

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

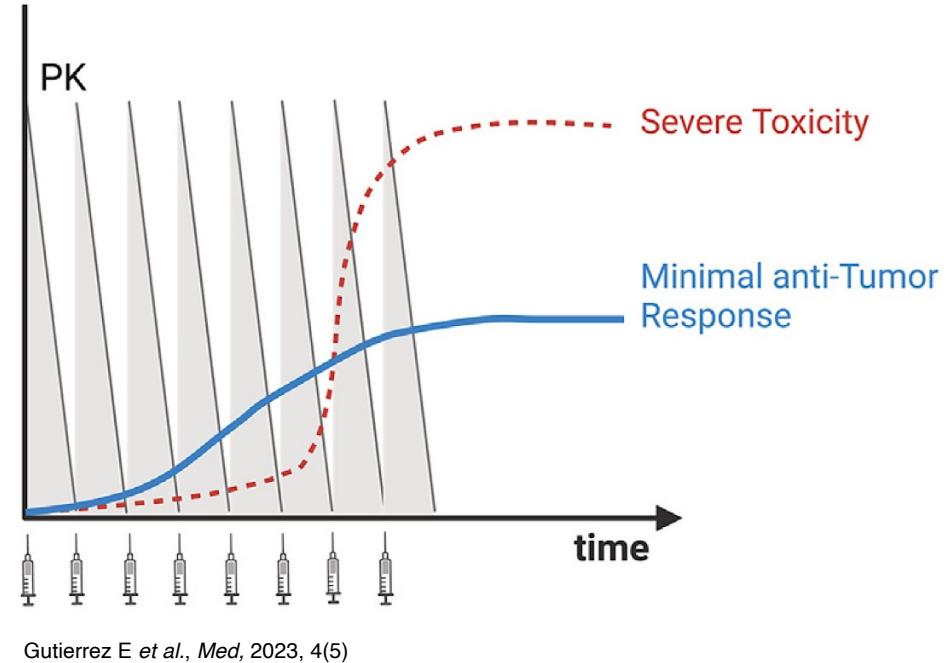
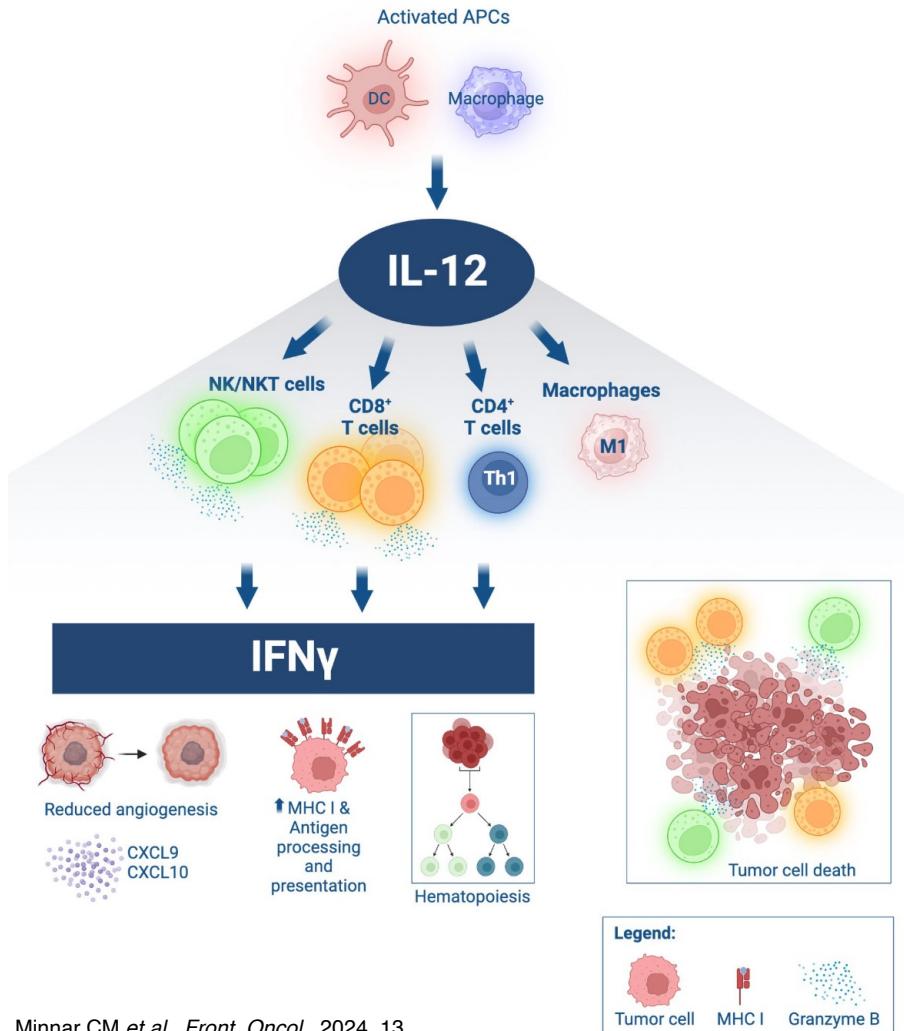
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Kayla G. Sprenger, C. Wyatt Shields IV

