



An Oral Nanoparticle-embedding Hydrogel for Targeted cGAS-STING Inhibition in Inflammatory Bowel Disease

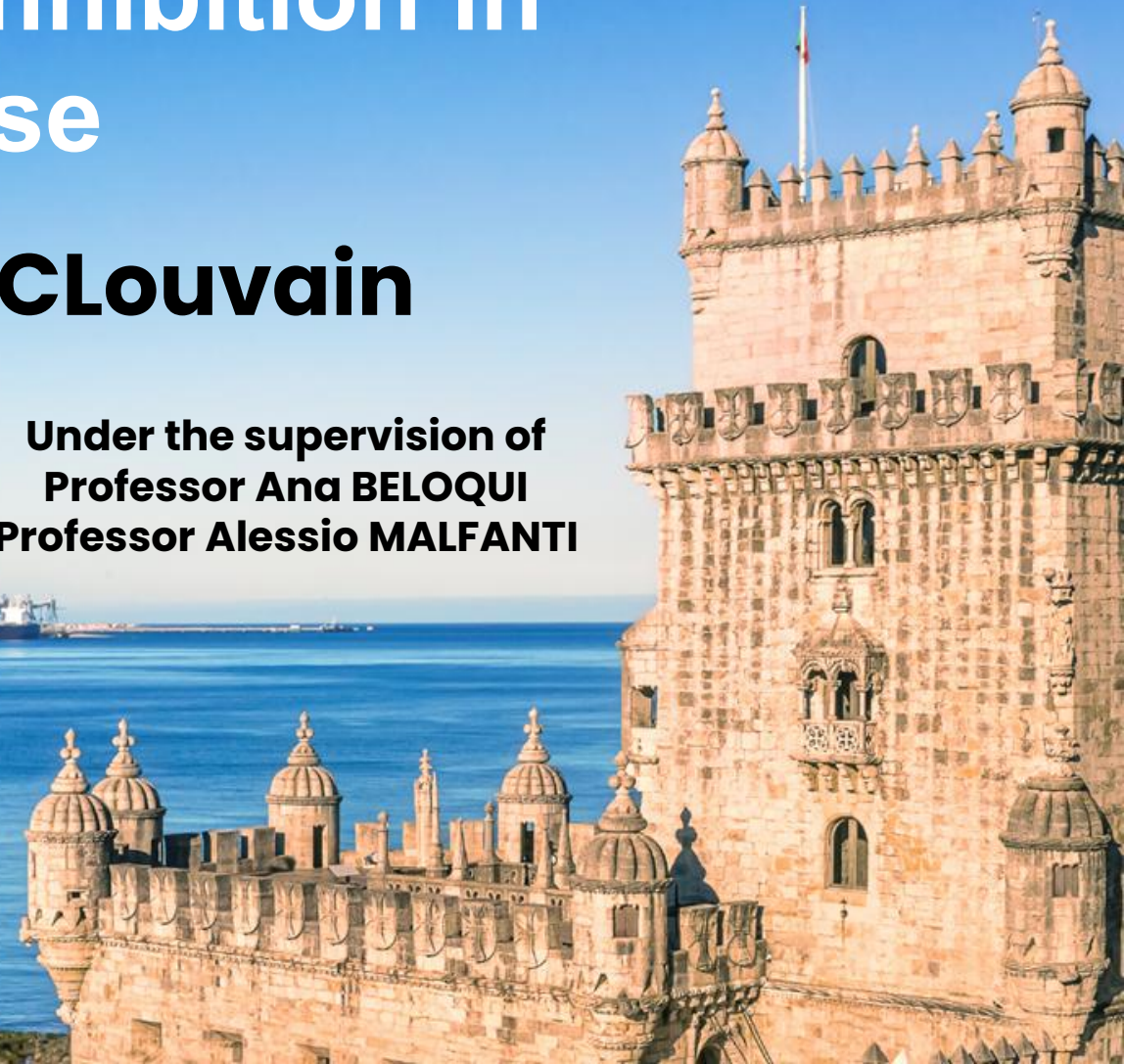
Léo GUILBAUD, PhD Student, UCLouvain

**Under the supervision of
Professor Ana BELOQUI
Professor Alessio Malfanti**

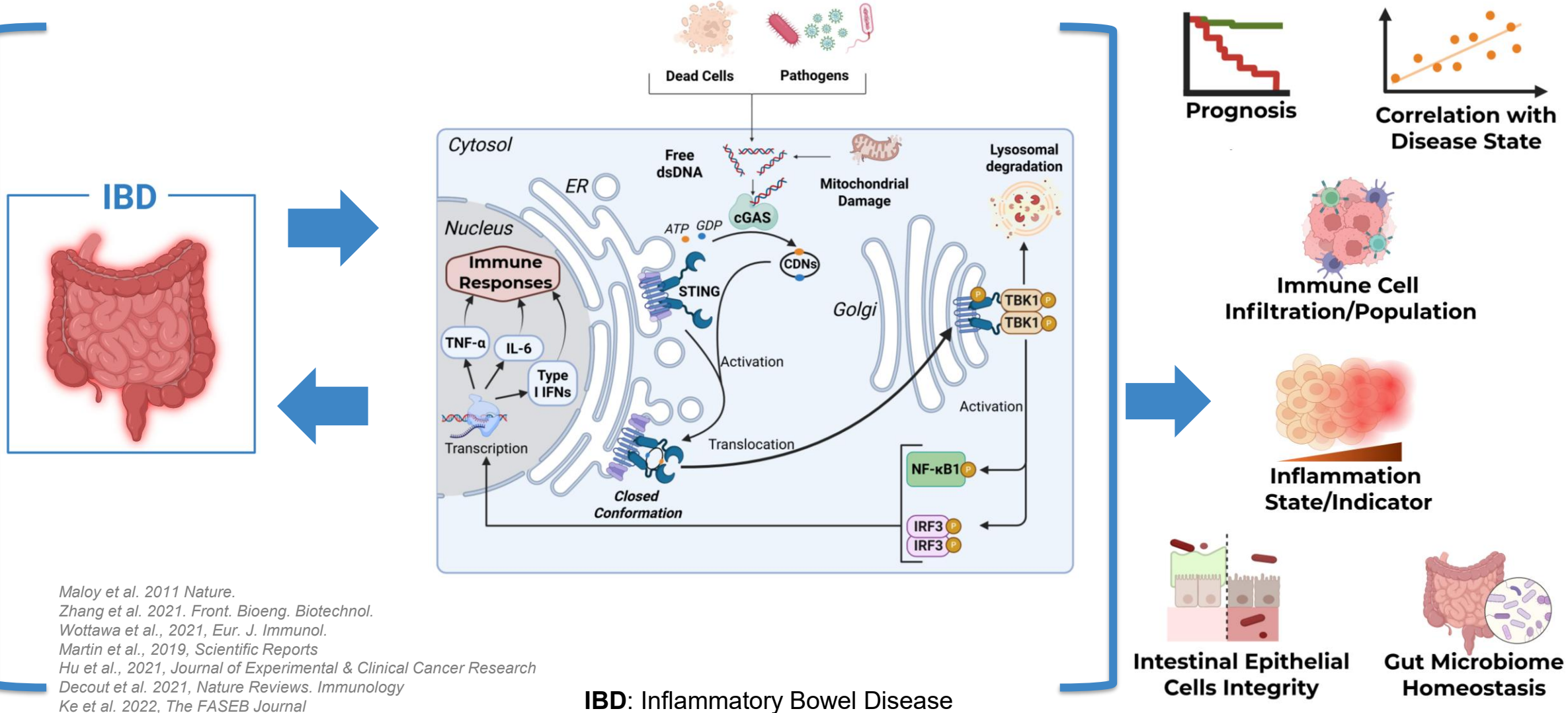
 **CRS2026**
ANNUAL MEETING & EXPOSITION
LISBON
— PORTUGAL —

