

Principles for enhancing the stability of cytokines in polymeric nanoparticle delivery platforms

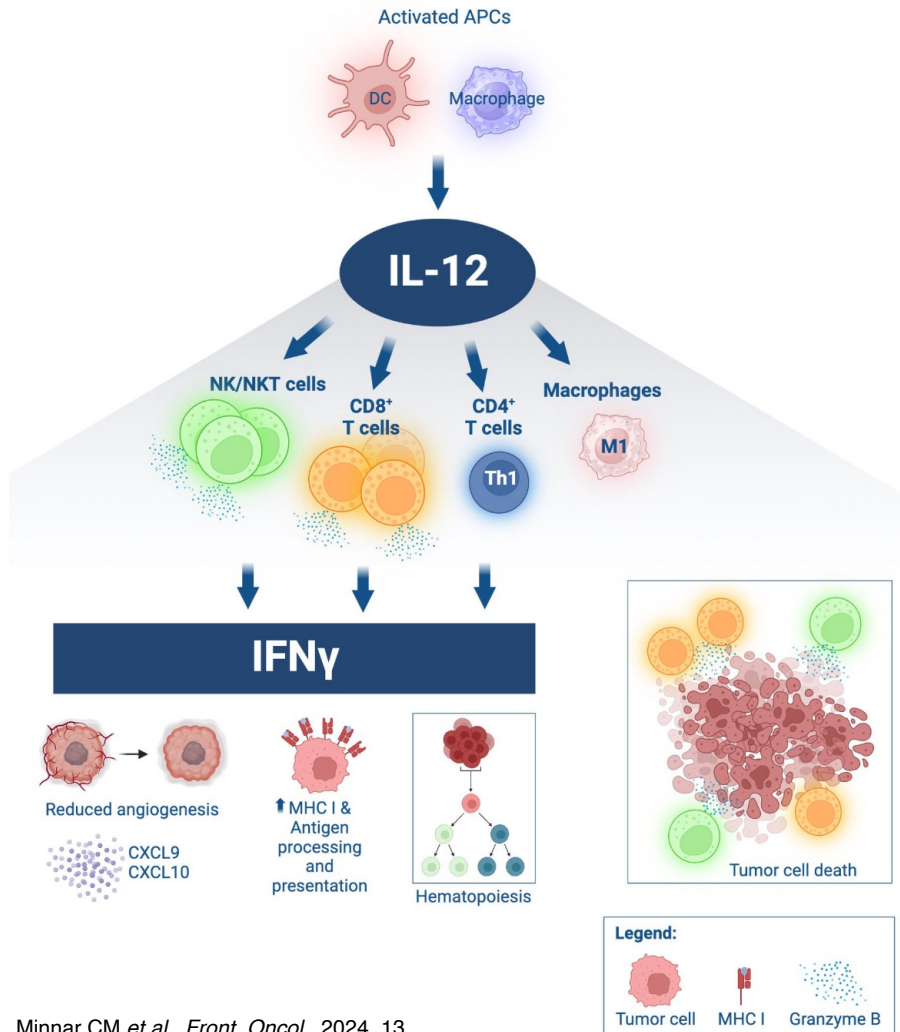
Nicole B. Day, Emily R. Rhodes, Emma C. Aldrich,
Kayla G. Sprenger, C. Wyatt Shields IV