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University of Colorado Boulder

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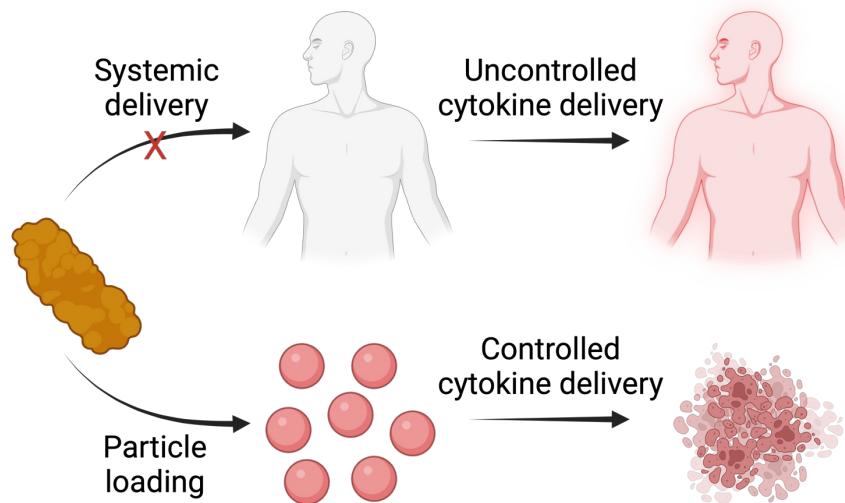