MULTISECTOR
INNOVATION
for ADVANCING
DELIVERY SCIENCE

JULY 6-9, 2026

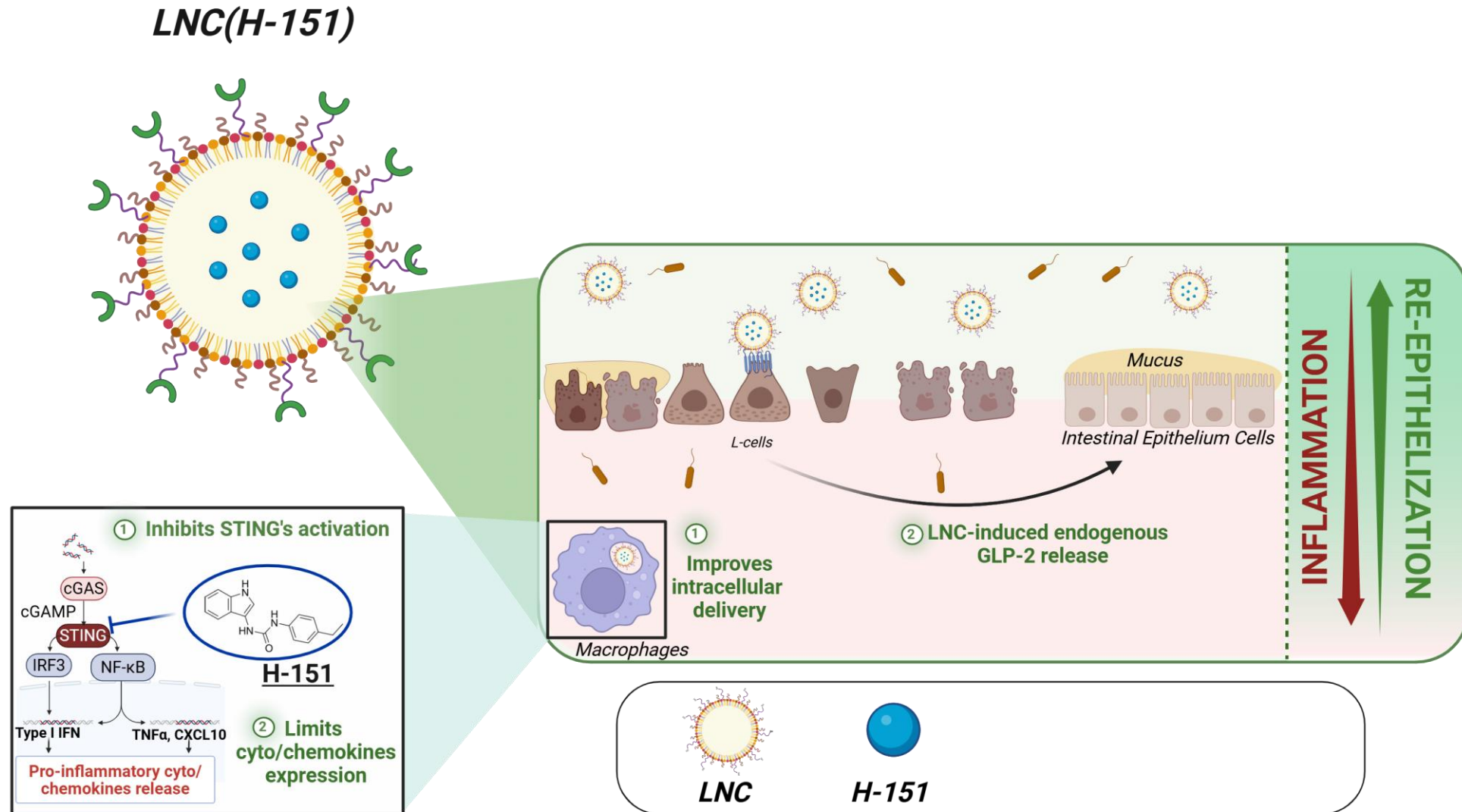


From DNA Sensing to Gut Inflammation: The cGAS-STING Axis in IBD

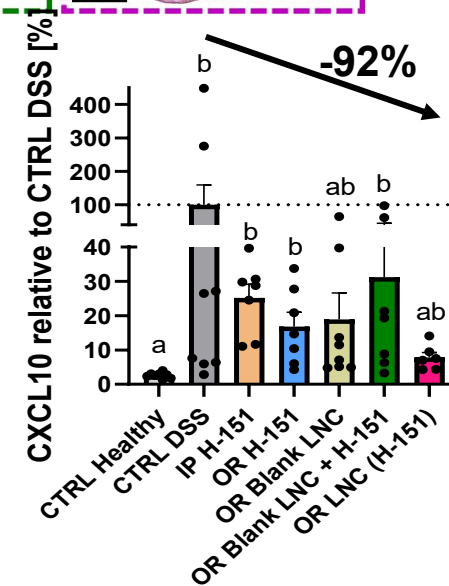
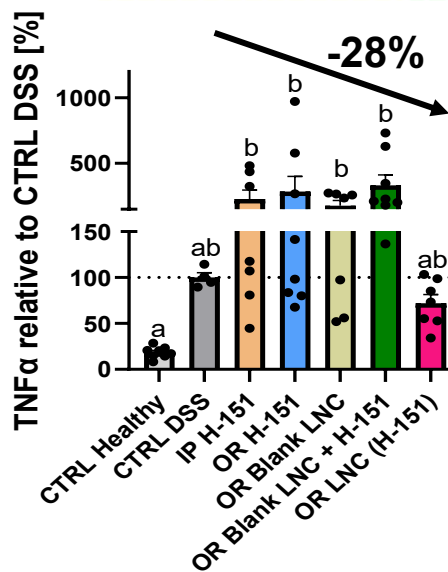
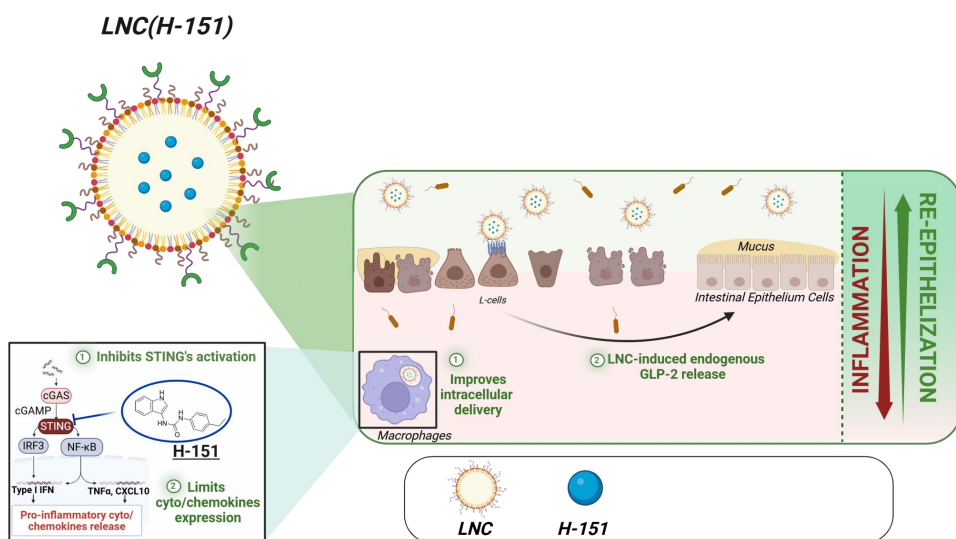
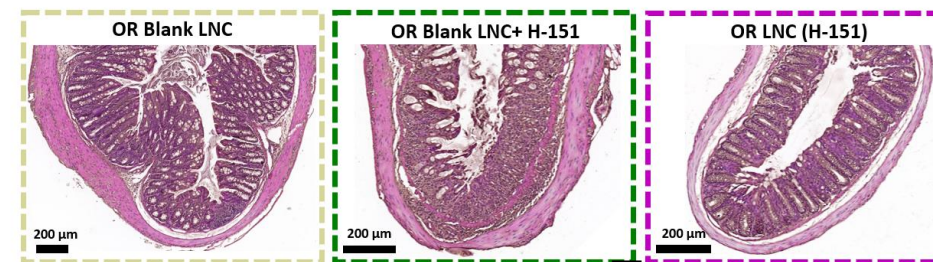
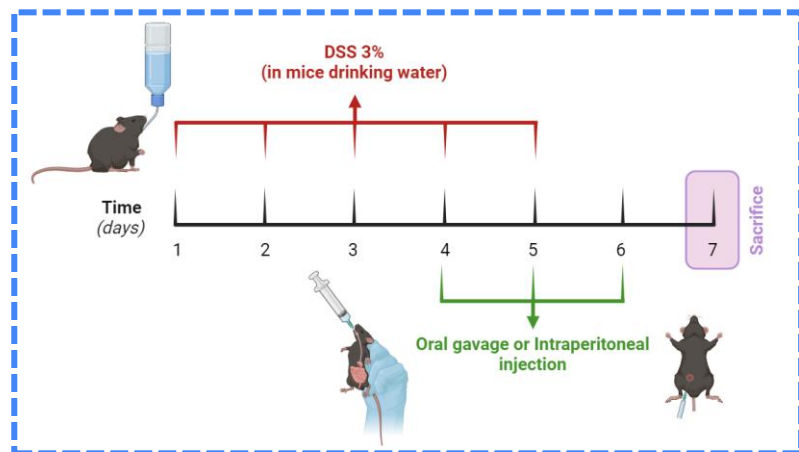


Maloy et al. 2011 Nature.
 Zhang et al. 2021. Front. Bioeng. Biotechnol.
 Wottawa et al., 2021, Eur. J. Immunol.
 Martin et al., 2019, Scientific Reports
 Hu et al., 2021, Journal of Experimental & Clinical Cancer Research
 Decout et al. 2021, Nature Reviews. Immunology
 Ke et al. 2022, The FASEB Journal

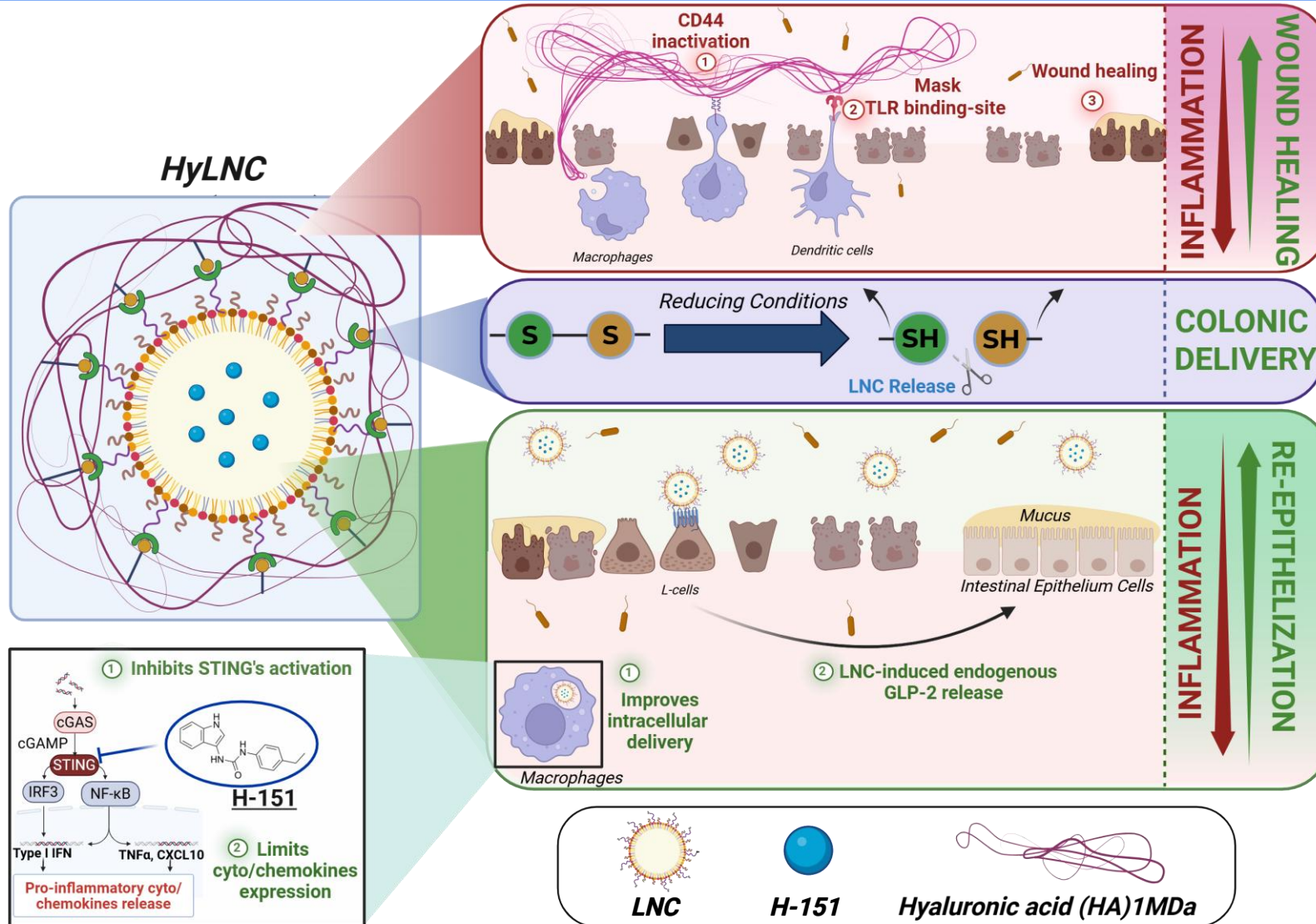
Dual-Effect Lipid Nanoparticles for cGAS-STING Inhibition in IBD



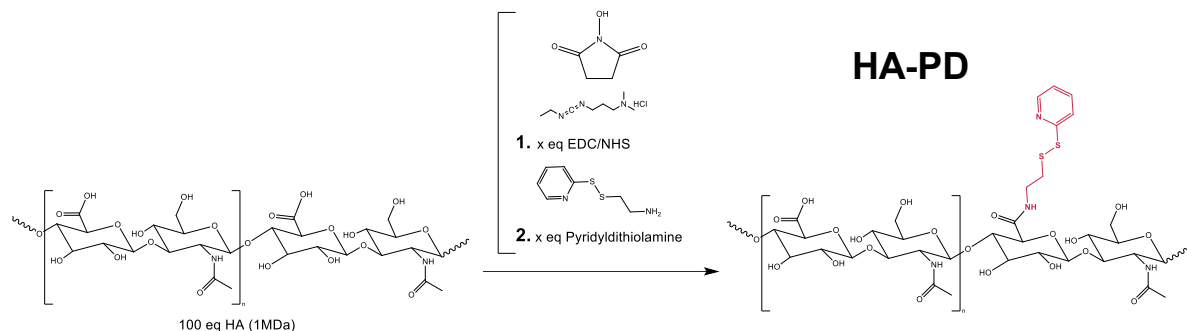
Oral LNC(H-151) are Alleviating Colitis in a DSS-induced Mice Model



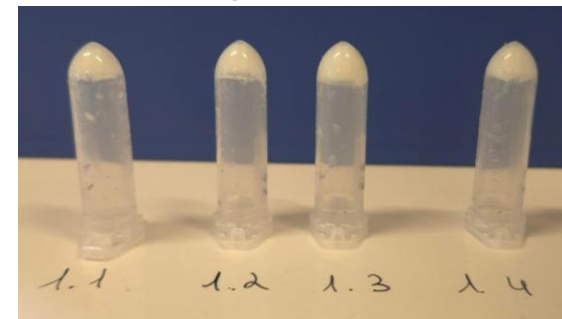
HyLNC for Localized and Prolonged Delivery of LNC(H-151)



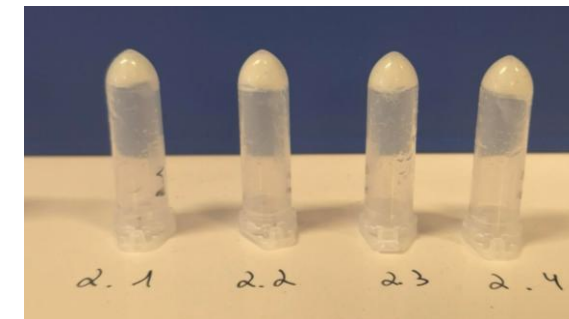
HA-PD and LNC-DSPE-PEG-SH are forming HyLNC



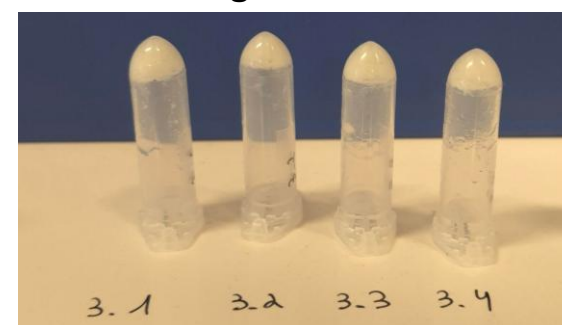
5 mg/mL of HA



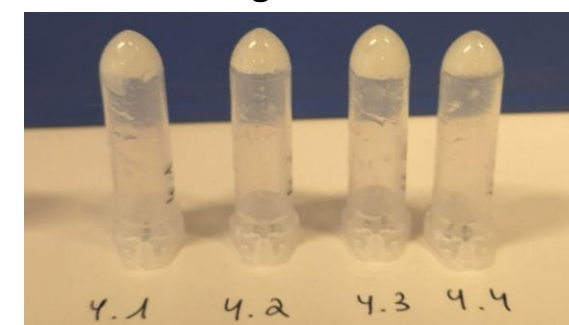
10 mg/mL of HA



15 mg/mL of HA



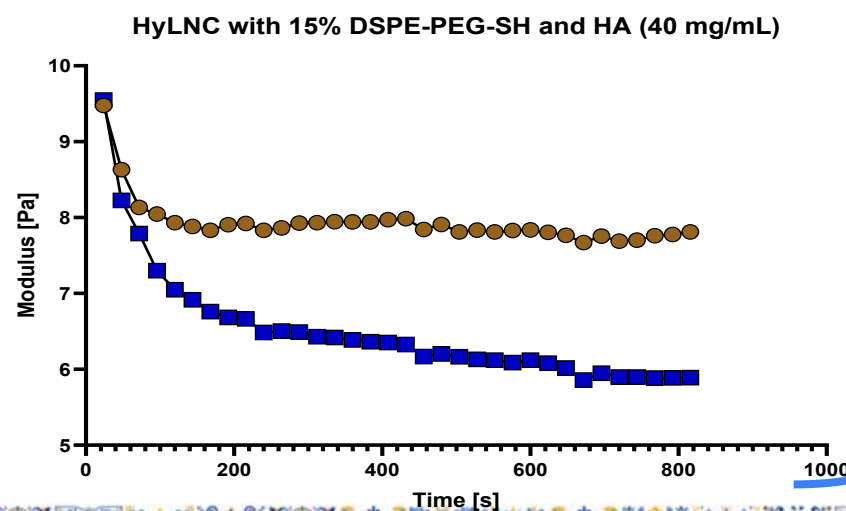
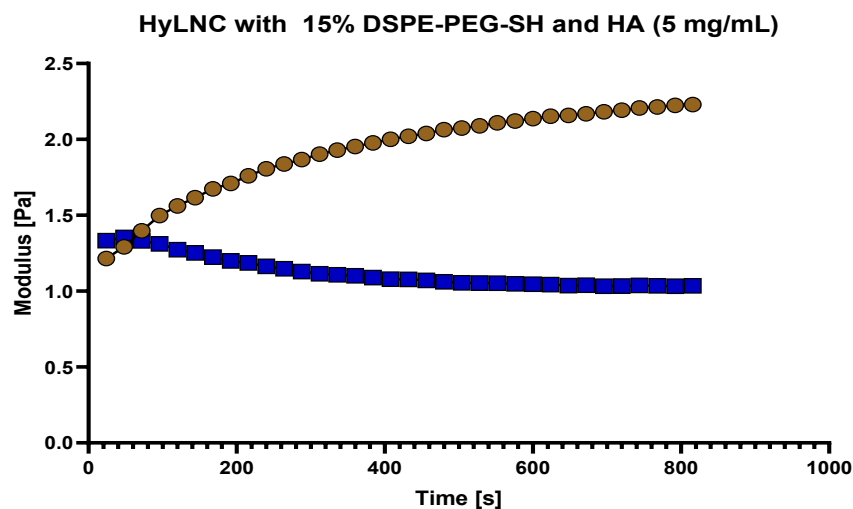
20 mg/mL of HA