Department of Chemical and Biological Engineering
University of Colorado Boulder

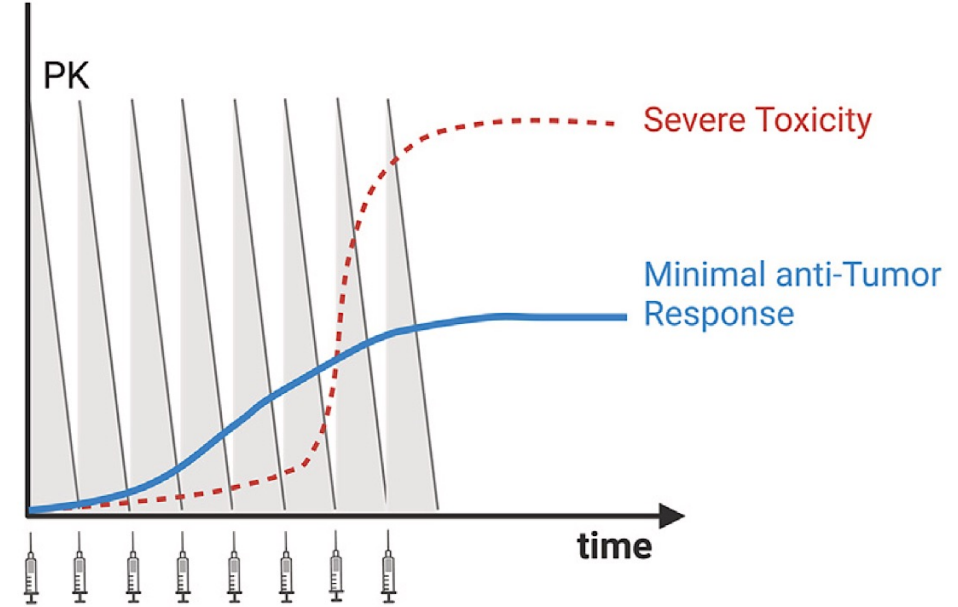
July 11th, 2024



Therapeutic IL-12 in the clinic



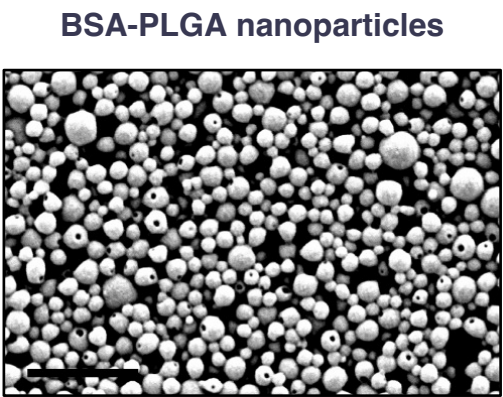
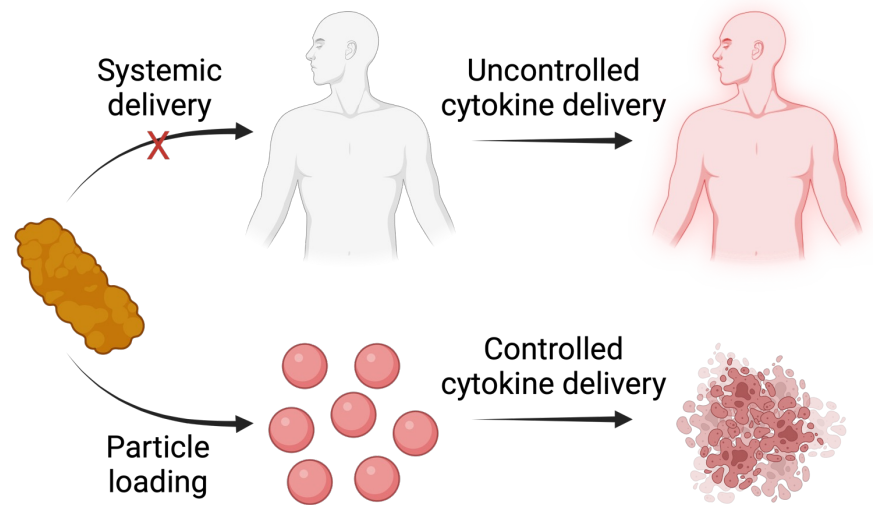
Minnar CM *et al.*, *Front. Oncol.*, 2024, 13



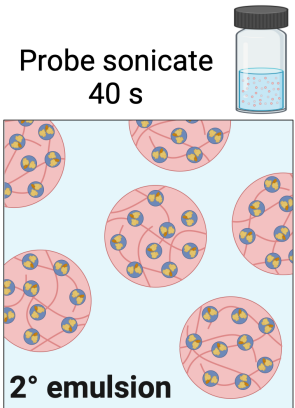
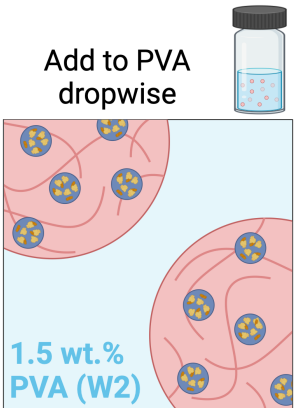
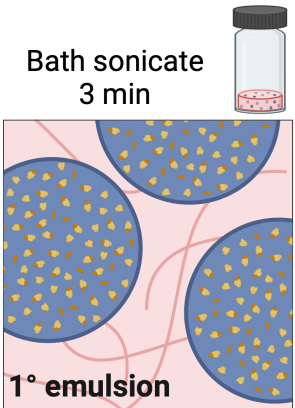
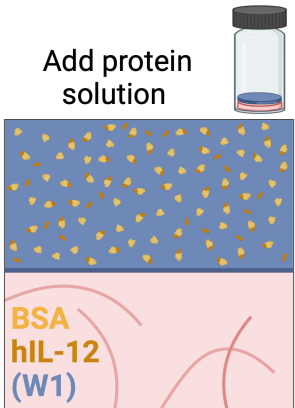
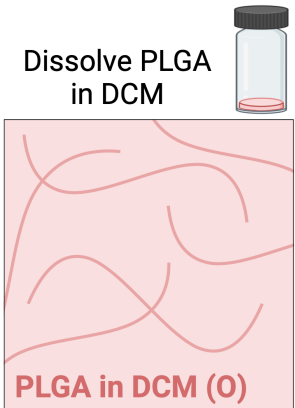
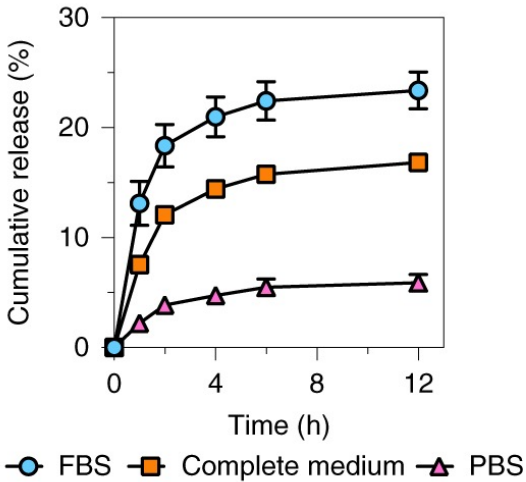
Gutierrez E *et al.*, *Med*, 2023, 4(5)

