

Tech Session 3: Transdermal and Mucosal Delivery

A. Sofia Barros

CRS 2022 Annual Meeting & Expo

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

Advanced Delivery Science





Stimulus Responsive Nanosystem to Manage Inflammatory Bowel Disease

Tech Session 3: Transdermal and Mucosal Delivery

A. Sofia Barros, PhD Student

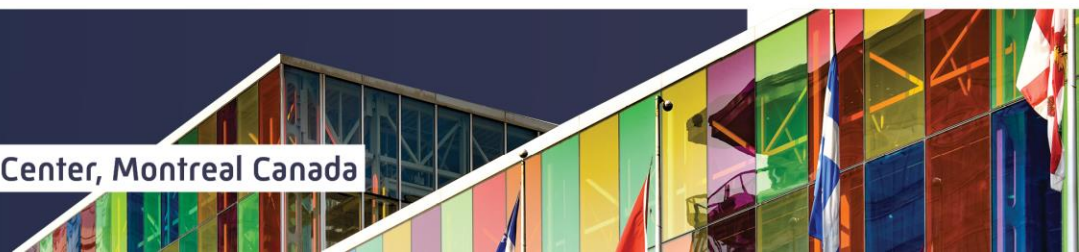
July 14, 2022 Montreal, Canada

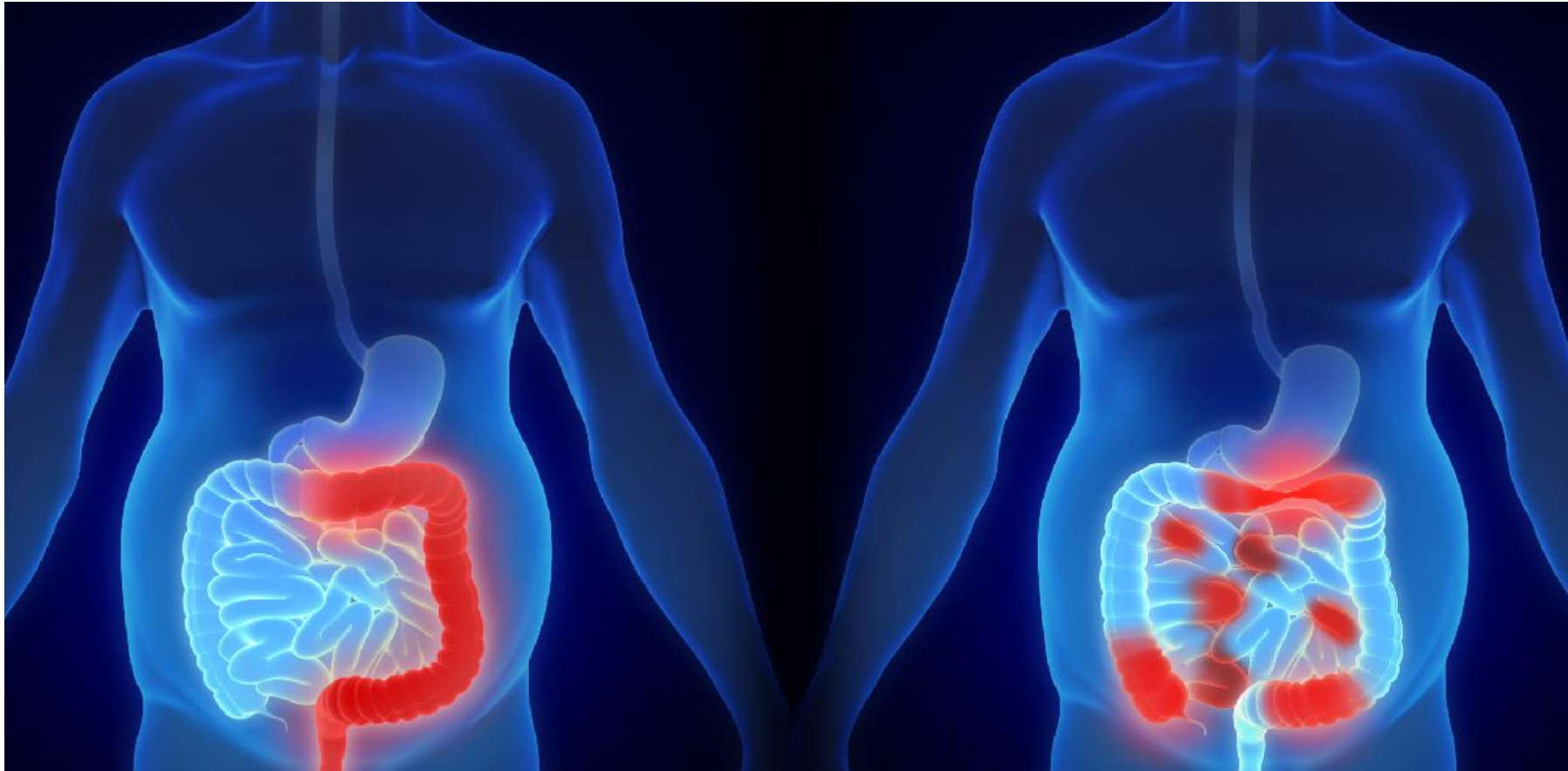


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Ulcerative colitis

Crohn's disease

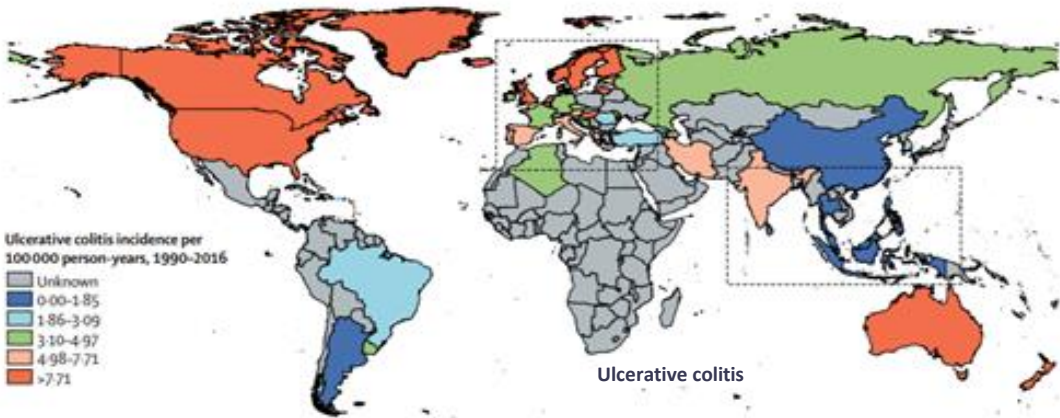
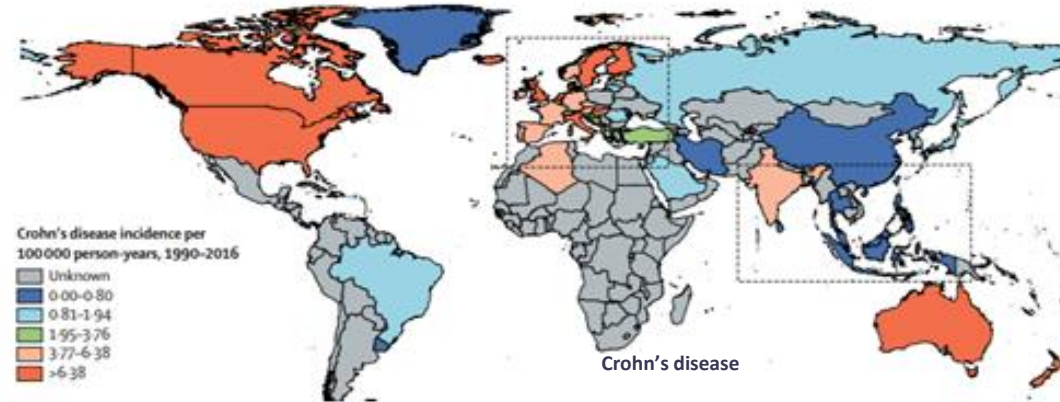