Recipe	Size[nm] PDI [-]	Zeta Potential [mV]
LNC(H-151)-DSPE-PEG-SH 5%	170.1 ± 1.48 0.1165 ± 0.03	-15.17 ± 0.64
LNC(H-151)-DSPE-PEG-SH 10%	170.3 ± 2.04 0.0663 ± 0.04	-32.11 ± 0.28
LNC(H-151)-DSPE-PEG-SH 15%	179.2 ± 1.096 0.0971 ± 0.03	-34.69 ± 0.51

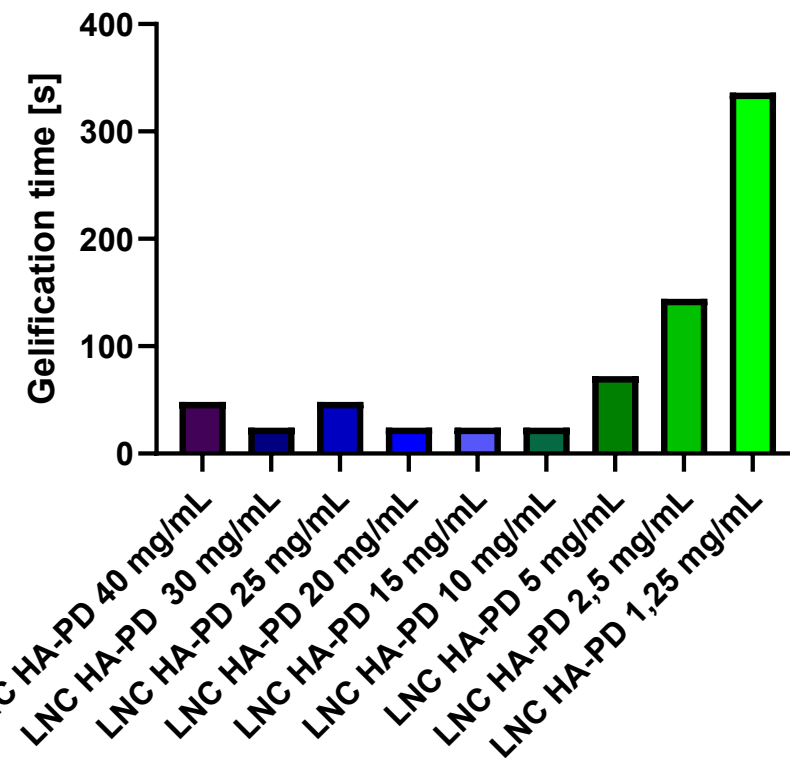


HyLNC are Forming Instantly After Mixing - Rheology



Gelification Point
Almost Instant
→ < 1 min

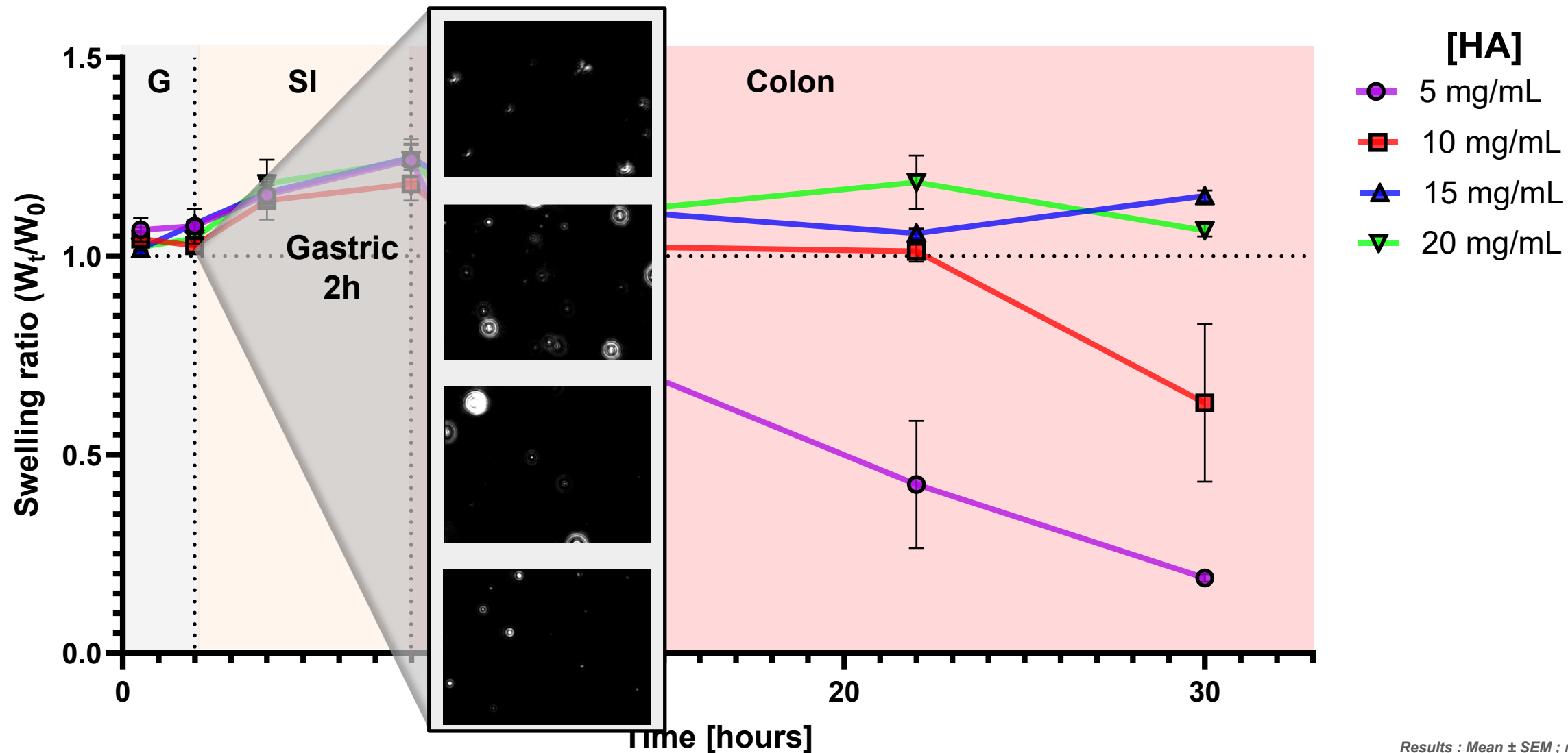
—●— Storage Modulus G'
—■— Loss Modulus G''



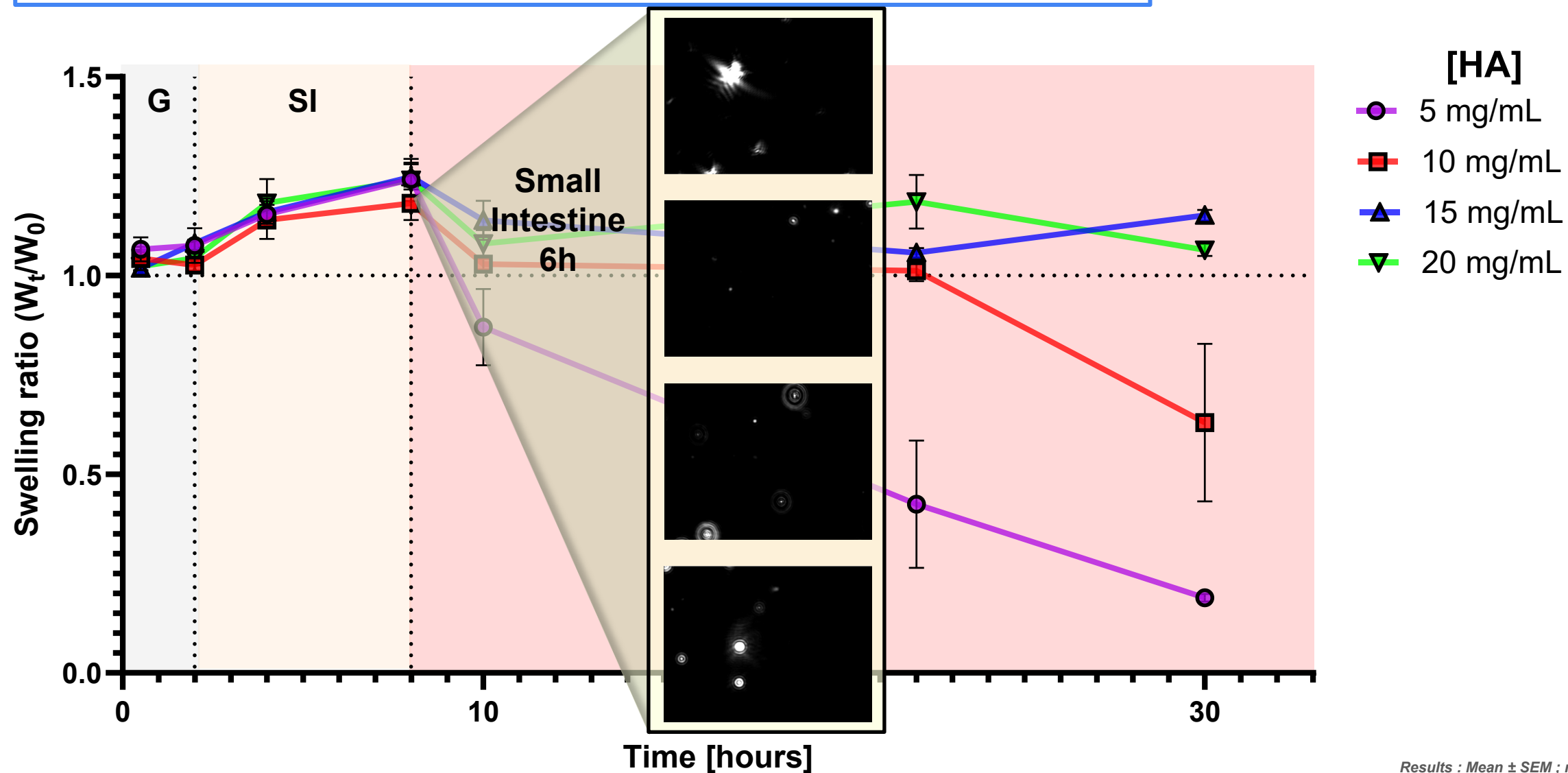
With [HA-PD] increasing → Gelification is happening faster then plateau

Results : Mean $\pm$ SEM ; $n=1$

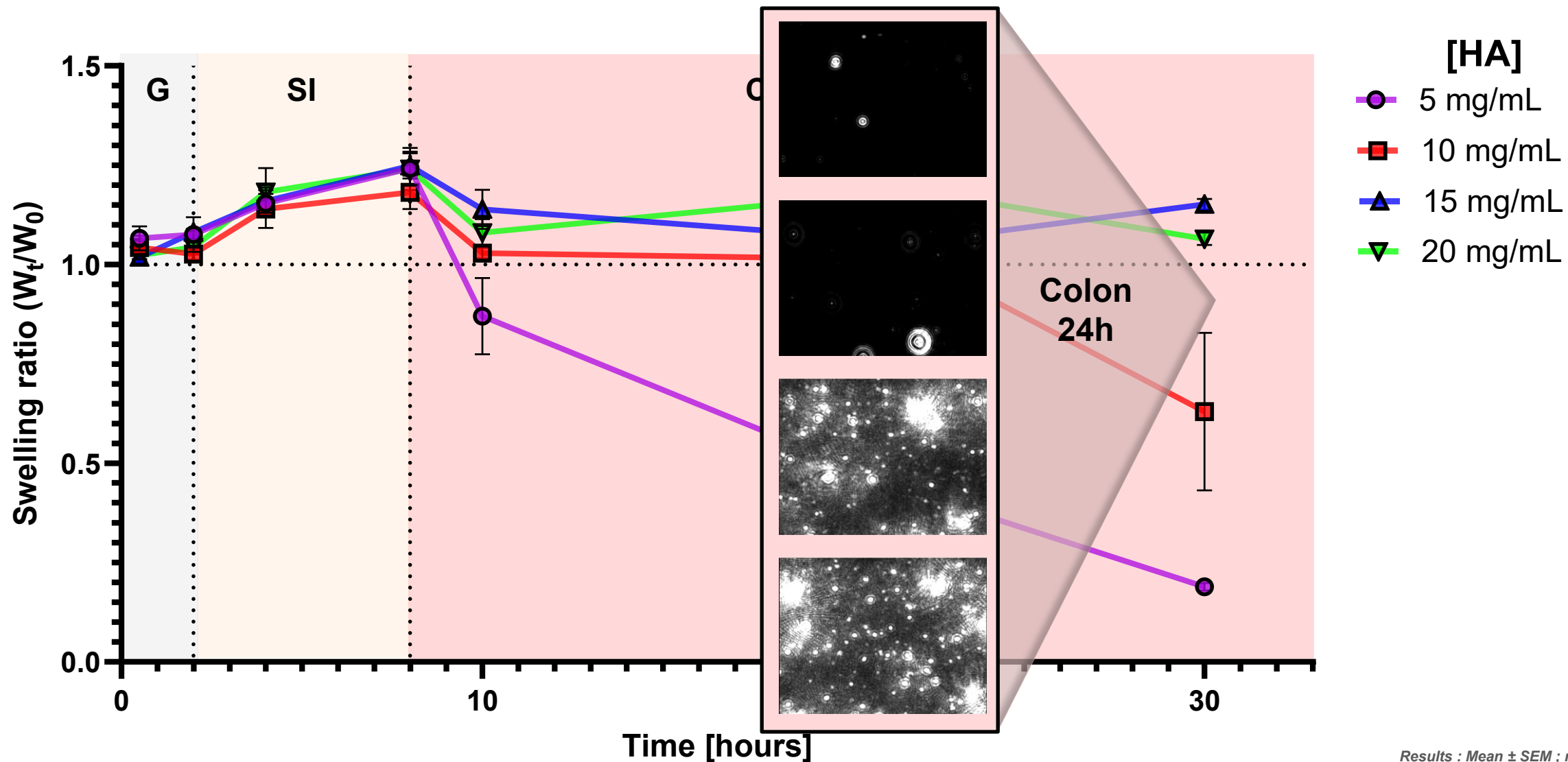
HyLNC (5mg/mL) and (10mg/mL) are Degraded in Colonic Fluid