1. Short circulation time and half-life
2. Off-target effects due to systemic delivery

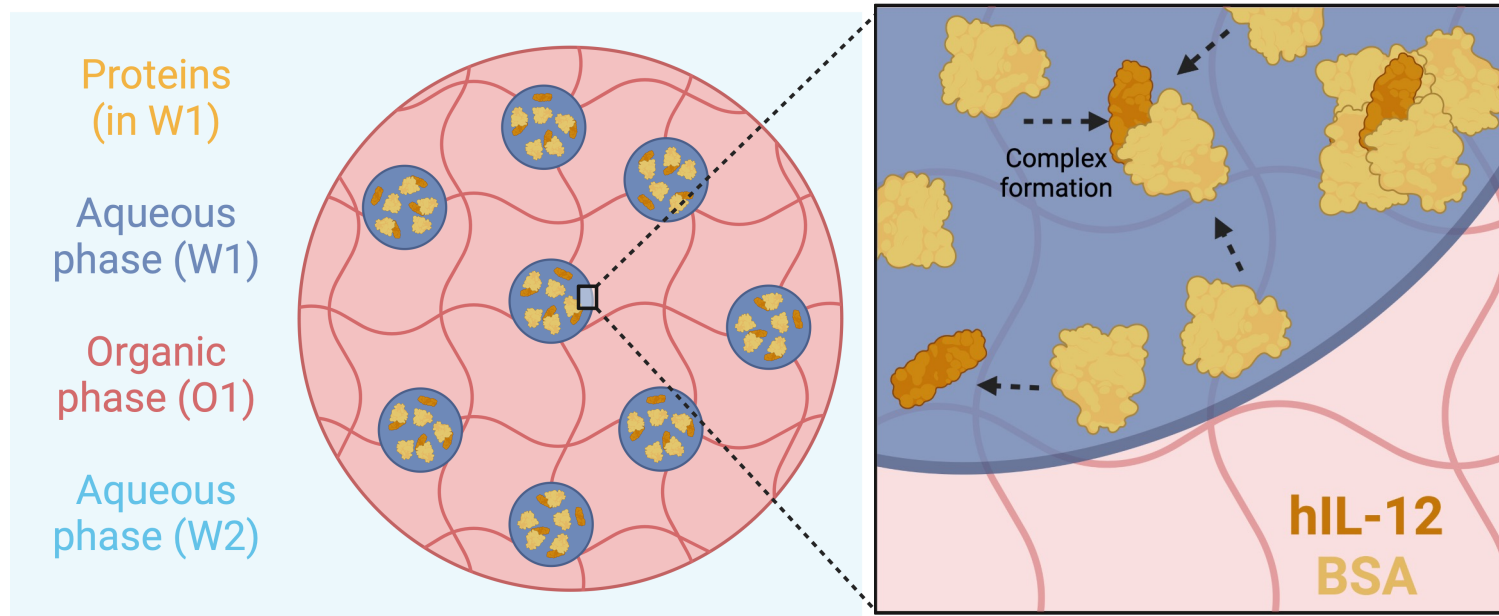
Particle-based controlled delivery of IL-12



Zhao Z et al., Nat. Biomed. Eng., 2021, 5



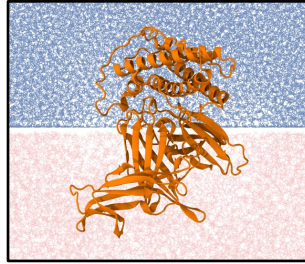
How can we elucidate principles of stabilization for the design of better cytokine carriers?



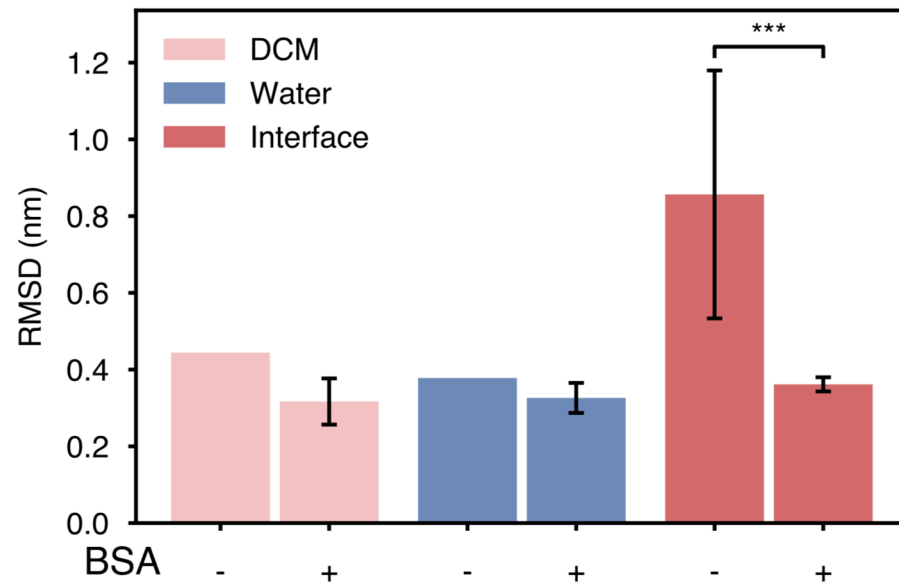
Hypotheses:

1. hIL-12 unfolds at the W/O **interface**
2. hIL-12 can be stabilized by **BSA binding**
3. hIL-12 can be stabilized by **interfacial crowding**