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**Portugal (2019):
0.05%**

**Europe (2020):
0.20%**

Santiago, M., et al., (2022). *Clinical and Translational Gastroenterology*, 13(5).
Zhao, M., et al., (2021). *Journal of Crohn's and Colitis*, 15(9).



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There is no cure for IBD!!!

Europe (2020):
0.20%

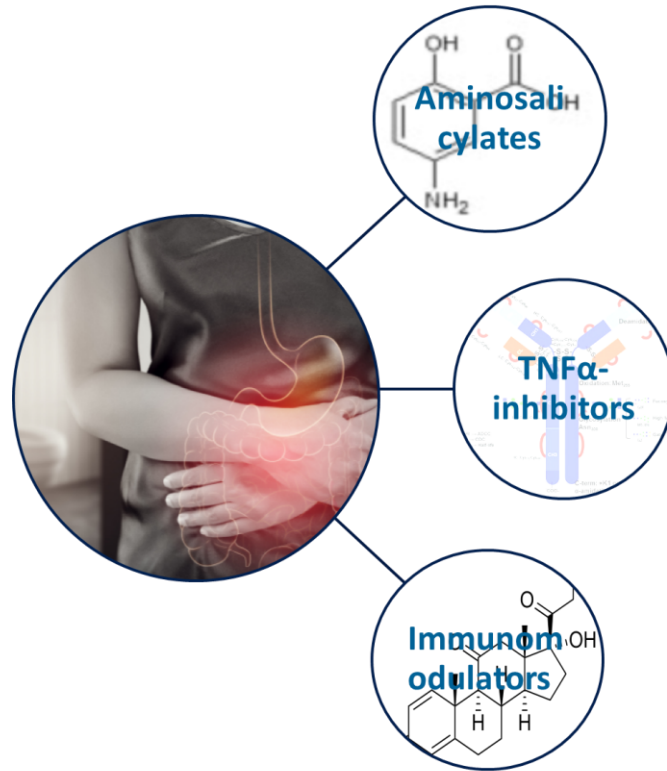


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Ineffective;

**Significant
infectious
and
neoplastic
side effects.**

✓ The current treatment options are often impaired by serious adverse effects and limited therapeutic efficacy.