Results : Mean $\pm$ SEM ; n= 3

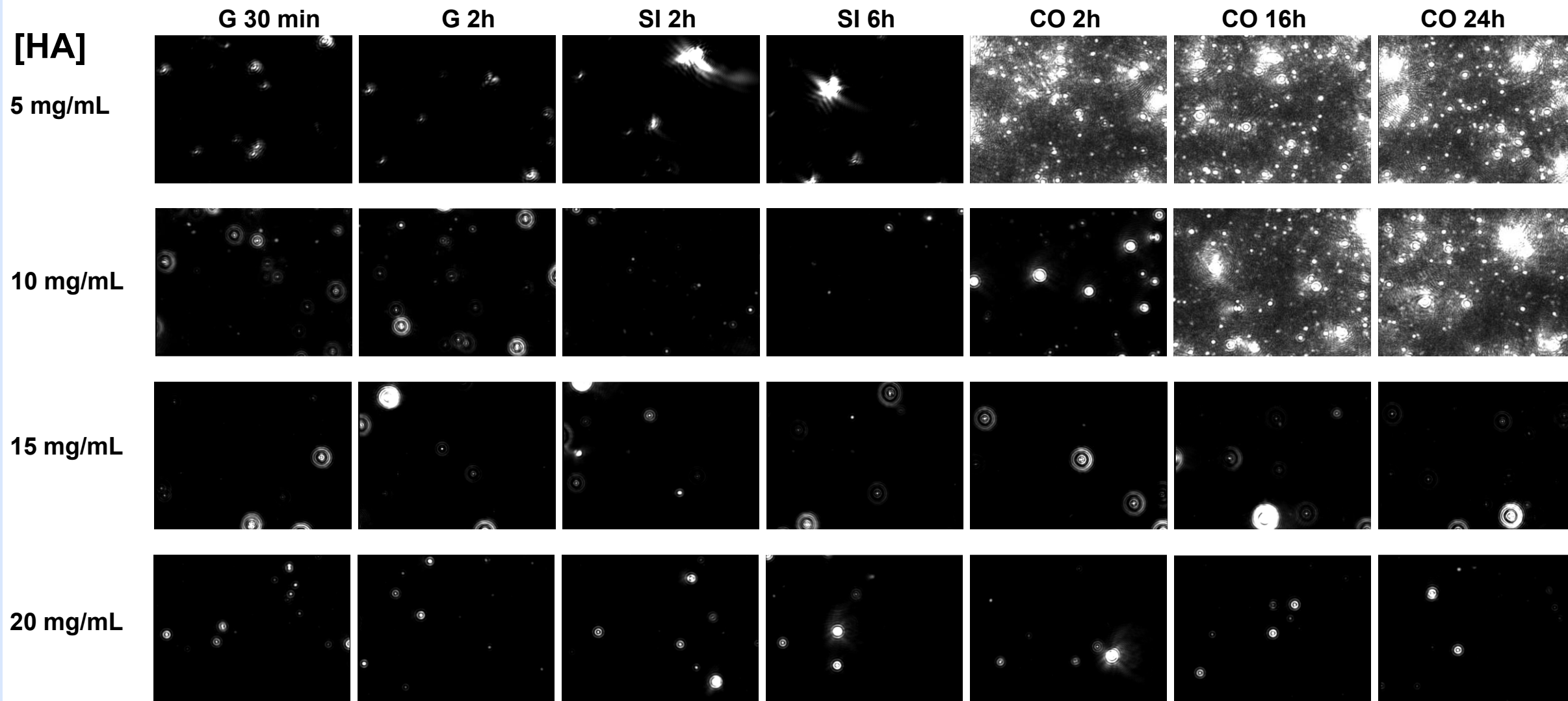
HyLNC (5mg/mL) and (10mg/mL) are Degraded in Colonic Fluid

Results : Mean $\pm$ SEM ; n= 3

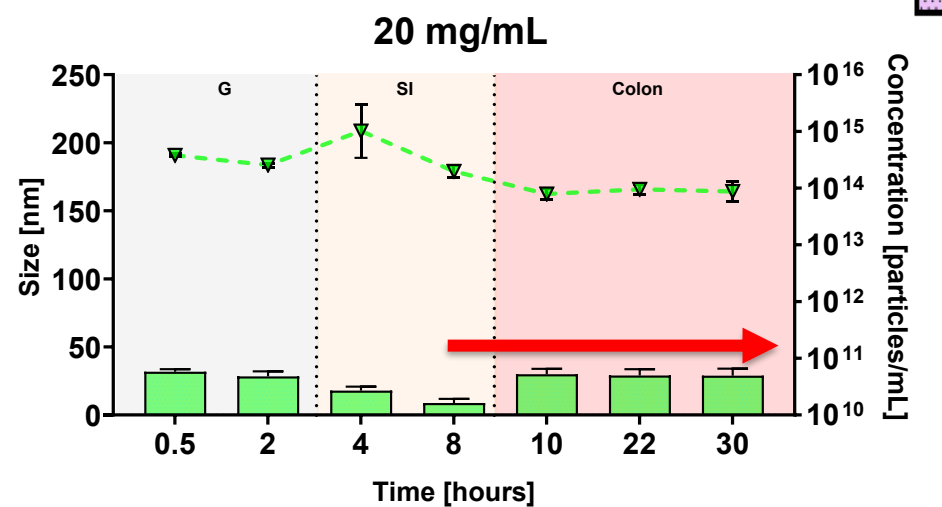
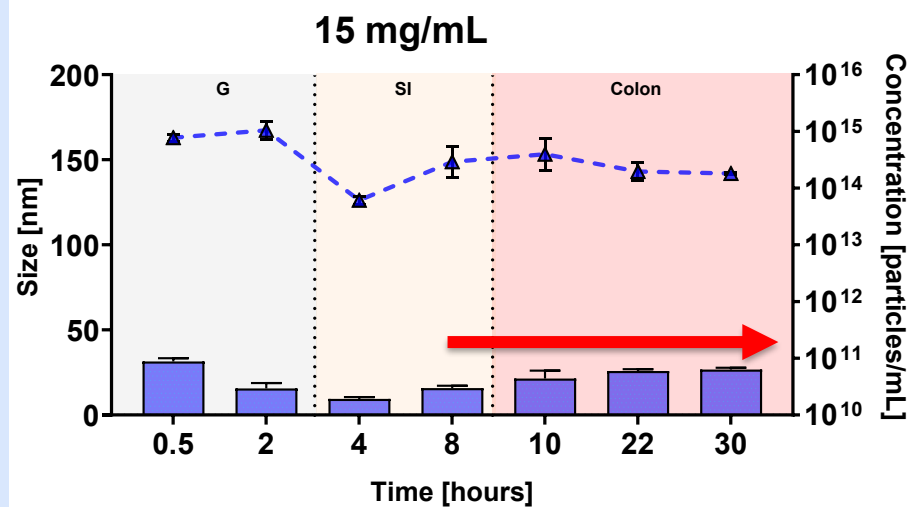
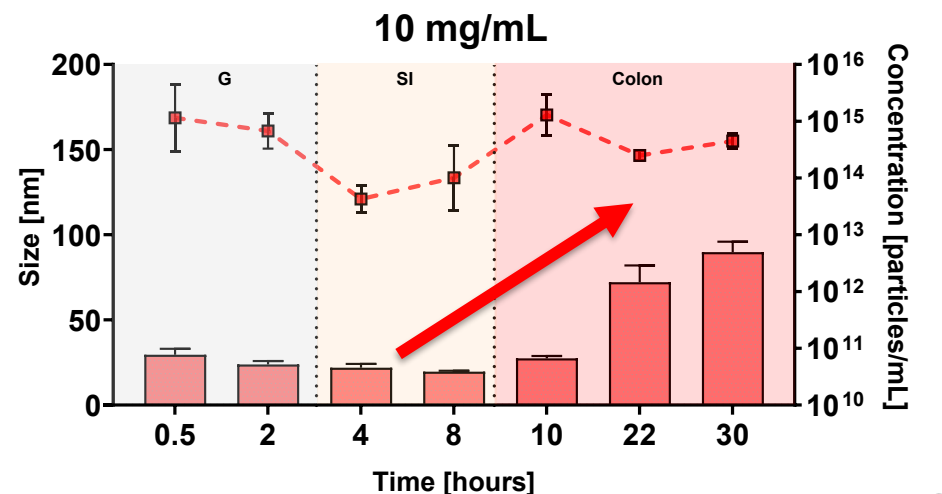
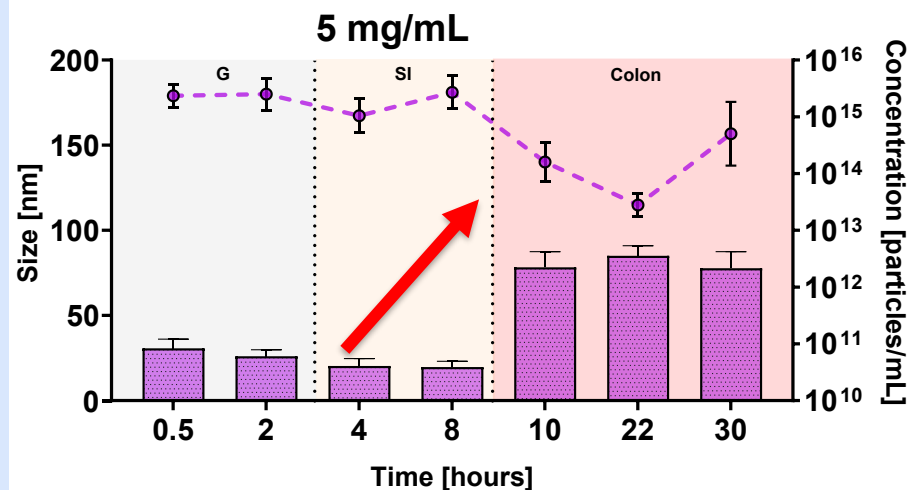
HyLNC (5mg/mL) and (10mg/mL) are Degraded in Colonic Fluid

Results : Mean $\pm$ SEM ; n = 3

NTA Results – Qualitative analysis



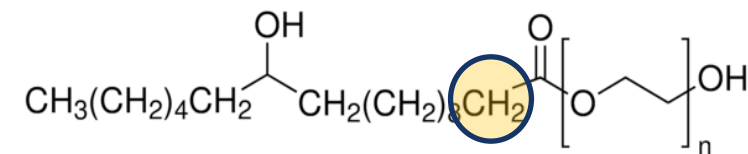
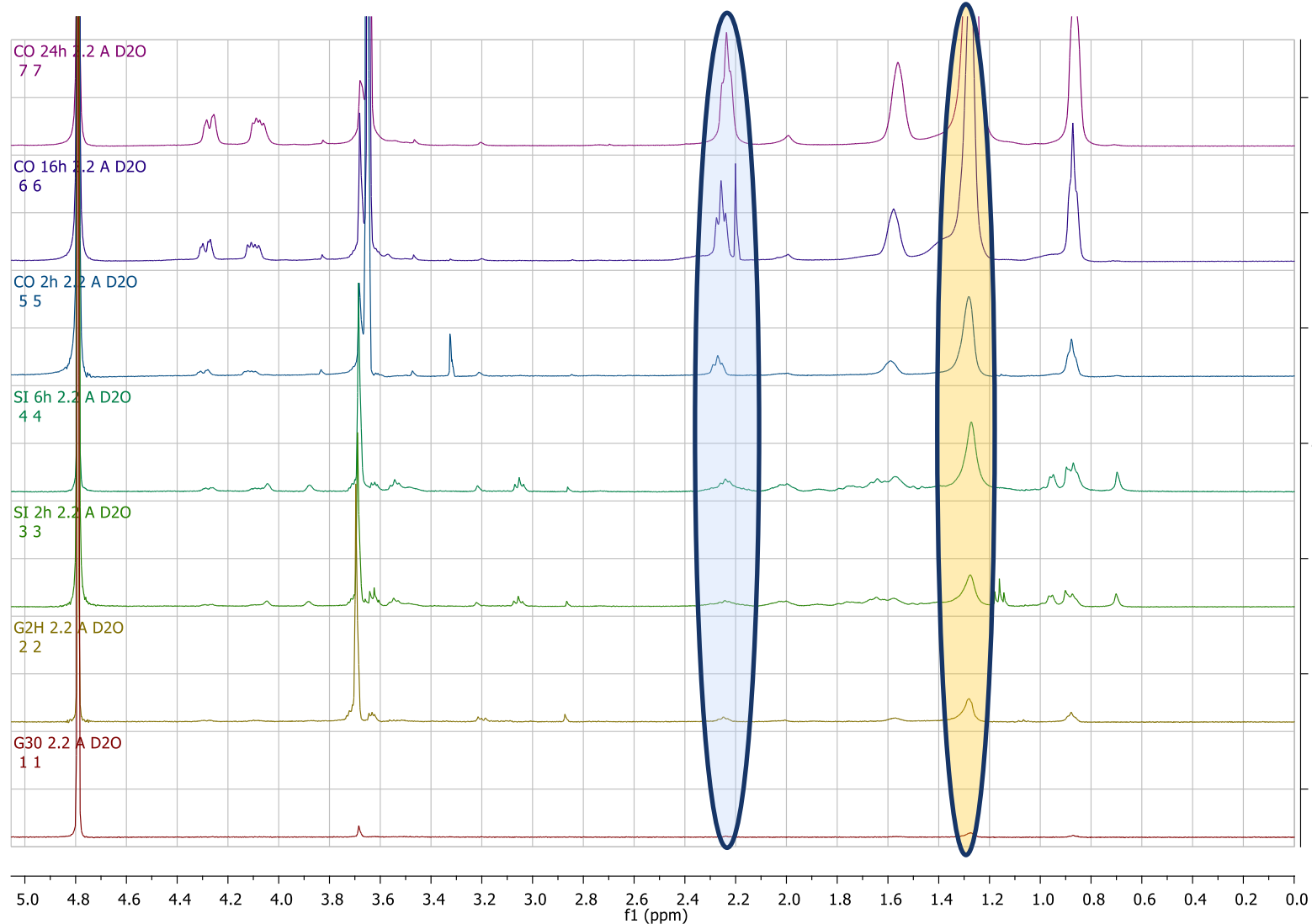
NTA- HyLNC (5mg/mL) and (10mg/mL) are Releasing LNC(H-151) in Colonic Fluid