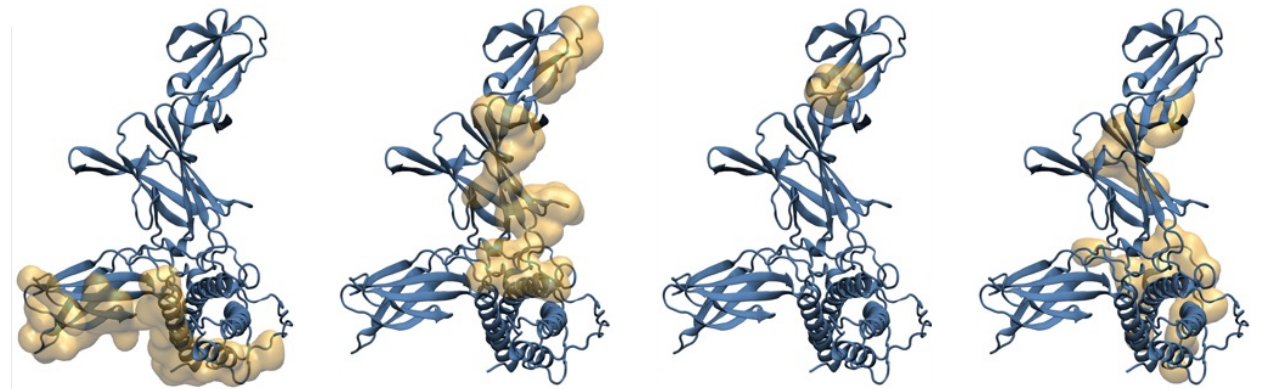
MD analysis demonstrates that hIL-12 destabilization at the W/O interface is dampened by BSA



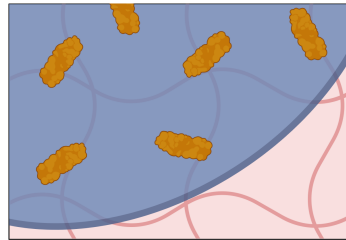
Dr. Kayla Sprenger,
University of Colorado Boulder



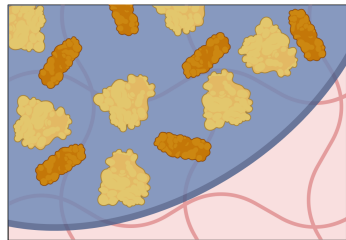
hIL-12 crystal structure + BSA binding locations



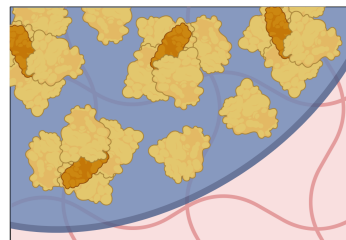
hIL-12 release from particles indicates stabilization by BSA occurs through multiple mechanisms



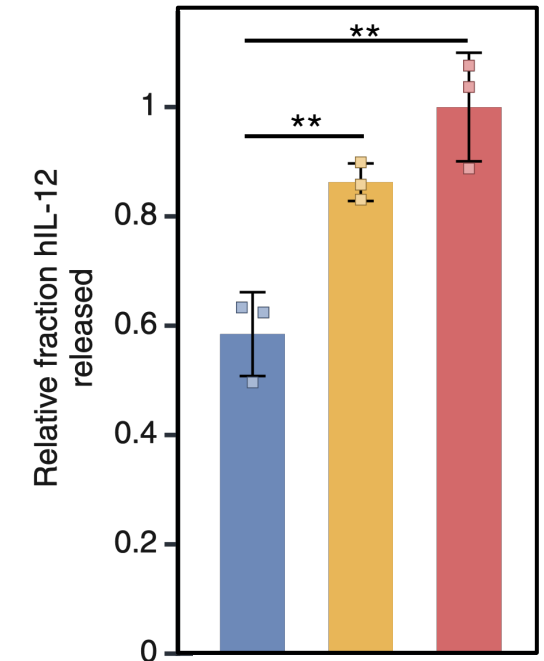
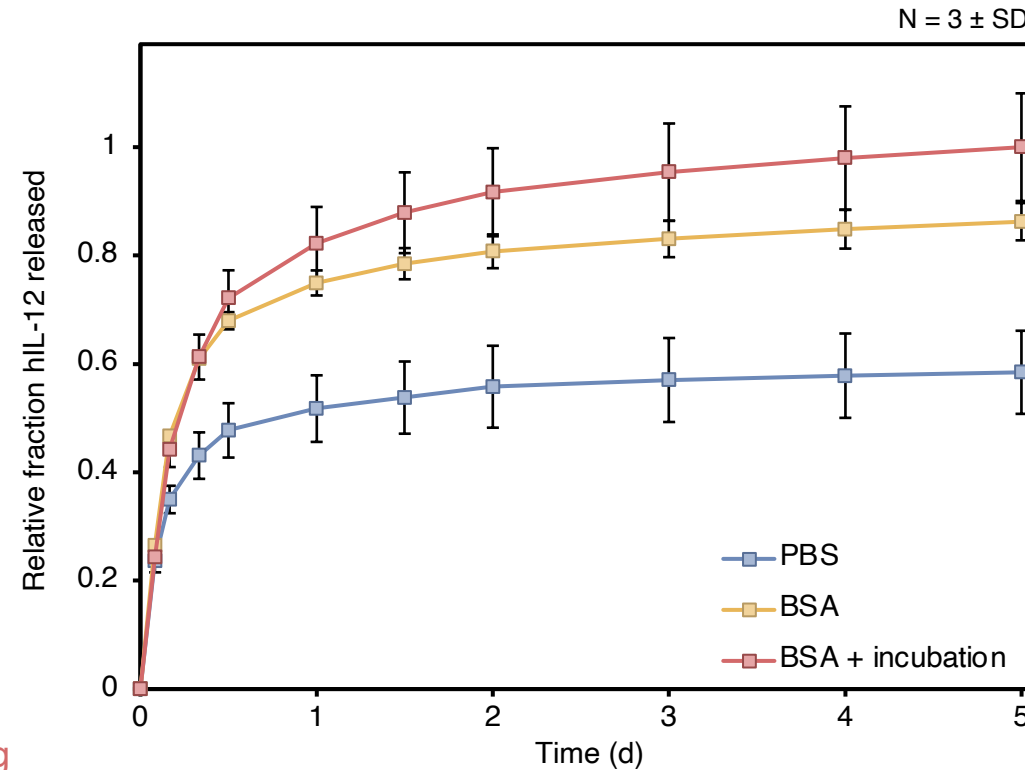
No stabilization
(PBS)