Nanomedicine





Nanomedicine



PLGA matrix



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Nanomedicine

Peptides



PLGA matrix

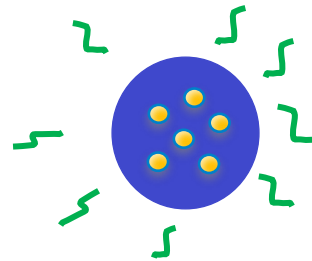




Nanomedicine



PLGA matrix



PEGylation

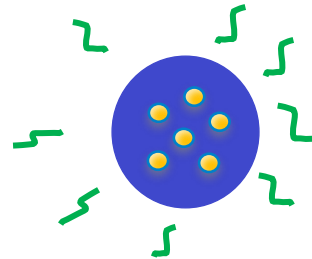




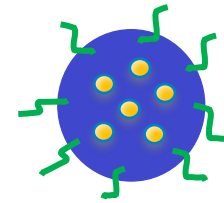
Nanomedicine



PLGA matrix



PEGylation

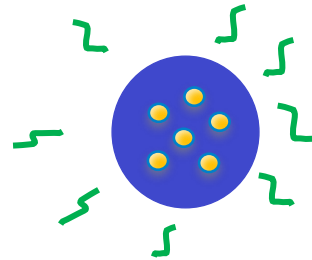




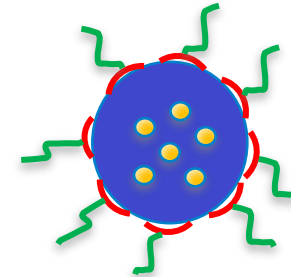
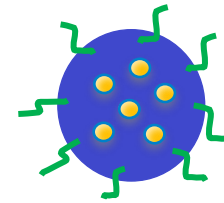
Nanomedicine



PLGA matrix

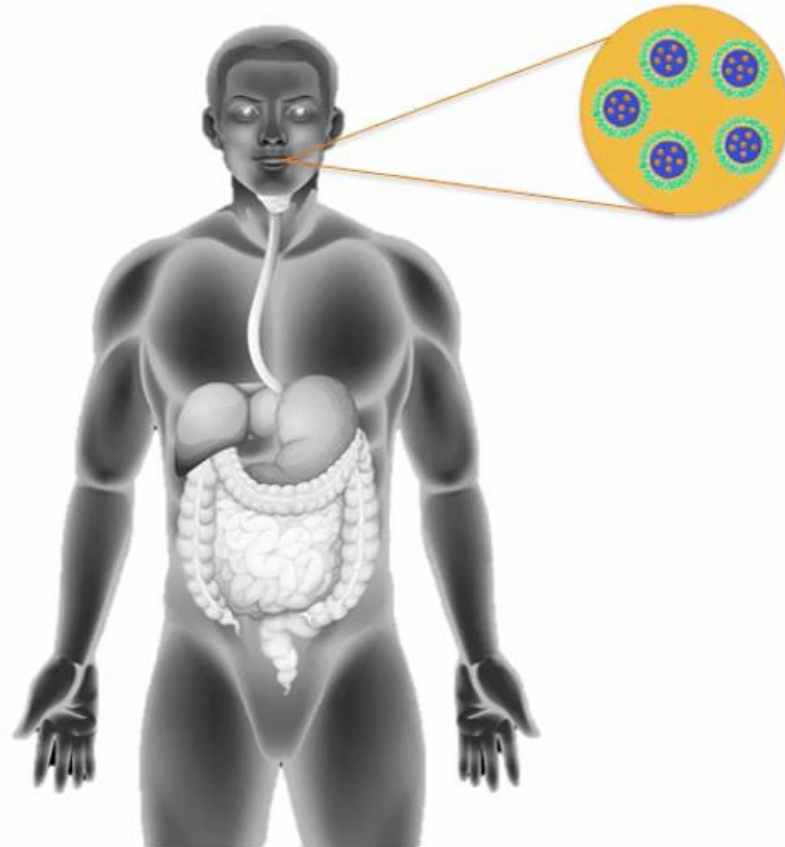


PEGylation



Stimulus-responsive linker



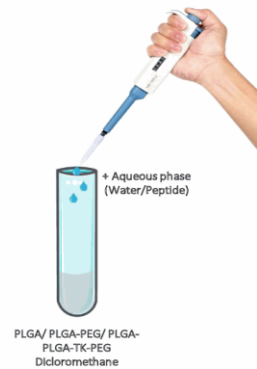


-  cPEG-NPs
-  cPEG-NPs-in-OPs
-  PEG
-  Thioketal linker
-  PLGA
-  Peptide
-  Immune cells