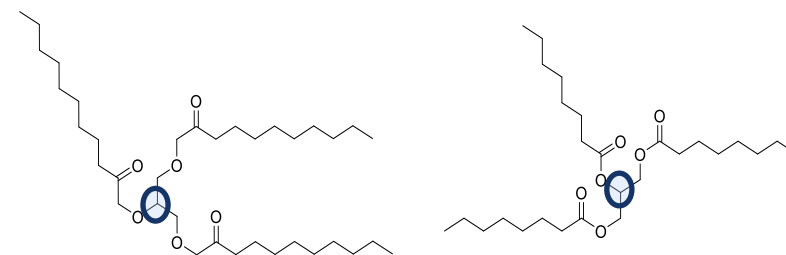
● ■ ▲ ▼ Size
■ ■ ■ ■ Concentration

Results : Mean $\pm$ SEM ; n= 3

Example: Stacked Qualitative Spectra Samples 2.2



**Kolliphor
HS15**

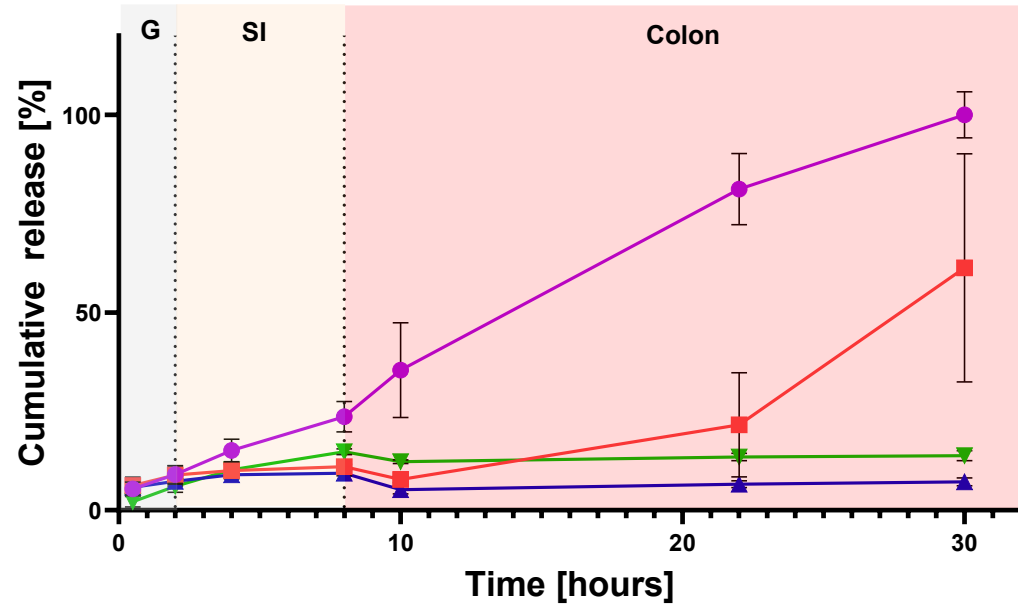


Labrafac

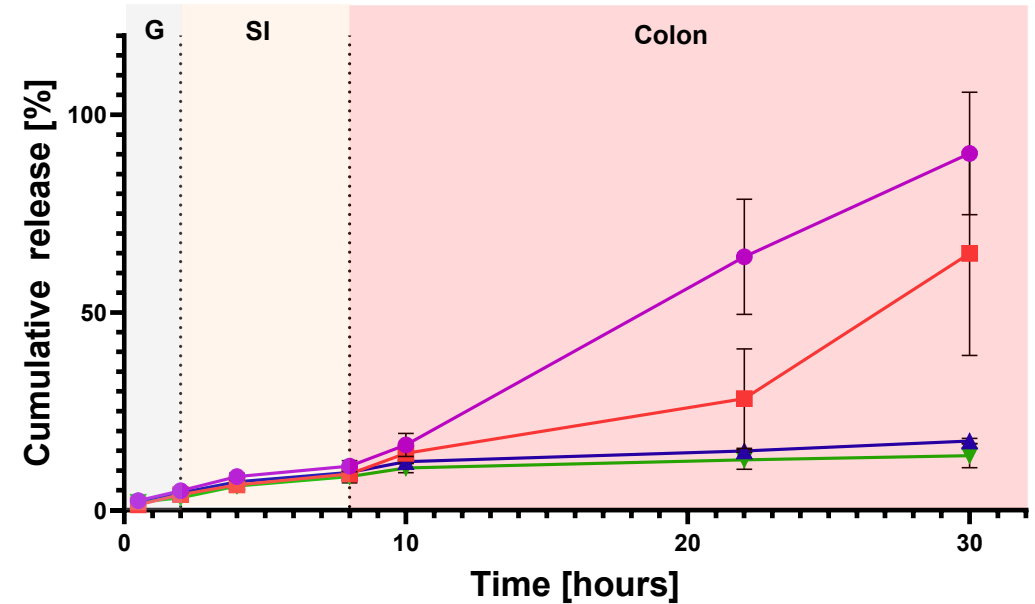


HyLNC (5mg/mL) and (10mg/mL) are released LNC components in Colon

Labrafac 2.3ppm



Kolliphor HS15 1.5 ppm

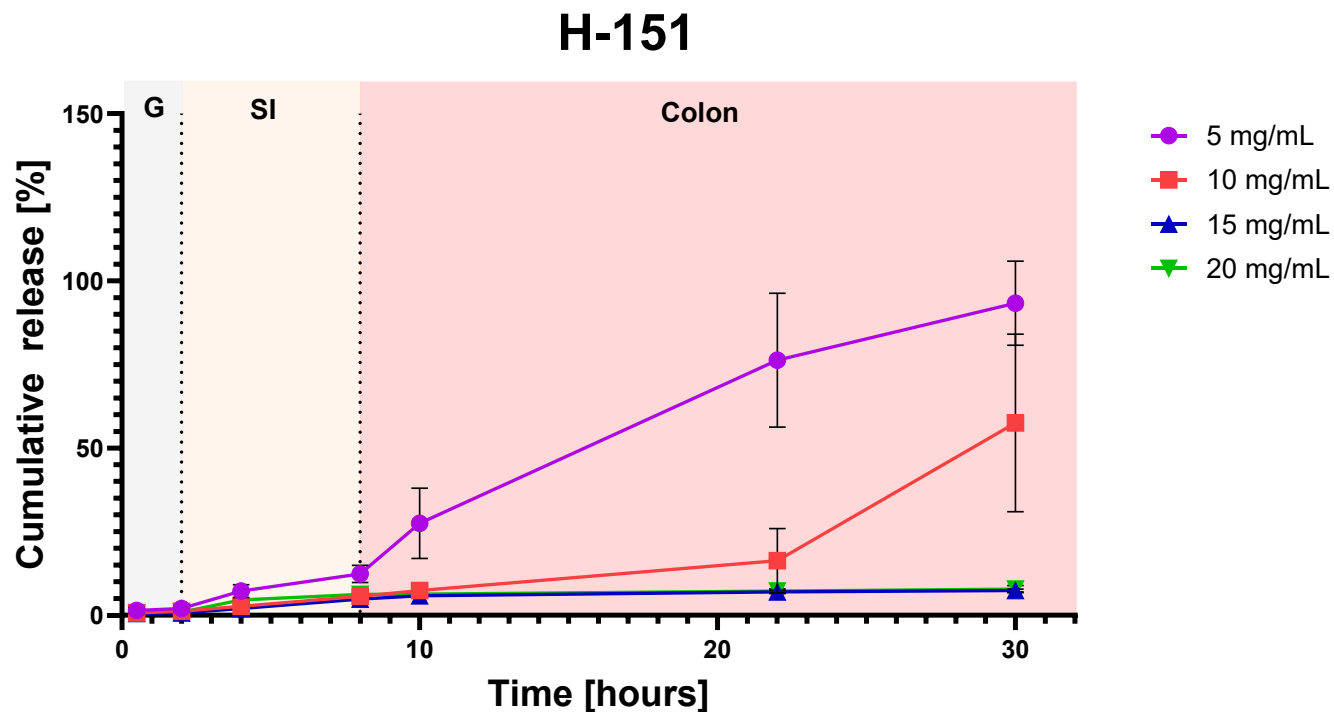


5 mg/mL
10 mg/mL
15 mg/mL
20 mg/mL

Results : Mean $\pm$ SEM ; n= 3



HPLC- HyLNC (5mg/mL) and (10mg/mL) are Releasing H-151 in Colonic Fluid

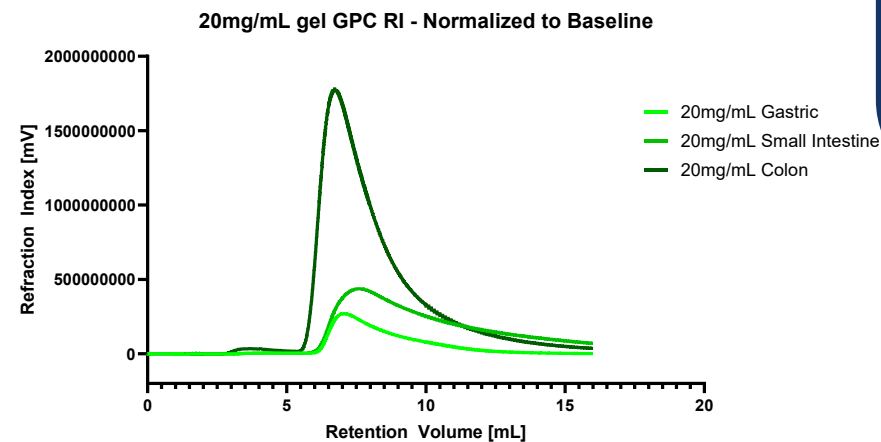
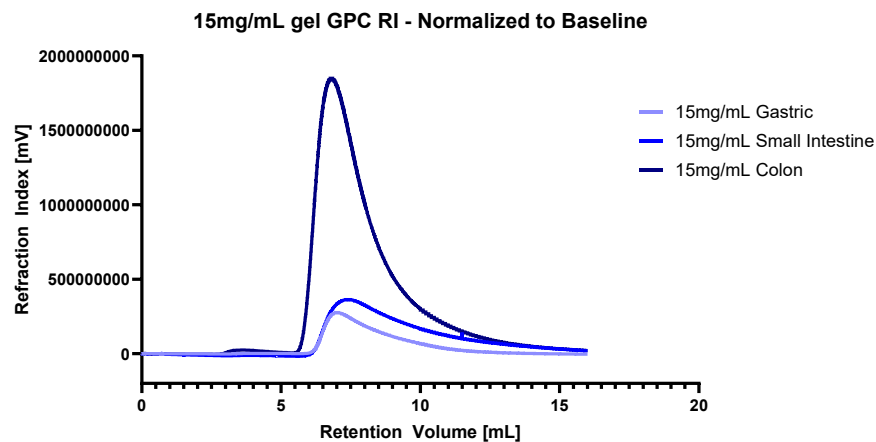
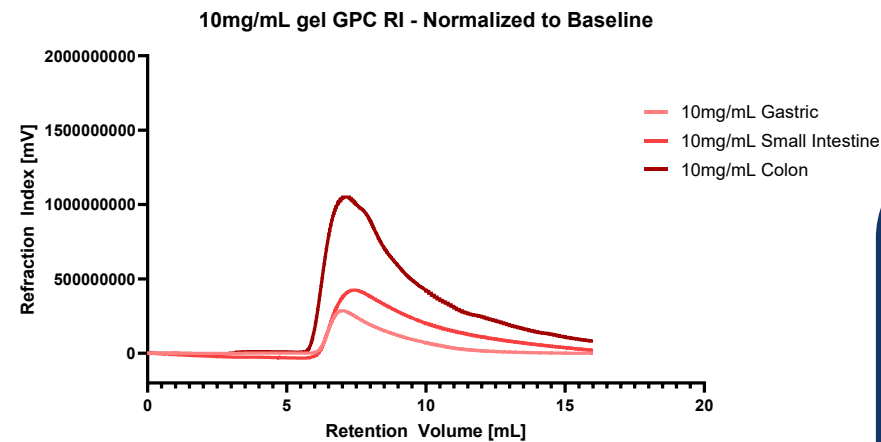
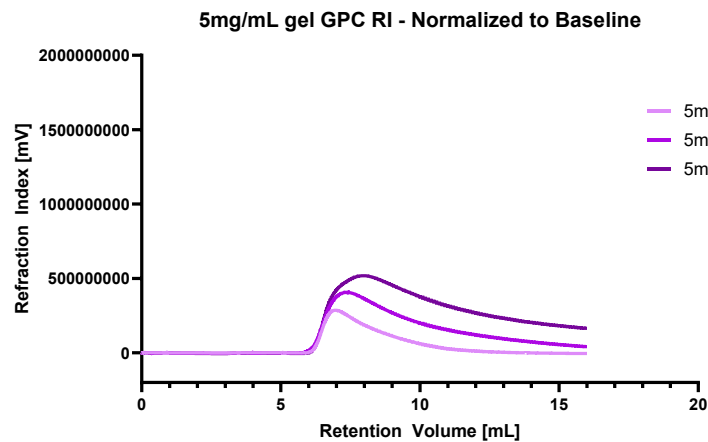