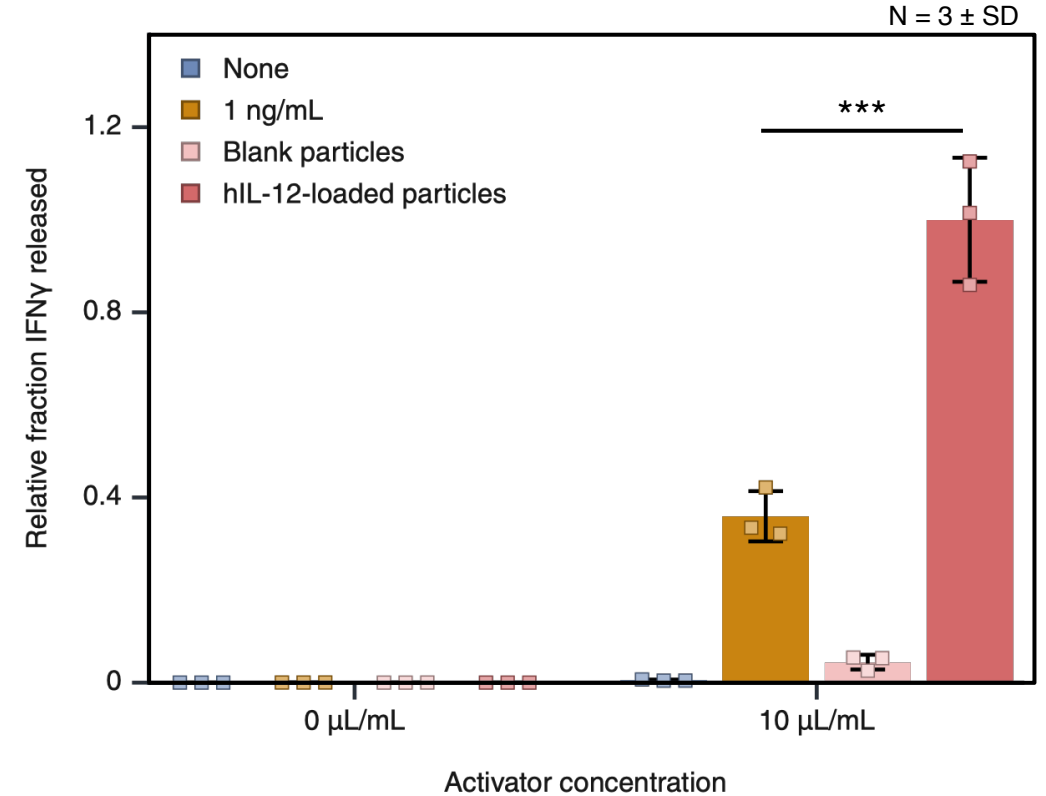
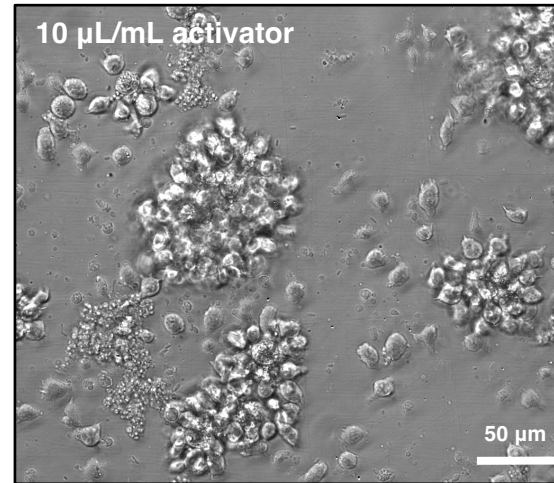
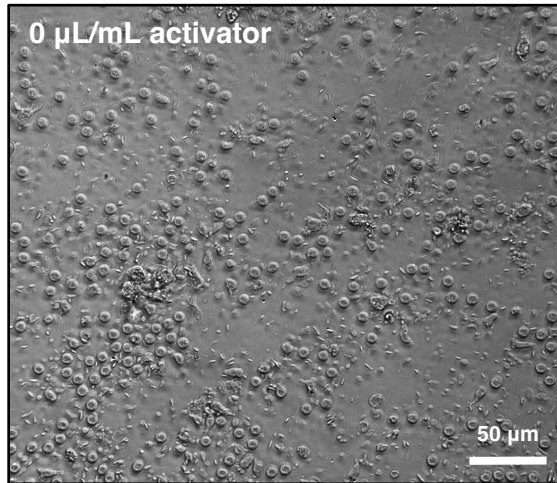
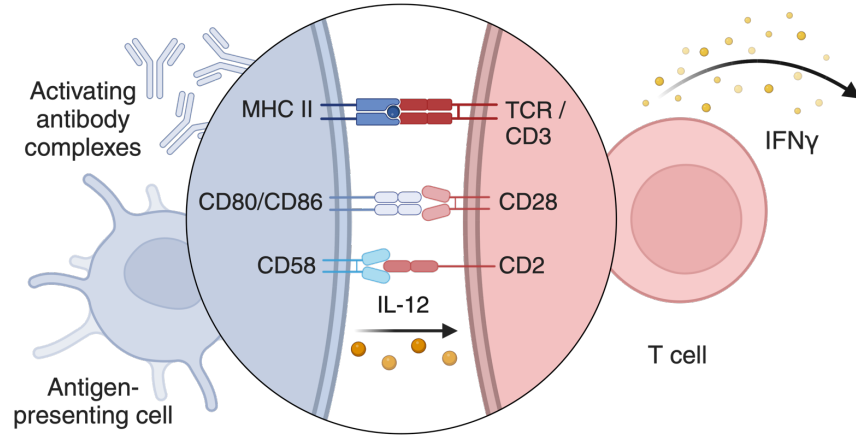
Interfacial
crowding only
(BSA)