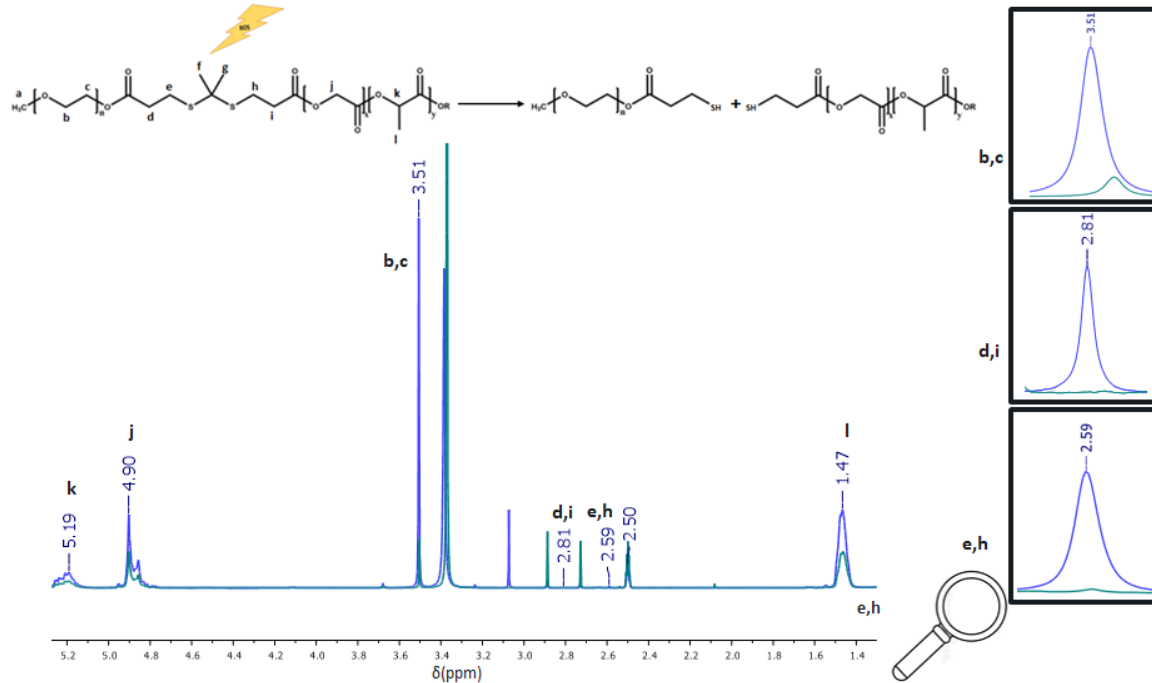
1. NPs production and characterization

Samples	Size-Average (nm)	PDI	ZP (mV)	Quantification method	AE (%)	DL (%)
Empty mPEG-TK-PLGA:PLGA NPs	194 ± 7	0.125 ± 0.029	-1.6 ± 0.2	---	---	---
Peptide-loaded mPEG-TK-PLGA:PLGA NPs	222 ± 4	0.217 ± 0.036	-0.8 ± 0.3	HPLC	71 ± 14	7.1 ± 1.4