All the release components identified are converging →
Clear increased release from HyLNC (5mg/mL) and (10mg/mL) in Colonic Fluid

Results : Mean $\pm$ SEM ; n= 3



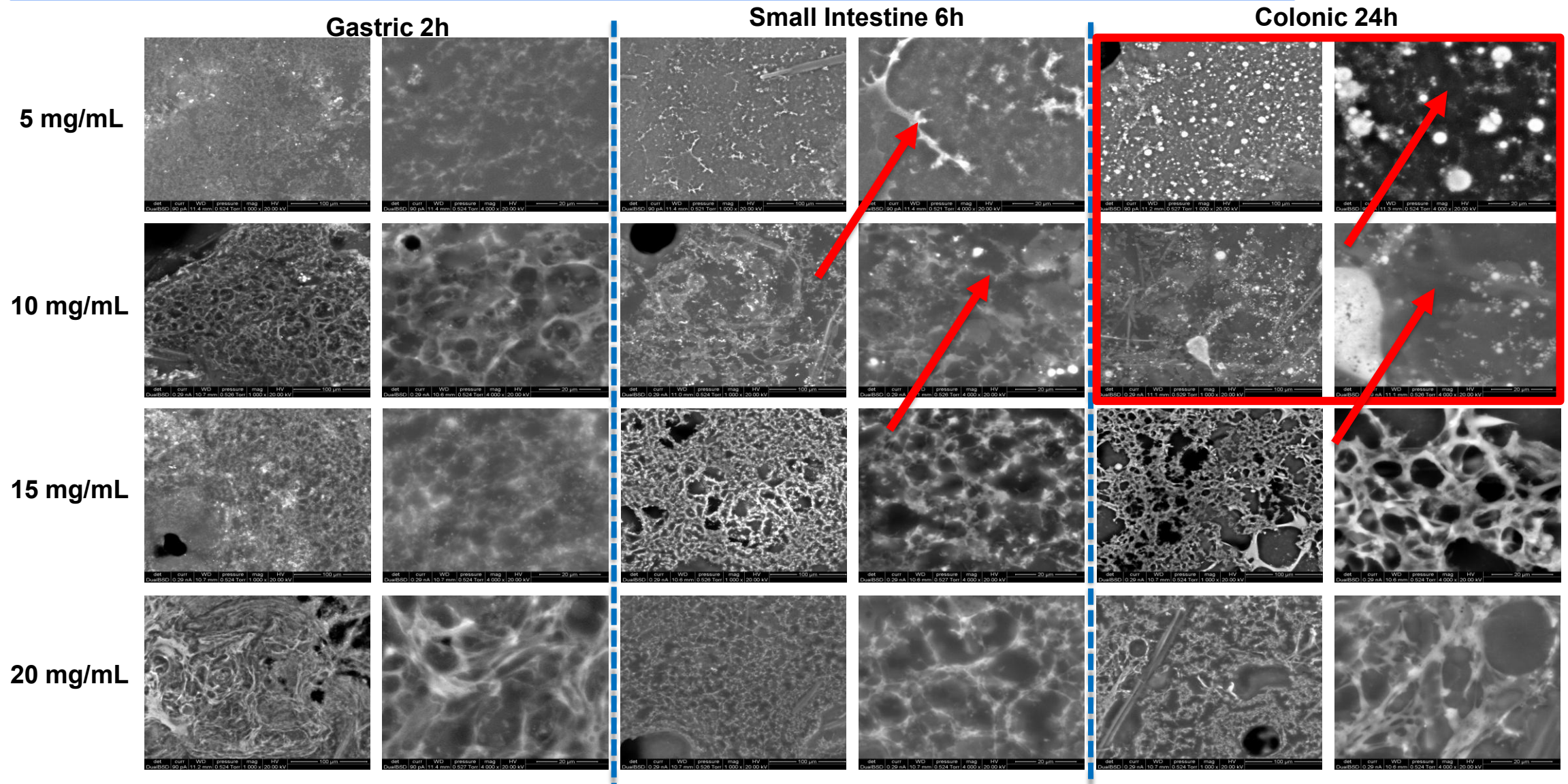
GPC – Increase of Release of HA in Colonic Fluid



Colonic fluid :
Increased signal and
shift left of HA
→ **More and higher**
molecular weight HA
is released

Results : Mean $\pm$ SEM ; n= 3

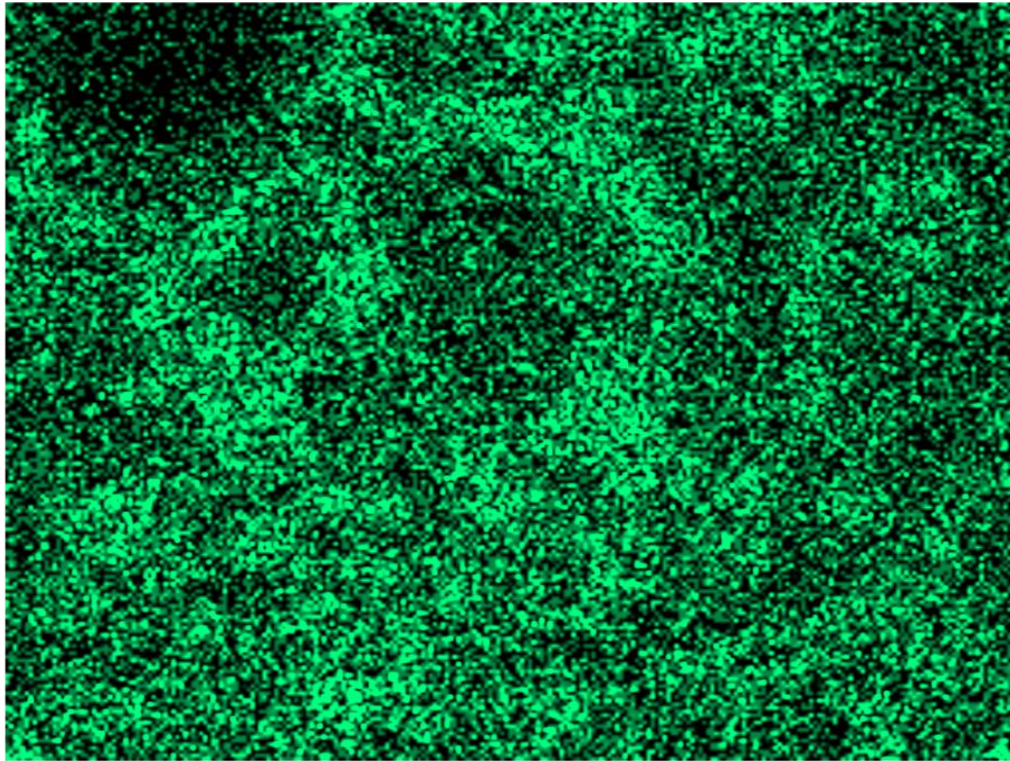
SEM - HyLNC (5mg/mL) and (10mg/mL) Network is Breaking Down in Colon



SEM (Sulfur Content) – Global Decrease of Sulfur Content when Reaching Colonic Fluid

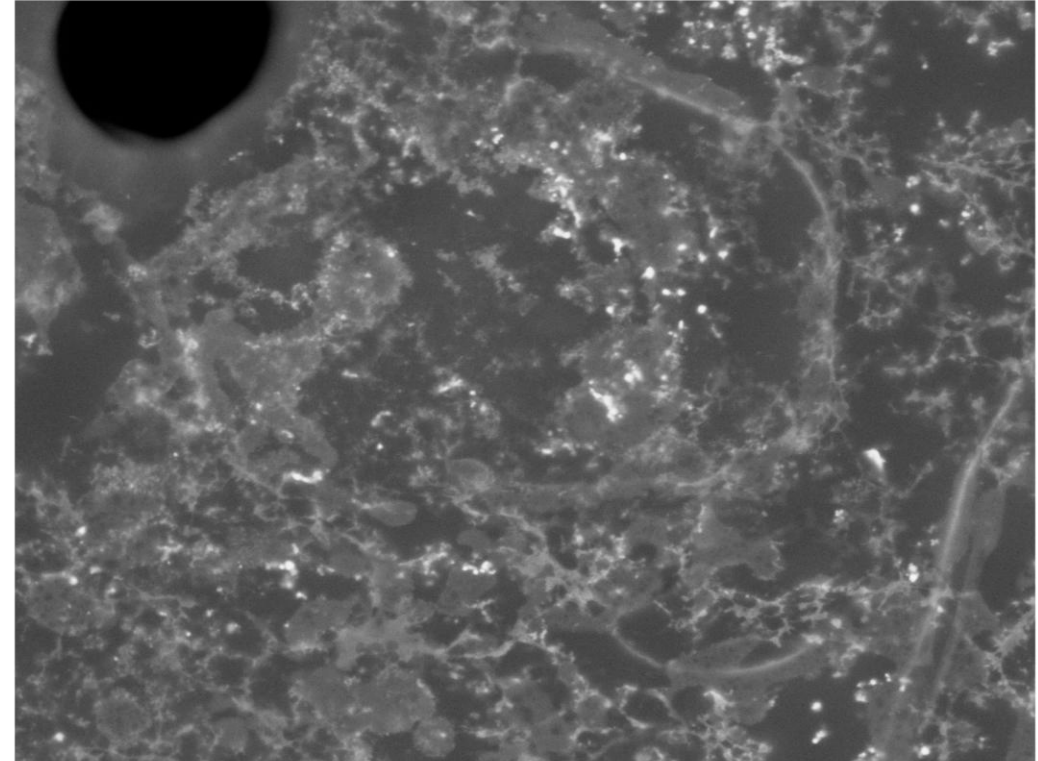
Results

S K α 1



100 μ m

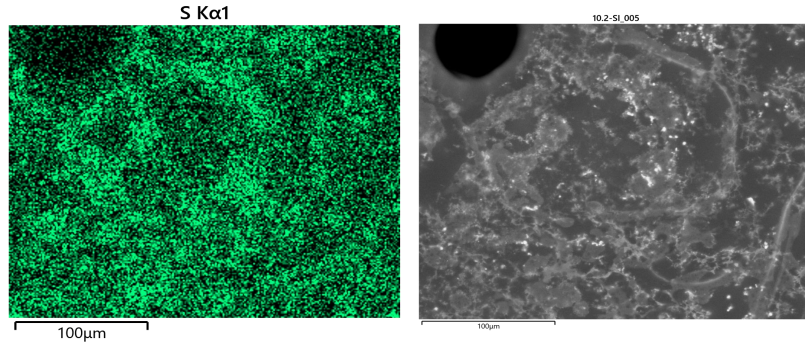
10.2-SI_005



100 μ m

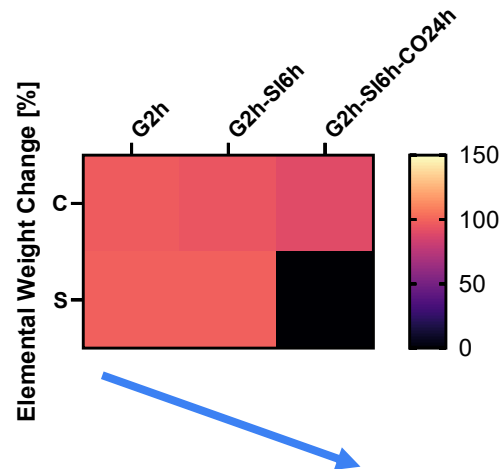


SEM (Sulfur Content) – Global Decrease of Sulfur Content when Reaching Colonic Fluid

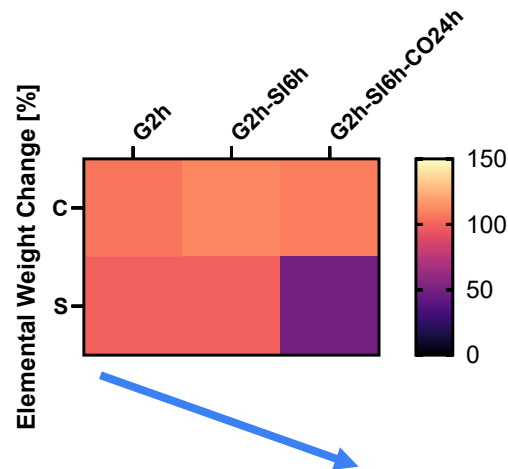


Decrease of the Elemental Sulfur Content →
**Loss of S-S bonding and
Release of LNCs with SH**