Therapeutic IL-12 in the clinic

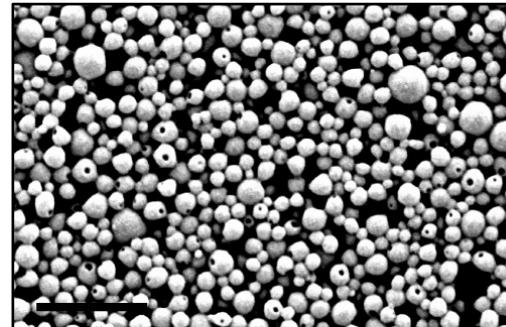


1. Short circulation time and half-life
2. Off-target effects due to systemic delivery

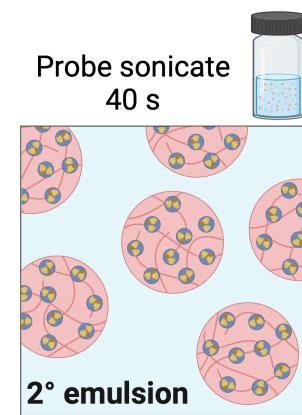
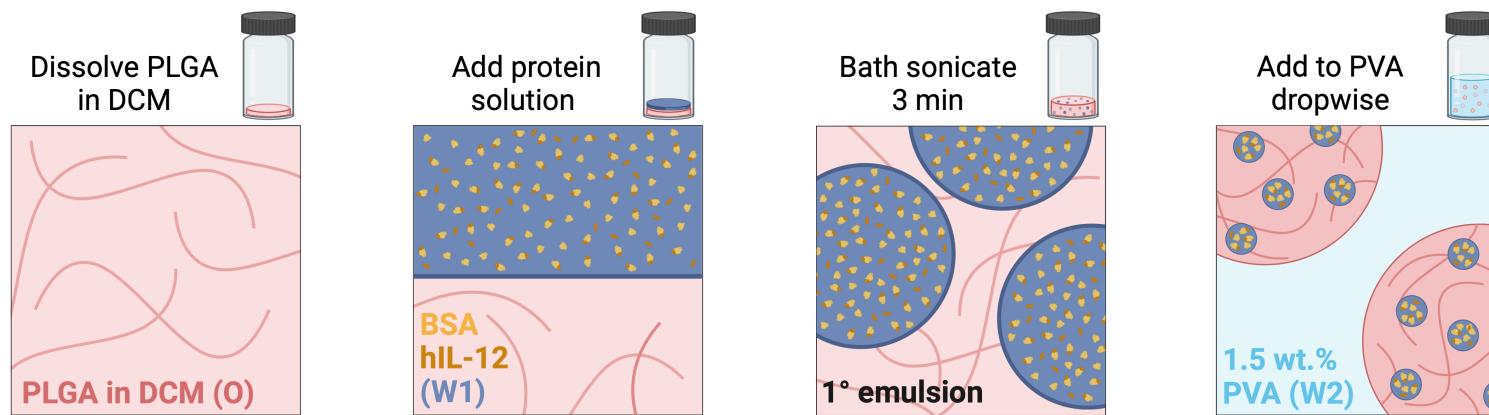
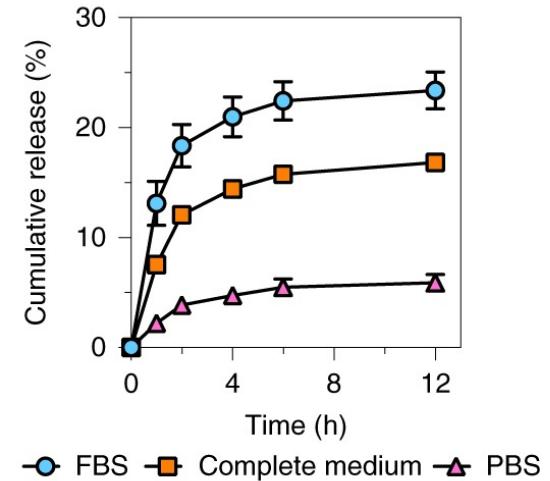
Particle-based controlled delivery of IL-12