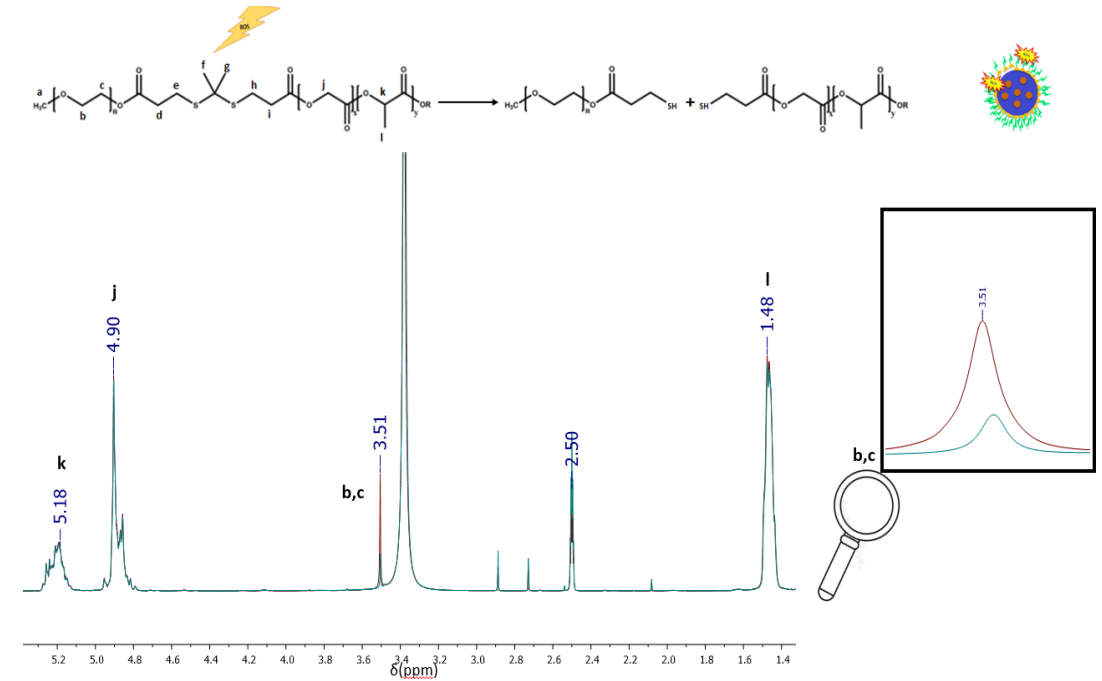


2. TK linker ROS-responsive profile

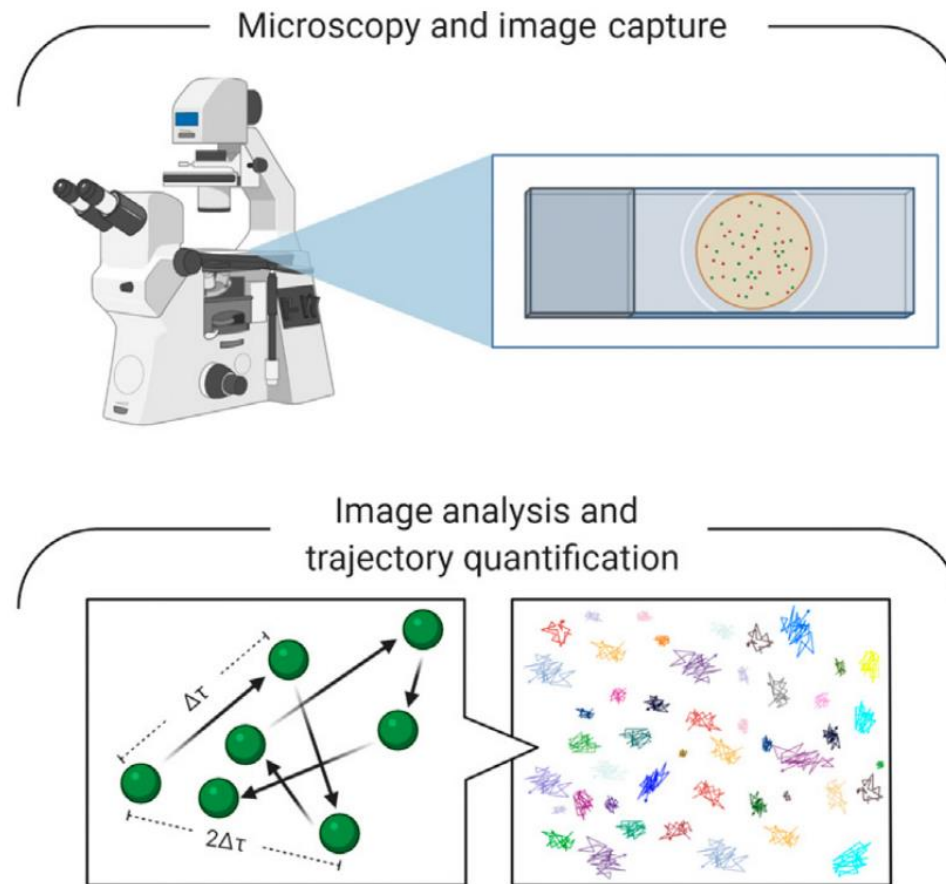
Co-polymer



NPs



3. Interaction of NPs with mucus



Zierden, H. C., et al., (2021). *Trends in Molecular Medicine*, 27(5), 436-450.

3. Interaction of NPs with mucus



Check
poster
259!!

Zierden, H. C., et al., (2021). *Trends in Molecular Medicine*, 27(5), 436-450.