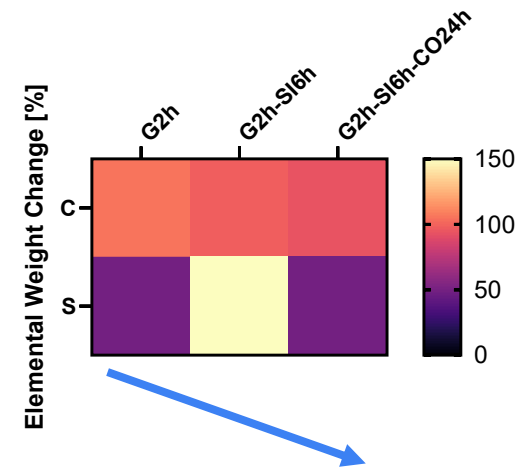
5 mg/mL relative to untreated



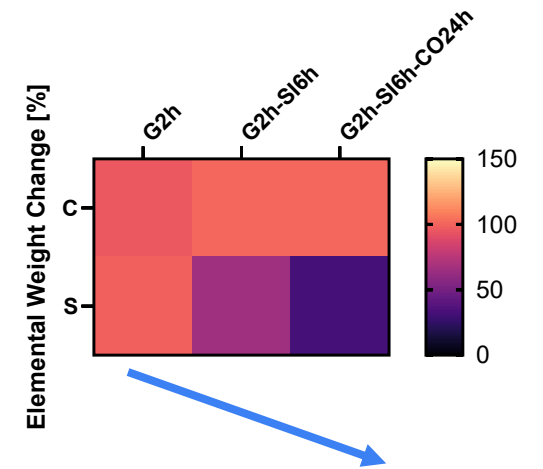
10 mg/mL relative to untreated



15 mg/mL relative to untreated



20 mg/mL relative to untreated



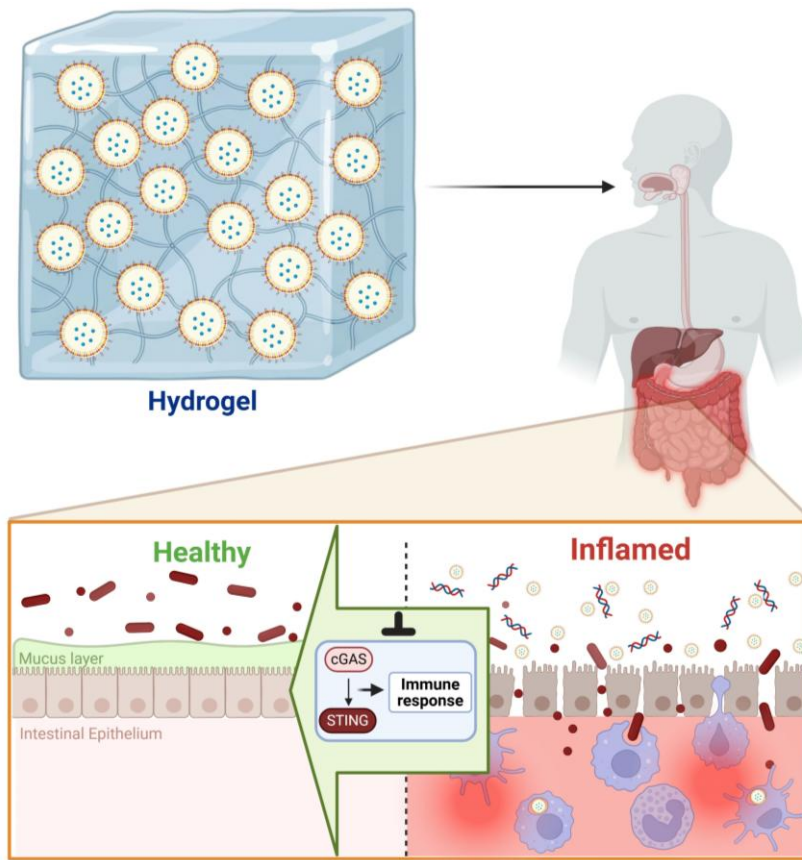
- We engineered an oral hydrogel platform that specifically disassembles in colon-like conditions, ensuring localized delivery of embedded nanoparticles to the colon
- We plan on doing an efficacy and biodistribution study in a DSS-induced mice model of colitis



Supervisor:
Professor Ana Beloqui

Group members:
Dr. Inês Ladeiro Domingues
Dr. Espoir Kambale Kavungere
Dr. Wunan Zhang
Dr. Cristina Pangua Irigaray
Dr. Tanya Saxena
Cheng Chen
Laurie Hoflack
Dan Ma
Valentina Marotti
William Van den Bossche
Hafsa Yagoubi

Any Questions?



Supervisor:
Professor Alessio Malfanti

Group members:
Dr. Riccardo Rampado
Dr. Nguyen Thao
Sofia Banzato
Vittoria Colladet
Milena Kuhn
Anna Maslova
Antonio Nardi
Francesco Rocca

Results

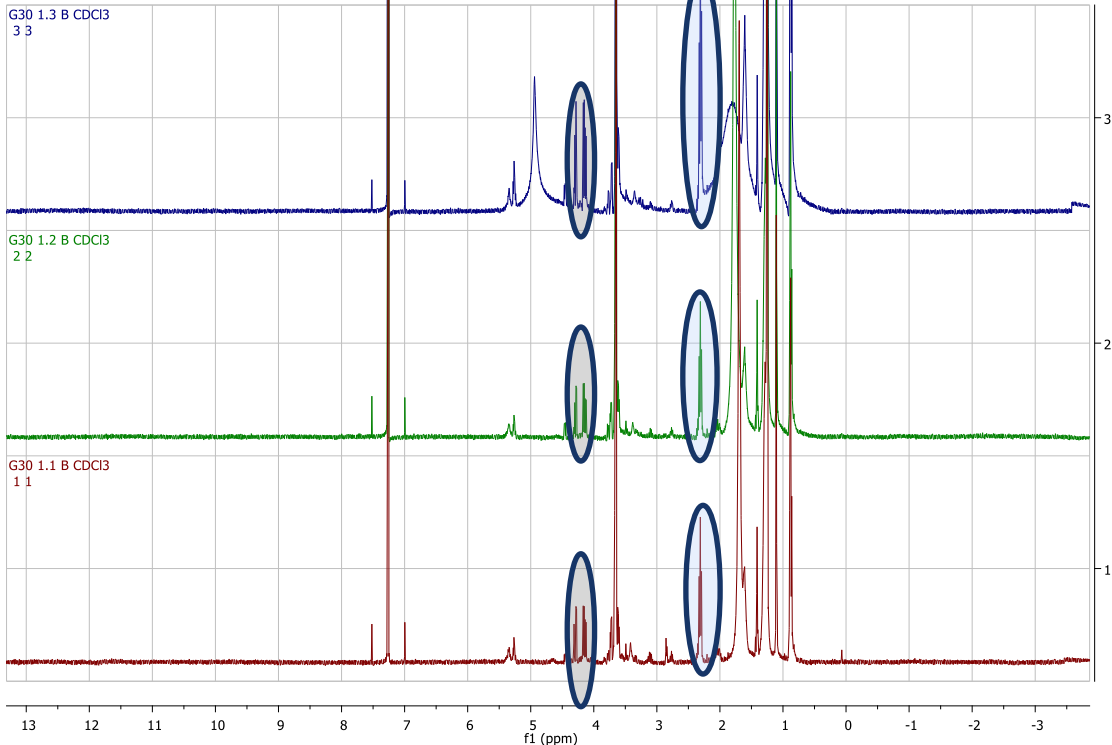




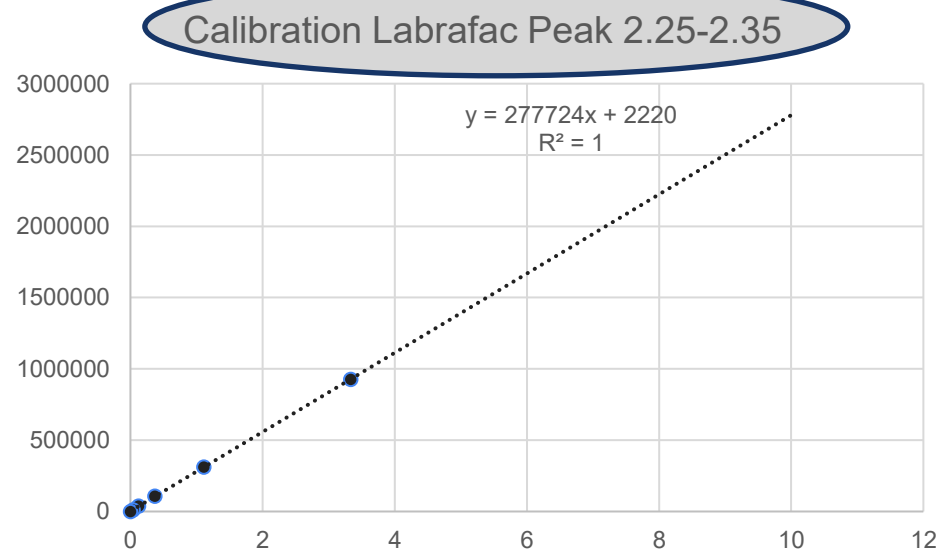
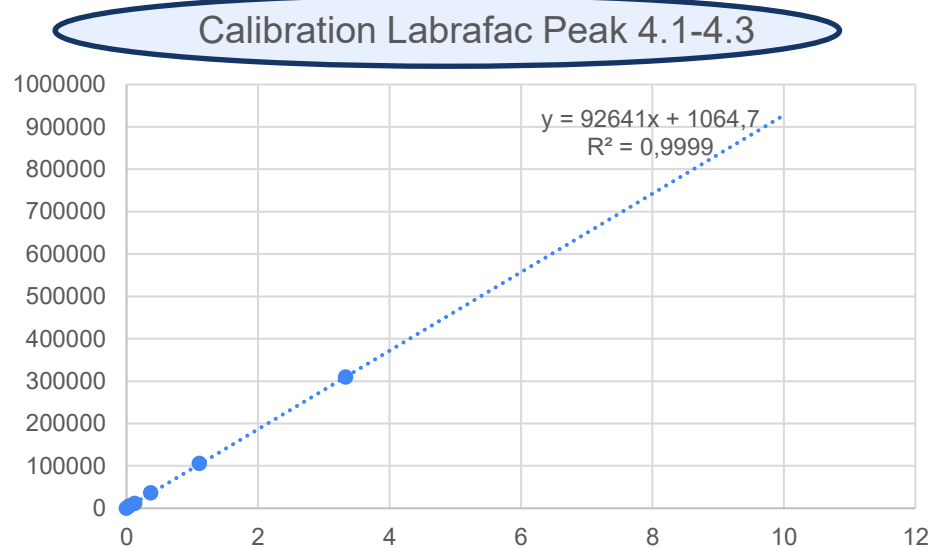
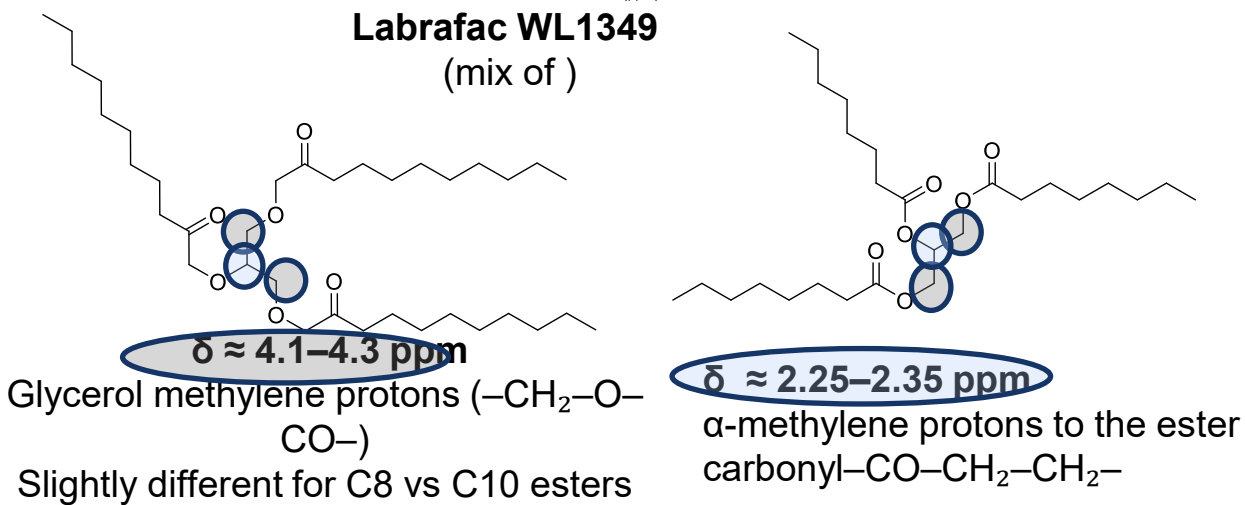
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qNMR – Calibration curve Labrafac



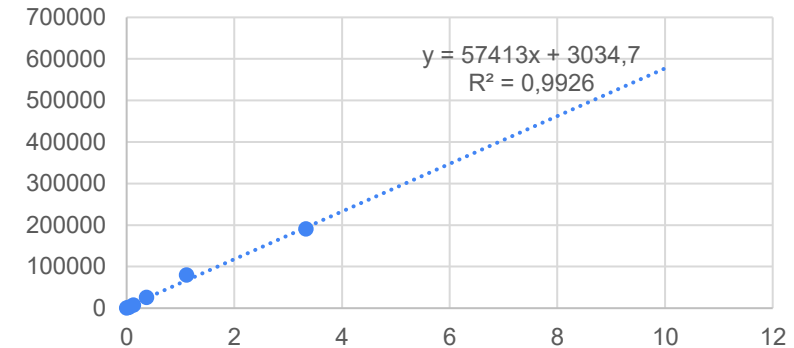
Labrafac WL1349
(mix of)



qNMR – Kolliphor HS15



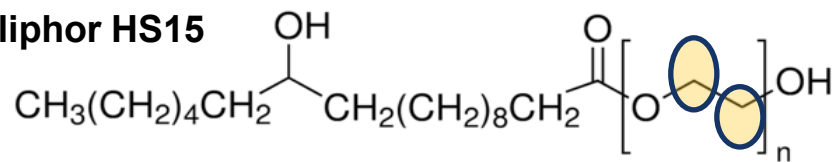
Calibration curve Kolliphor HS15 0,9 ppm