BSA-PLGA nanoparticles



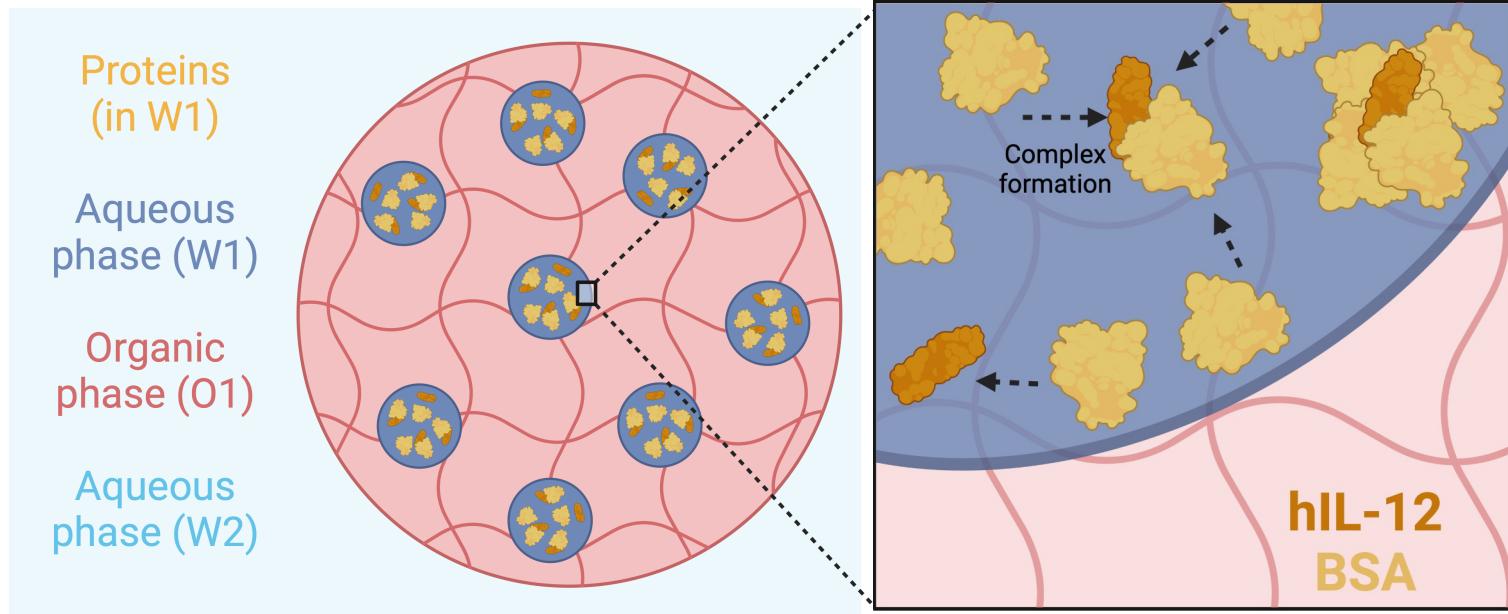
Zhao Z *et al.*, *Nat. Biomed. Eng.*, 2021, 5



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

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

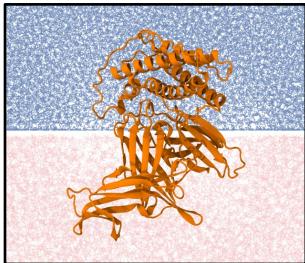


Hypotheses:

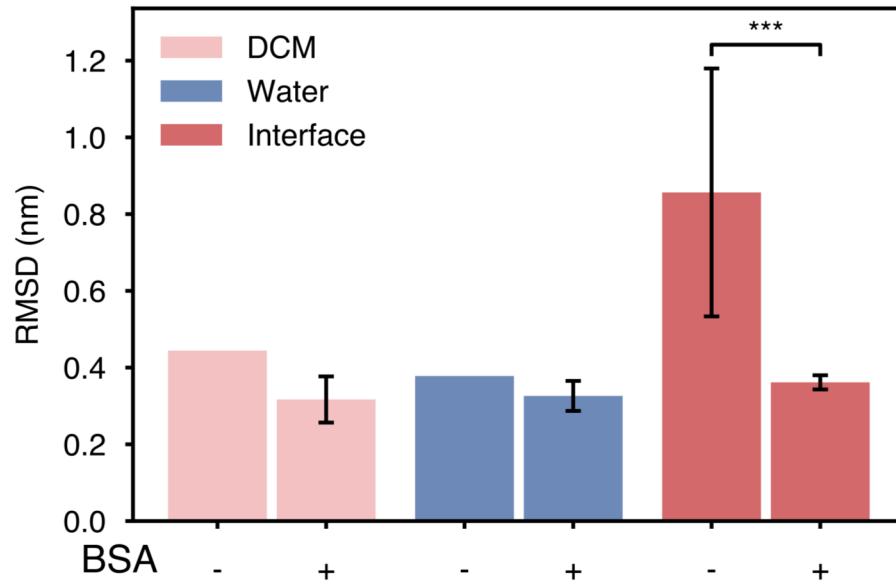
1. hIL-12 unfolds at the W/O interface
2. hIL-12 can be stabilized by BSA binding
3. hIL-12 can be stabilized by interfacial crowding