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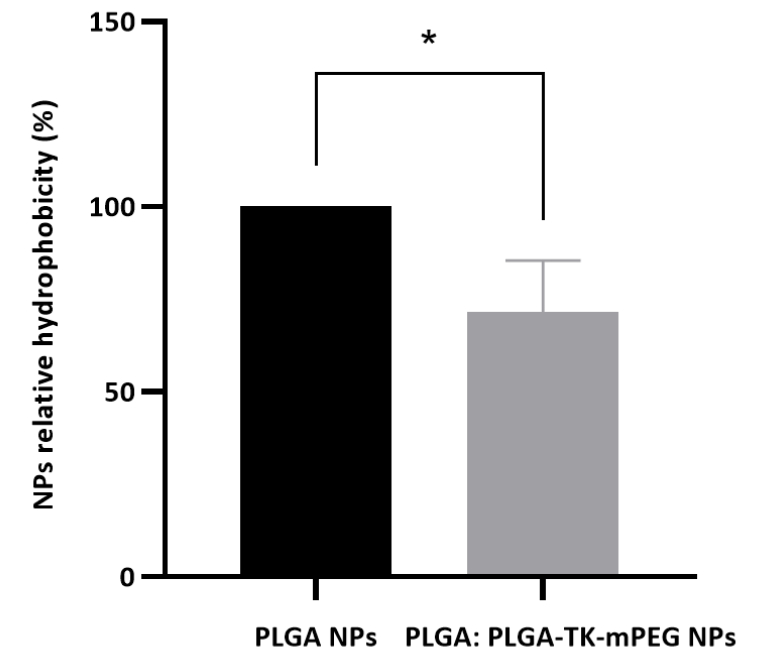
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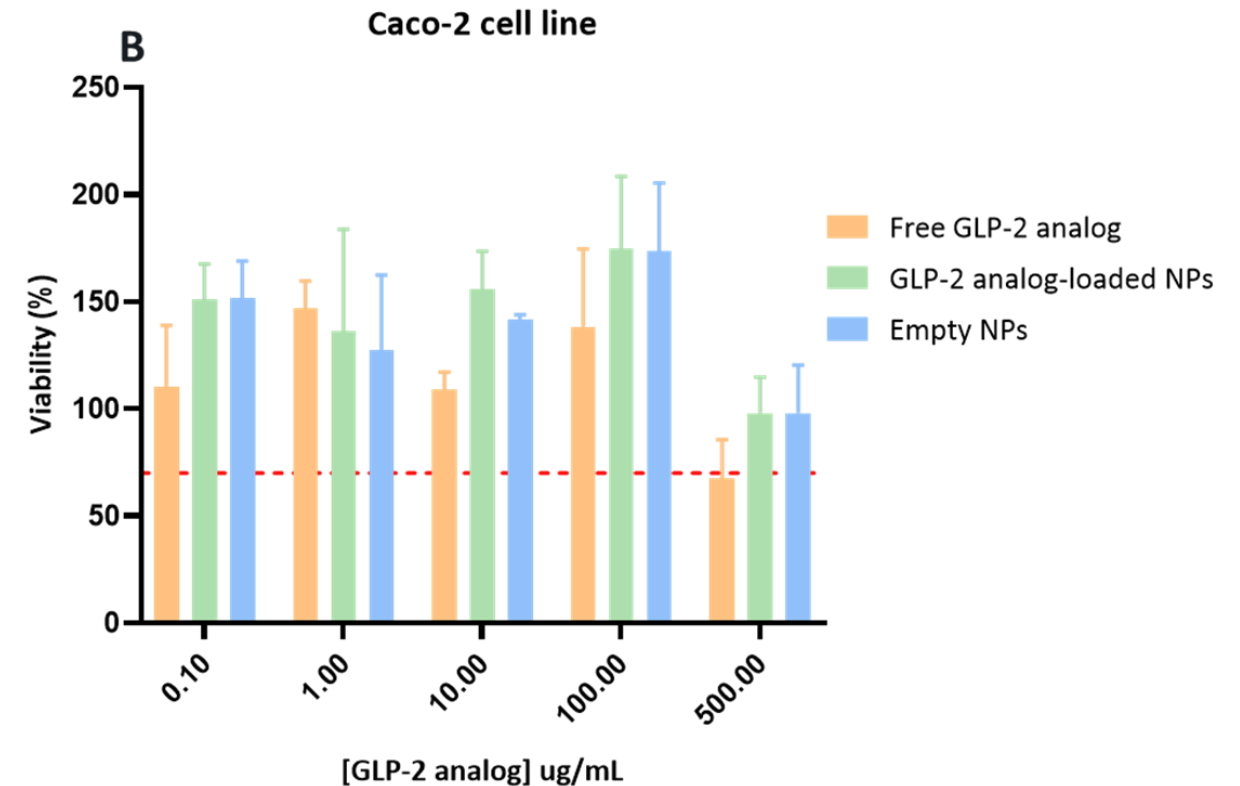
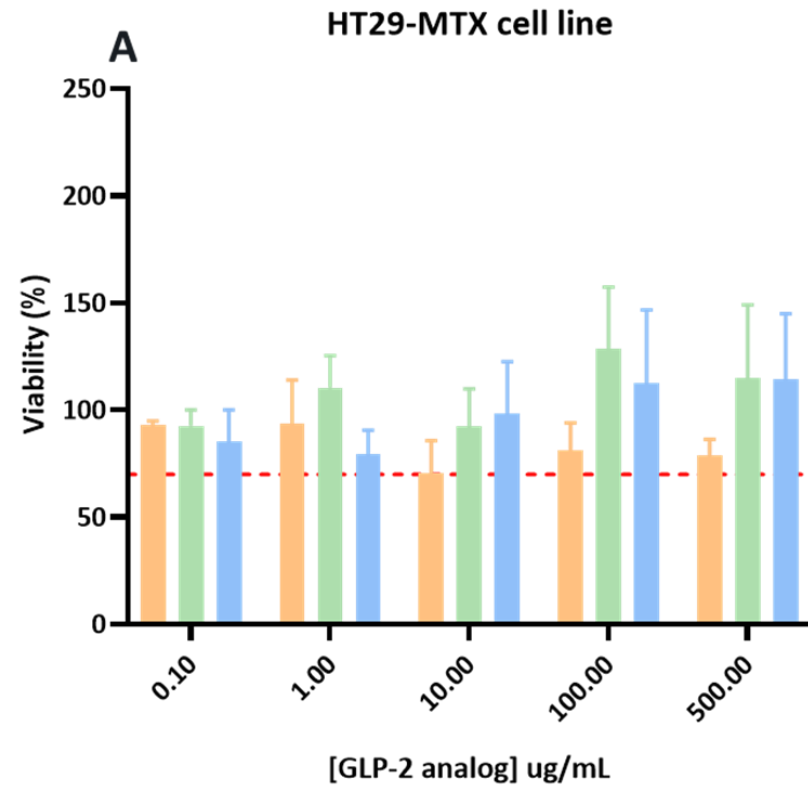