Colon not good →
Potential peak to detect at
2.25, 1.3-1.4 ppm, and 0.9
ppm

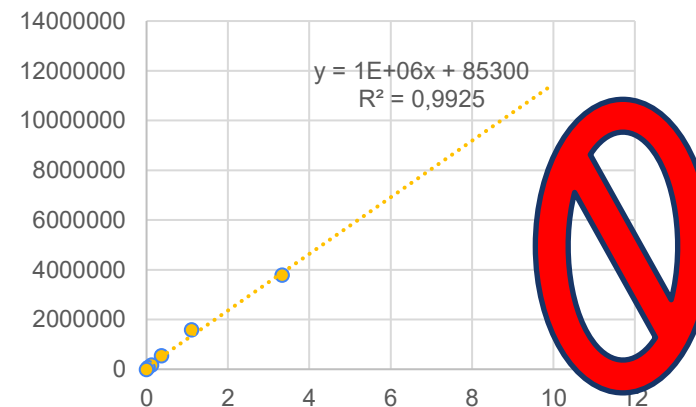
Kolliphor
HS15

Kolliphor HS15

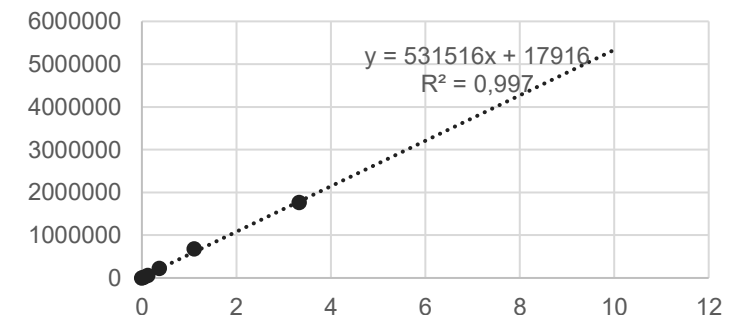


$\delta \approx 3.60-3.70$ ppm
–CH₂–CH₂–O– (repeating PEG
backbone)
Appears as a strong singlet

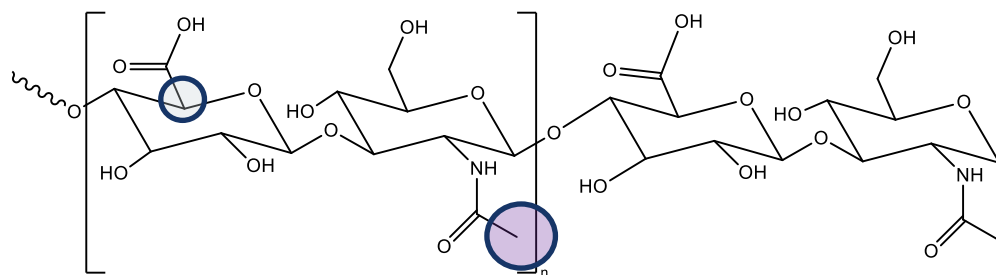
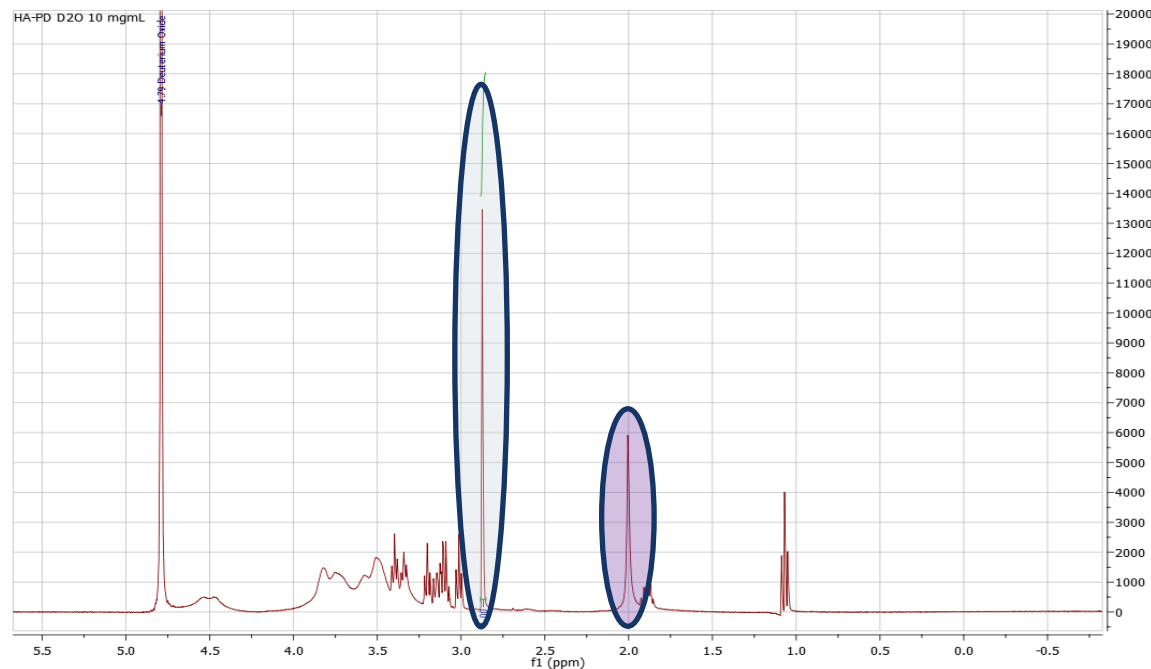
Calibration curve Kolliphor
HS15 3.60-3.70 ppm



Calibration curve Kolliphor HS15
1.3-1.5 ppm



qNMR – Calibration Curve HA-PD



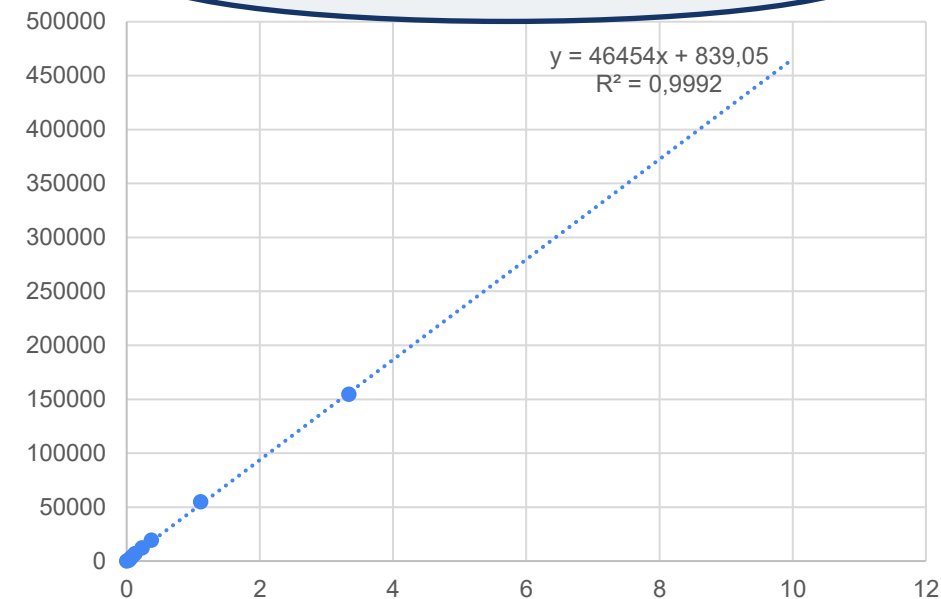
100 eq HA (1MDa)

$\delta \approx 2.7\text{--}2.8 \text{ ppm}$

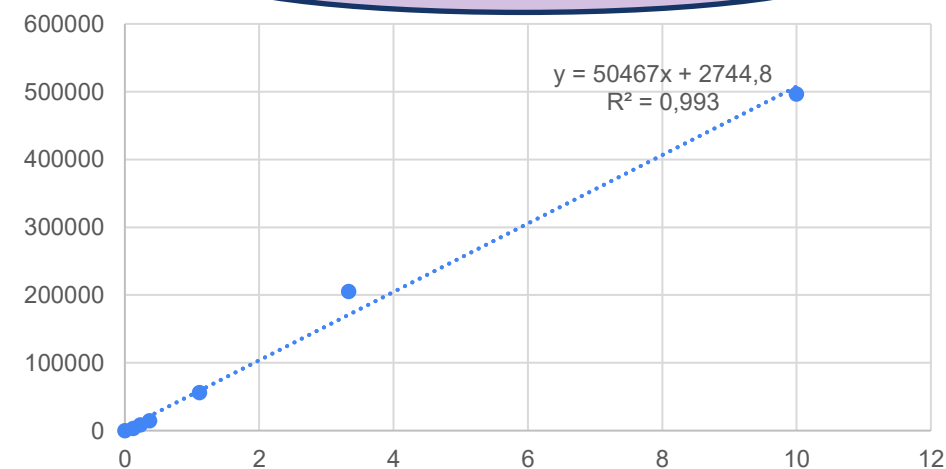
-CH proton(s) of D-glucuronic acid

Strongly deshielded by the nearby carboxylate ($-\text{COO}^-$) at C-6

Calibration Curve HA-PD 2,7-2,8 ppm

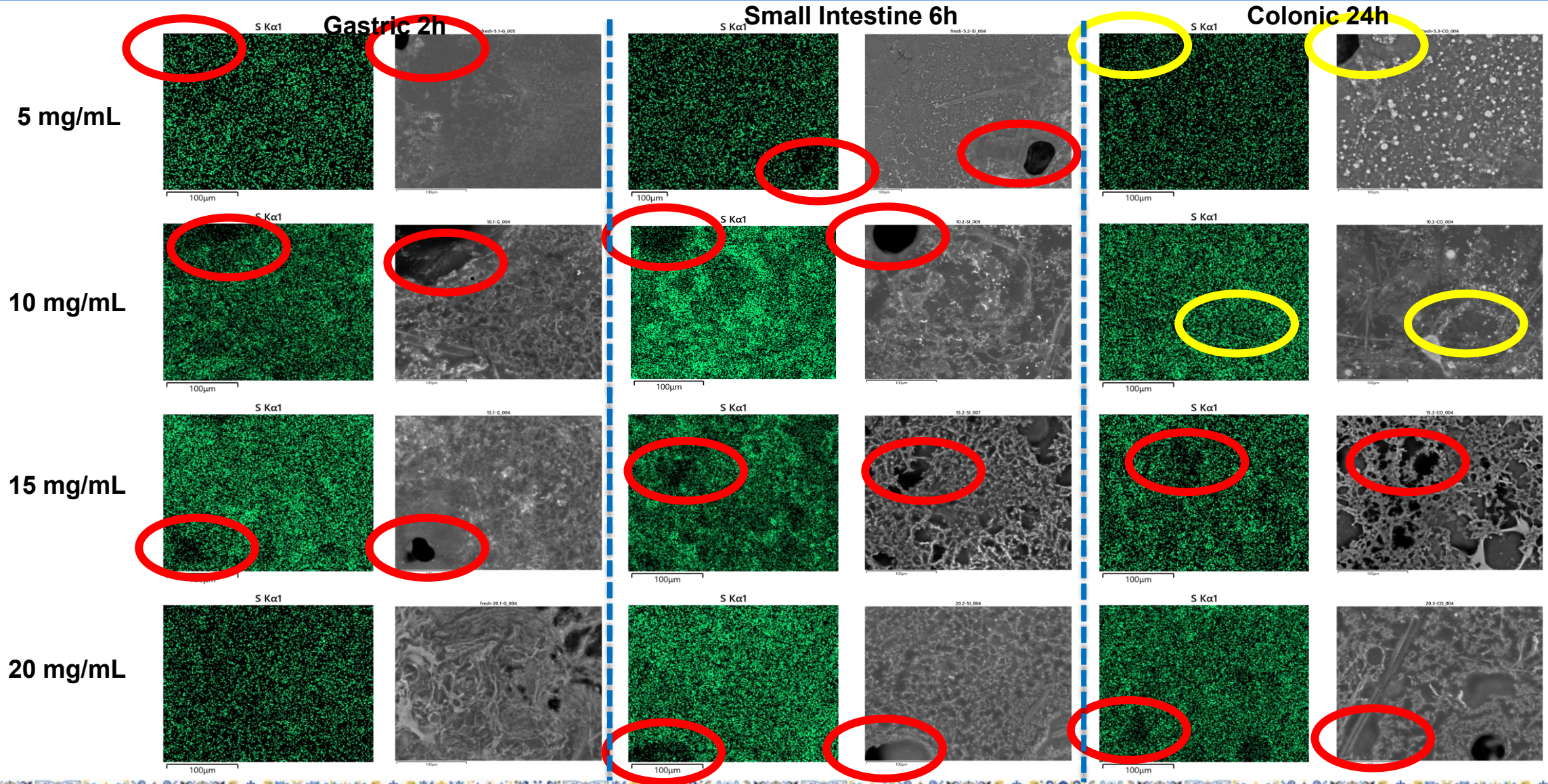


Calibration curve HA 2.1 - 1.9 ppm



SEM (Sulfur Content) - HyLNC (5mg/mL) and (10mg/mL) Network is Breaking Down in Colonic Fluid

Results



NTA Results – Qualitative analysis