Protein-protein
binding &
interfacial crowding
(BSA + incubation)

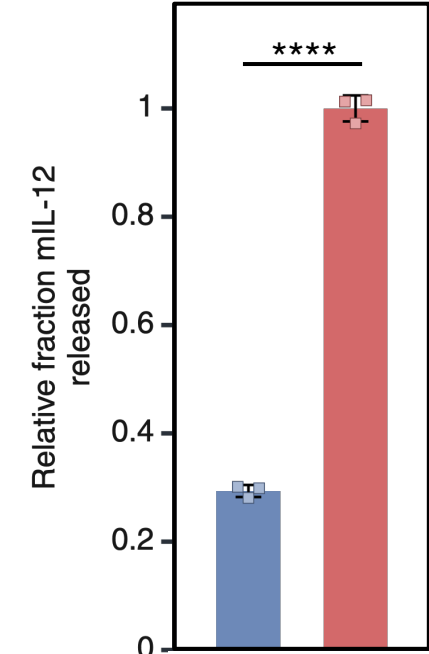
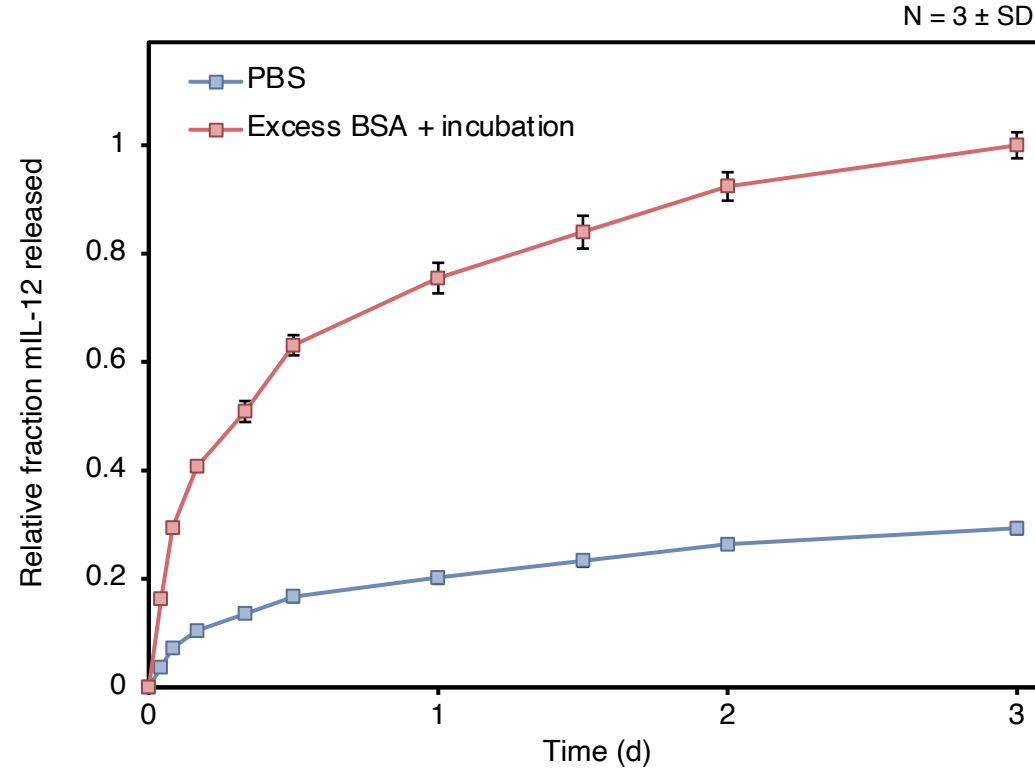
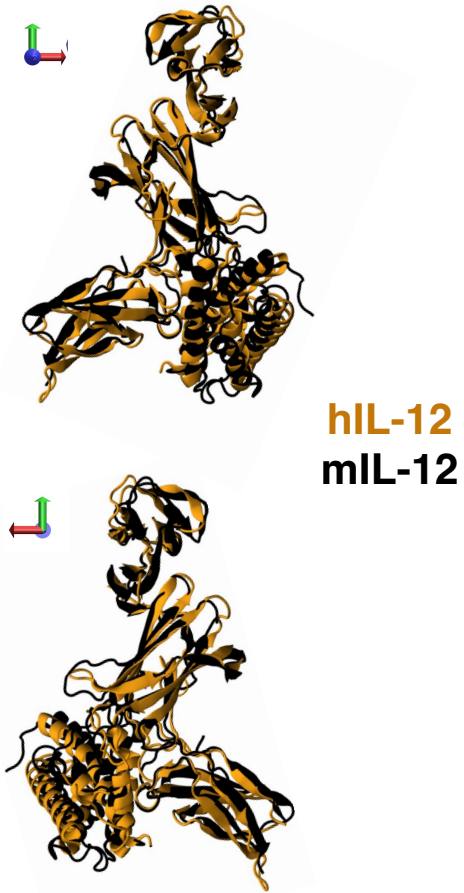