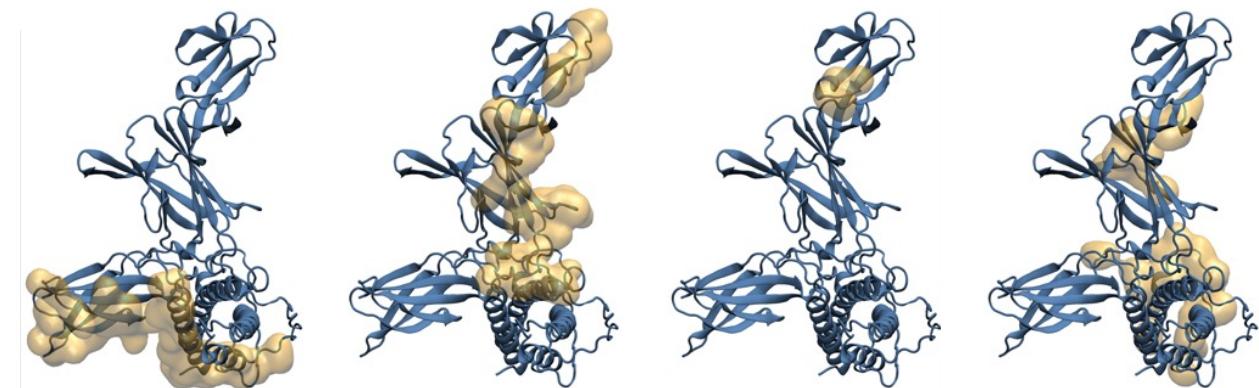
MD analysis demonstrates that hIL-12 destabilization at the W/O interface is damped by BSA



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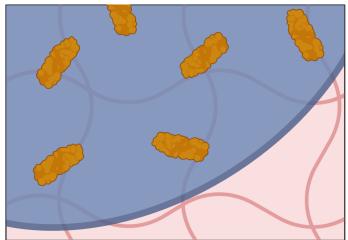
hIL-12 crystal structure + BSA binding locations



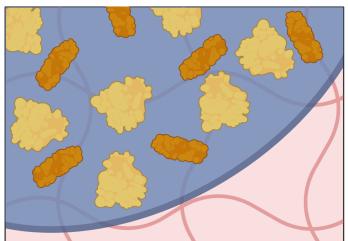
Day N and Rhodes E *et al.*, submitted

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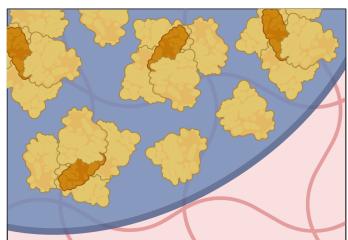
hIL-12 release from particles indicates stabilization by BSA occurs through multiple mechanisms