3. Interaction of NPs with mucus

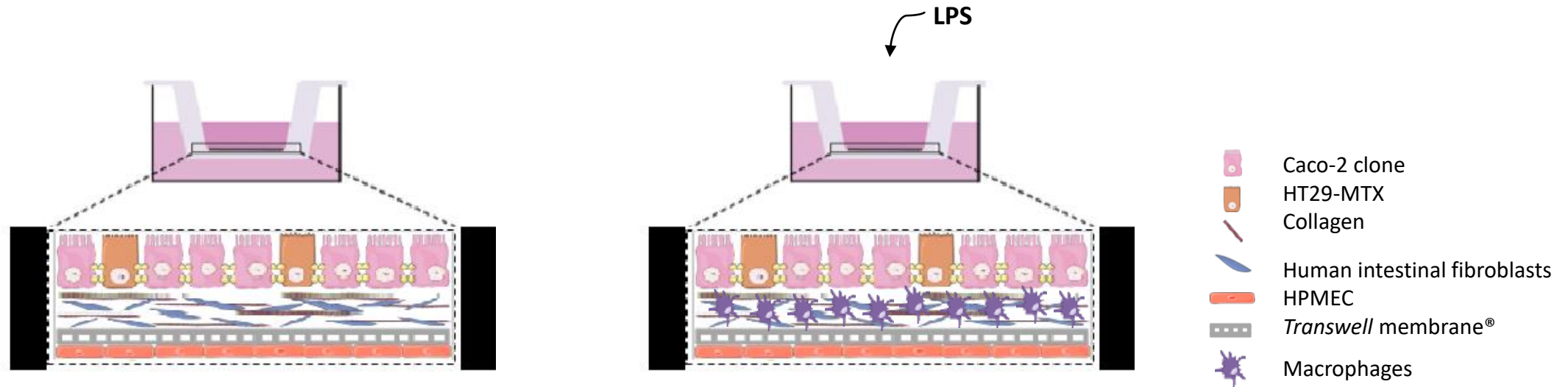
Transport Mode	α	PLGA:PLGA-Rho		PLGA: mPEG-PLGA: PLGA-Rho		PLGA: PLGA-TK-mPEG: PLGA-Rho	
Immobile	0.000-0.199	<slope> = STD =	0.769 0.121	<slope> = STD =	0.650 0.342	<slope> = STD =	0.523 0.056
Sub-diffusive	0.200-0.899						
Diffusive	0.900-1.199						
Active	1.200+						



4. Interaction of NPs with cells



4. Interaction of NPs with cells



Contents lists available at ScienceDirect

Journal of Controlled Release

journal homepage: www.elsevier.com/locate/jconrel



All layers matter: Innovative three-dimensional epithelium-stroma-endothelium intestinal model for reliable permeability outcomes

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- ✓ Developed cleavable PEGylated nanosystems present suitable characteristics for intestinal drug delivery;
- ✓ The ability to lose the PEG chains once in the presence of ROS was achieved;
- ✓ Nanosystems are safe for intestinal cell lines in the tested concentrations.

Thus, the proposed nanosystems present potential to be used for the oral delivery of therapeutic GLP-2 analogs for IBD treatment.