hIL-12 released from stabilized particles maintains bioactivity in PBMCs

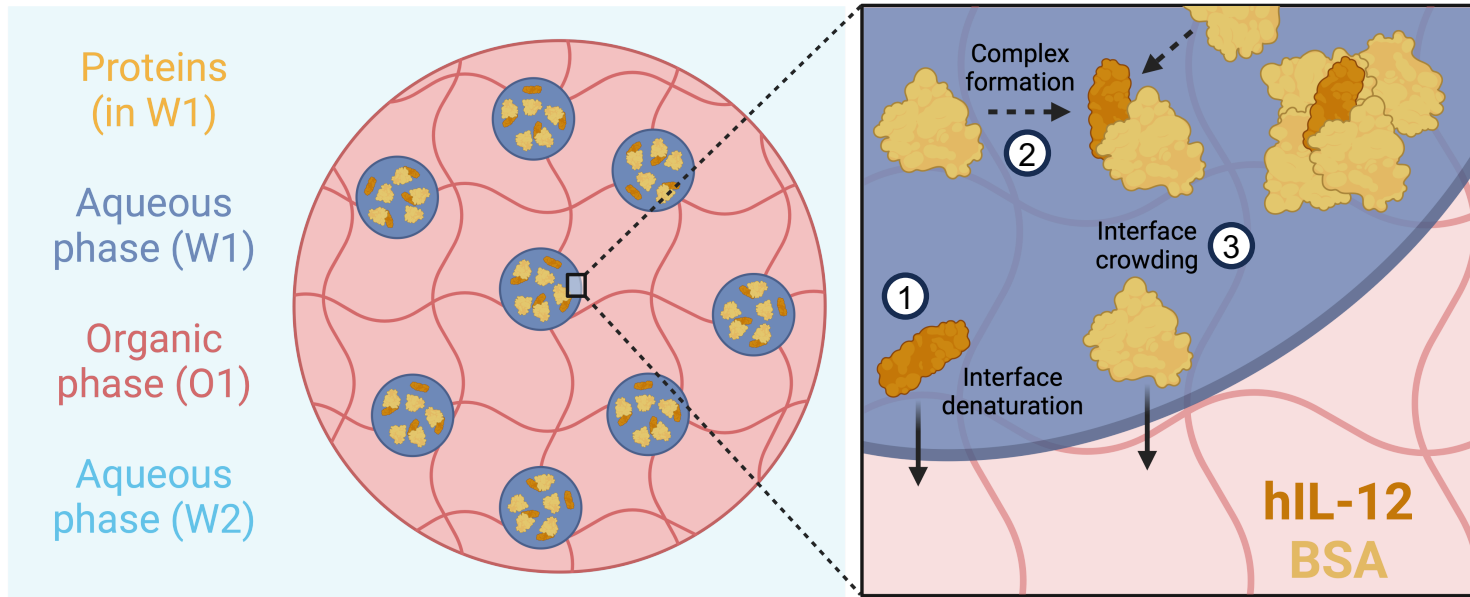


Day N and Rhodes E *et al.*, submitted

Murine IL-12 release is enhanced by BSA stabilization



Design principles for cytokine stabilization in particles



1. hIL-12 unfolds at the W/O interface
→ Reduce interfacial tension
2. hIL-12 is stabilized by BSA binding
→ Bind sensitive regions
3. hIL-12 is stabilized by interfacial crowding
→ Increase propensity for interface

Thank you!

C. Wyatt Shields IV

Shields Lab postdocs & grad students

- Taylor Ausec
- Courtney Bailey
- Alanna Duarte
- Dr. Ankit Gangrade
- Abigail Harrell
- Collin Kemper
- Kendra Kreienbrink
- Matthew Kwan
- Dr. Jin Lee
- Ritu Raj
- Cooper Thome
- Katherine Trese

Collaborators, CU Boulder

- Dr. Kayla Sprenger
- Emily Rhodes
- Emma Aldrich

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University of Colorado **Boulder**