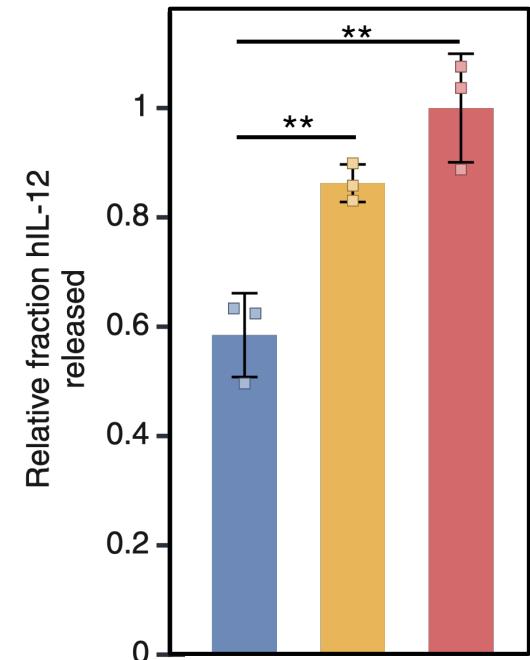
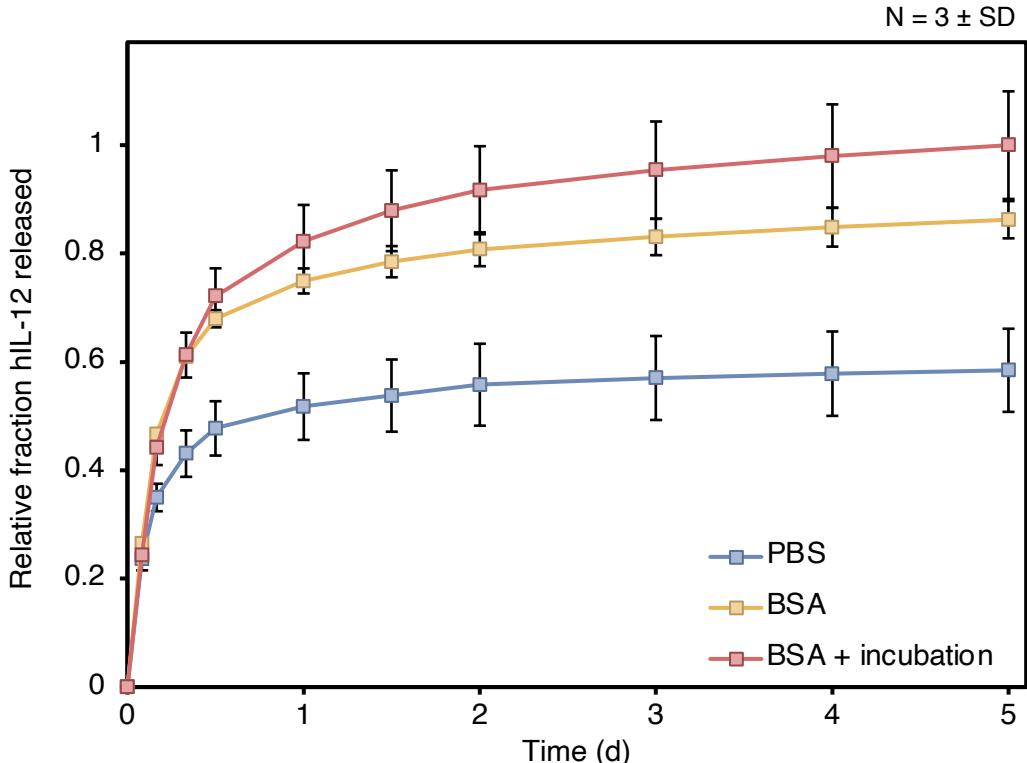
No stabilization
(PBS)



Interfacial crowding only
(BSA)



