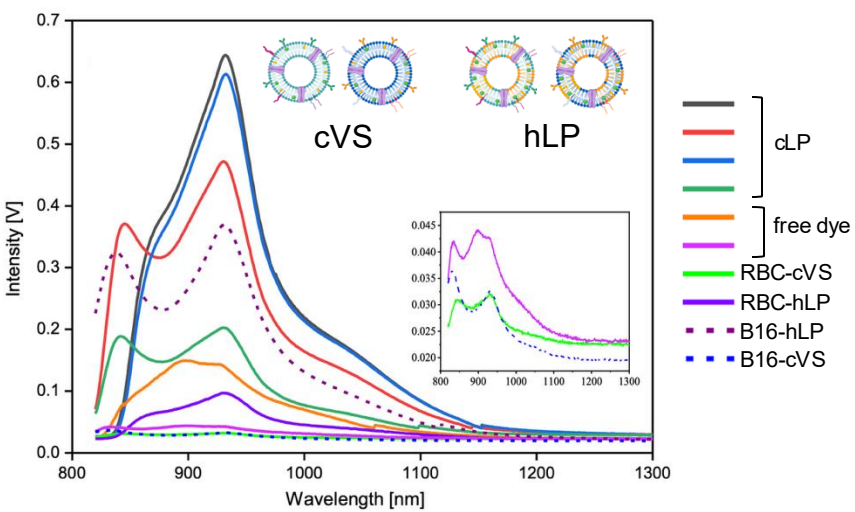
Biophysical outcome

Membrane rigidity enhances uptake, while membrane coating improves uptake only in specific cell types.

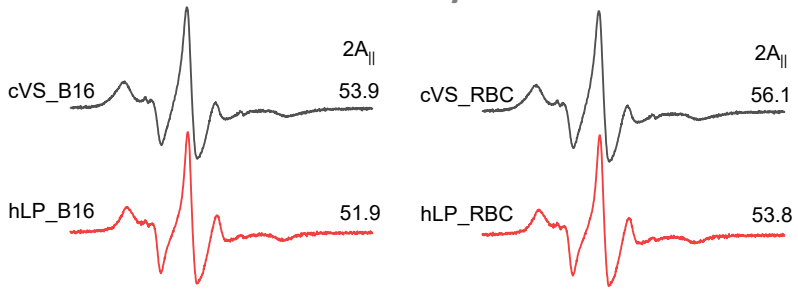
Photophysical aspects

UV-vis-NIR/Fluorescence analysis





ESR analysis



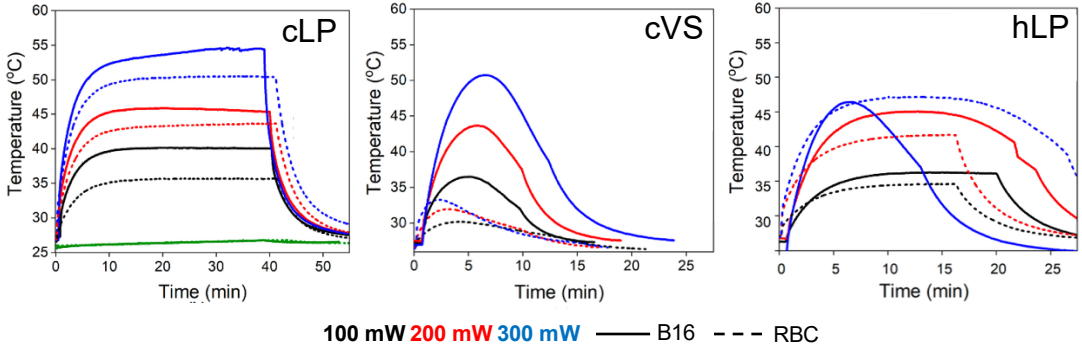
- hLP show stronger fluorescence emission and higher NIR absorbance than cVS, but lower than cLP, reflecting their intermediate membrane environment.
- cVS have more rigid membranes than hLP, causing stronger redshifts and greater quenching of IR780 fluorescence, likely due to membrane proteins and reduced dye mobility.
- cLP provide the highest photoluminescence, but hLP offer a better balance between imaging performance and biological relevance.

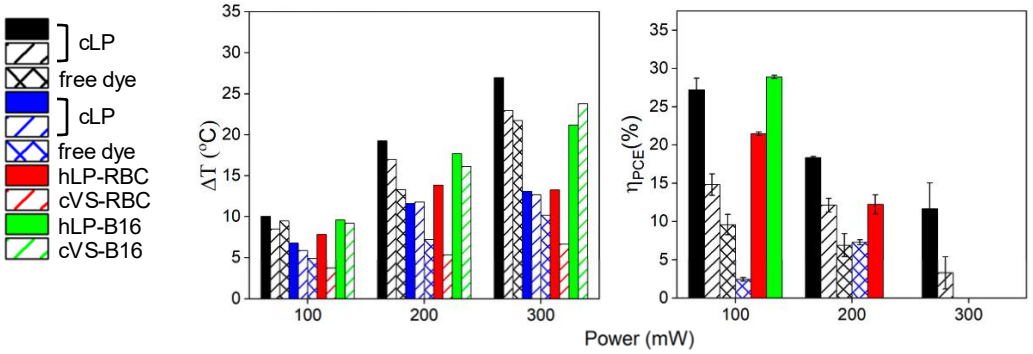
Biophysical outcome

Membrane rigidity reduces fluorescence and shifts optical properties

Photophysical aspects

PTT/PCE analysis





- hLP reach higher temperatures than cVS under laser irradiation, indicating better photothermal performance;
- cVS fail to reach therapeutic temperatures and photobleach earlier.
- cVS, show photobleaching at lower temperatures, while hLP resist photobleaching until surpassing 45 °C, reflecting greater thermal resilience.
- cLP outperform both hLP and cVS in photothermal conversion efficiency (PCE) but hLP maintain higher PCE than cVS, offering a functional balance between thermal performance and biomimicry.

Biophysical outcome

Rigid membranes reduce photothermal performance, while hybrid membranes enhance heat generation and stability

Take home message

- **Membrane hybridization increases rigidity, stability, and fusogenicity**, improving structural integrity and potential for controlled delivery.
- **Membrane rigidity enhances cellular uptake, especially** in cNPs, regardless of membrane origin.
- **Hybrid systems reduce protein adsorption**, achieving corona profiles similar to PEGylated controls.
- **Optical properties and photothermal performance are modulated by membrane structure**, with hybrid liposomes offering a balance between signal intensity and biological relevance.
- **Functional outcomes are governed more by membrane biophysics than by the membrane's cellular origin, highlighting the value of engineering physical state beyond simply choosing the source material.**

Acknowledgments

- Prof. Eliana M. Lima
  (Principal Investigator, FarmaTec)
- Prof. Andris F. Bakuzis
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- All students and technical staff from the FarmaTec group

For more about biophysics of hLP, cVs and cNP …

Membrane dynamics modulate the functional activity of biomimetic nanoparticles

Session: Nanomedicine and Nanoscale Delivery
Date/Time: Thursday, July 17 - 10:00 am-12:00 pm
Poster 115 hall E

Data Sharing Notice

Compositional, stability, protein interactions, and uptake data are currently under review — **please, do not share**.

Photophysical results have been published:
10.3390/pharmaceutics15020444

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