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Acknowledgments



Supervisors:

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Co-supervisor Dr. Rute Nunes



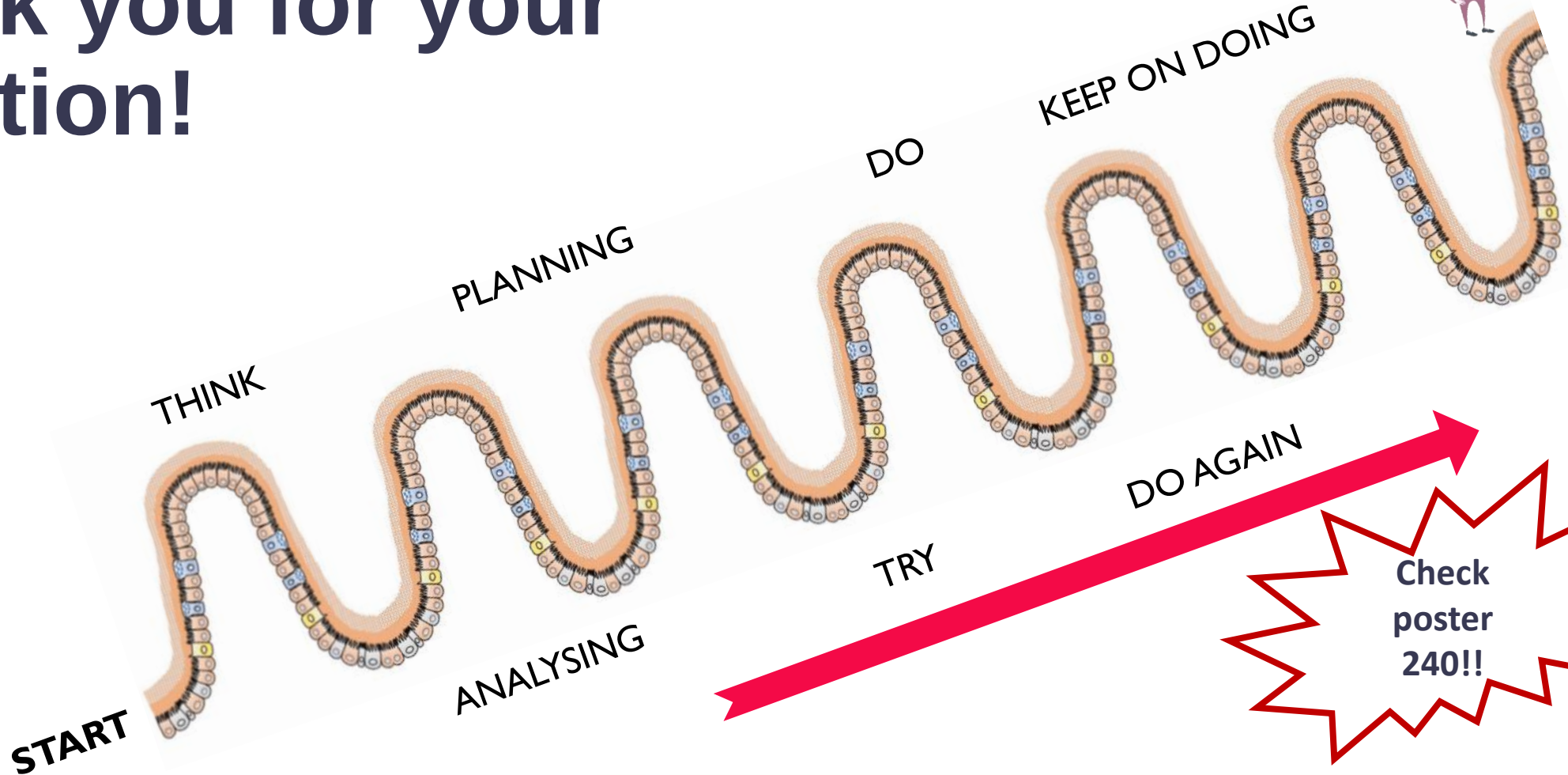
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Thank you for your attention!



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Samples	Production method	Size (nm)	PDI	ZP (mV)
75 PLGA: 25 PLGA-Rho	Nanoprecipitation (water with 0.1% Tween80)	152 ± 2	0.101 ± 0.012	-46.83 ± 2.02
65 PLGA: 10 PLGA-PEG: 25 PLGA-Rho	Nanoprecipitation (water)	125 ± 2	0.097 ± 0.013	-13.23 ± 1.21
65 PLGA: 10 PLGA-TK-PEG: 25 PLGA-Rho B	Nanoprecipitation (water)	164 ± 2	0.094 ± 0.001	-8.26 ± 0.36
50 PLGA: 25 PLGA-TK-PEG: 25 of PLGA-Rho	Nanoprecipitation (water)	69 ± 1	0.159 ± 0.013	-21.20 ± 0.93
25 PLGA: 50 PLGA-TK-PEG: 25 PLGA-Rho	Nanoprecipitation (water)	72 ± 1	0.114 ± 0.003	-13.60 ± 0.62
75 PLGA-TK-PEG: 25 PLGA-Rho	Nanoprecipitation (water)	85 ± 0	0.124 ± 0.012	-7.62 ± 0.33



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