Nicole.b.day@Colorado.edu



@shields_lab



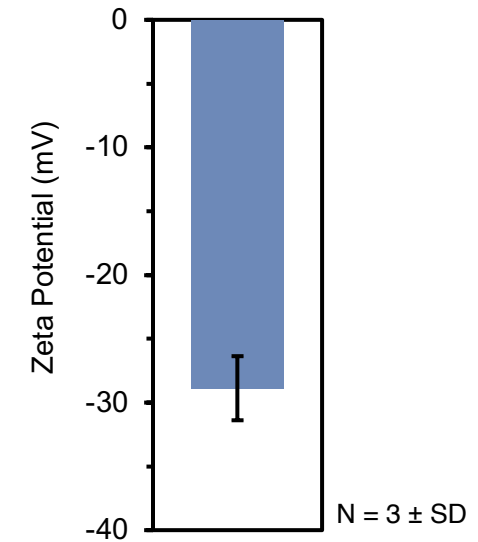
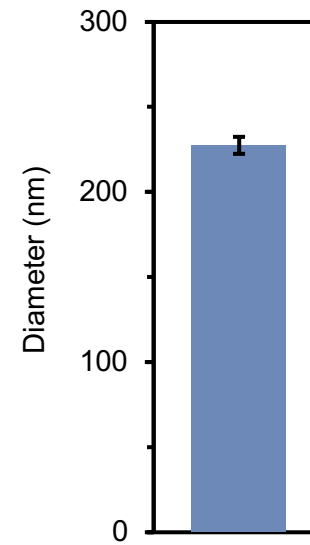
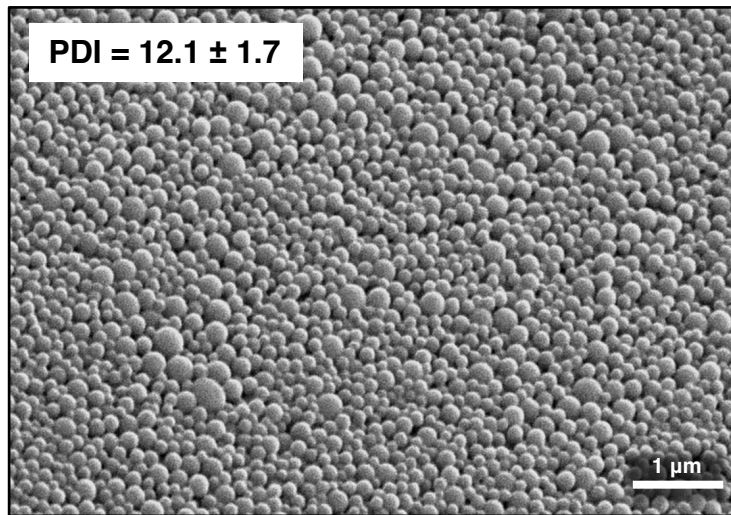
@WyattShieldsIV

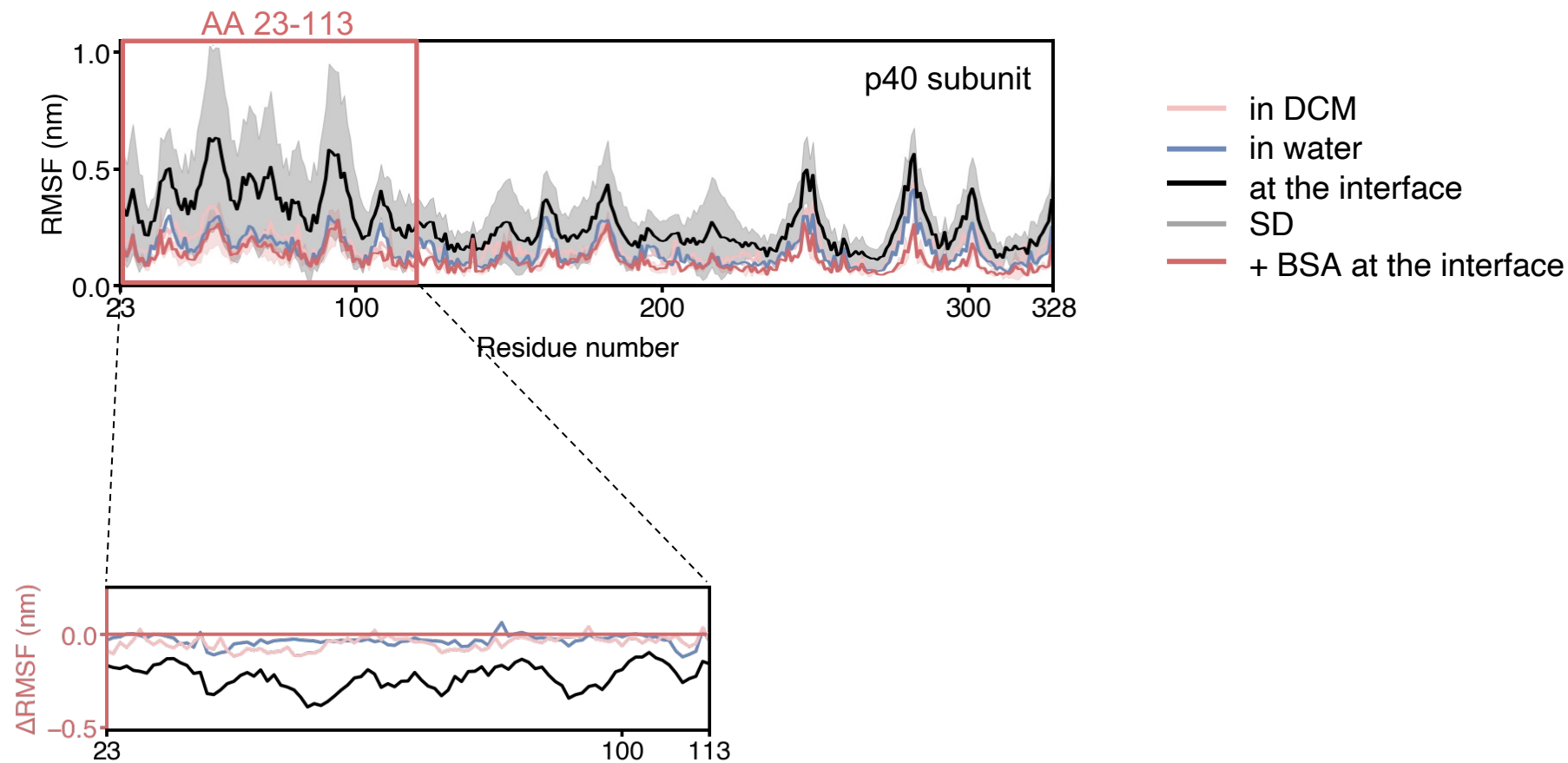


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