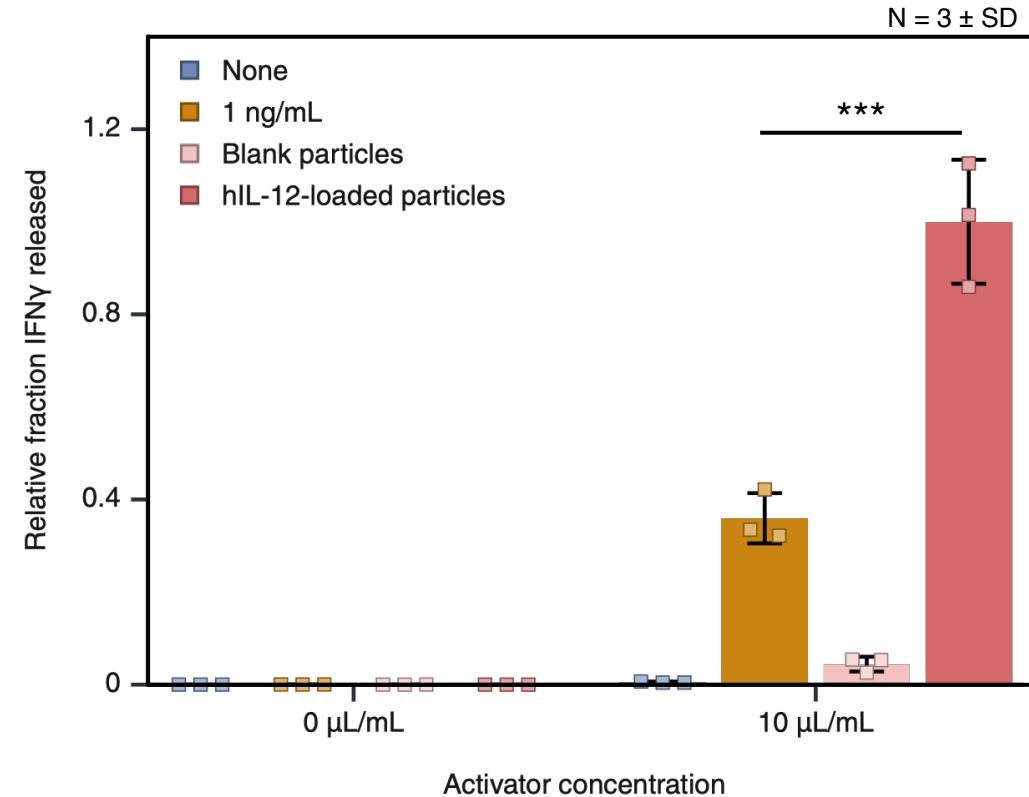
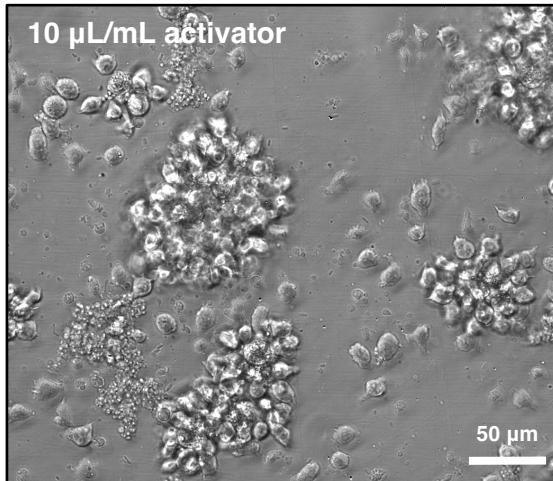
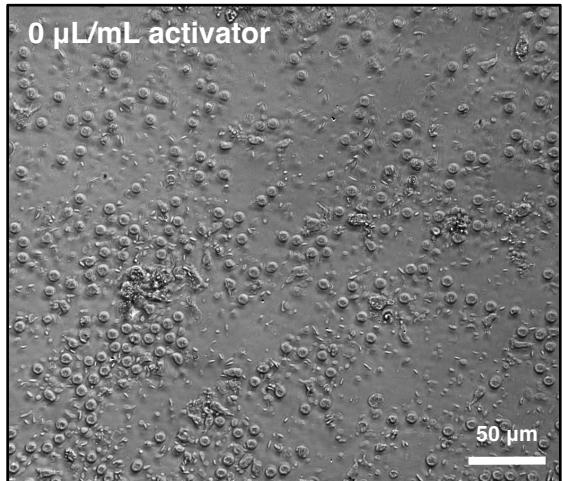
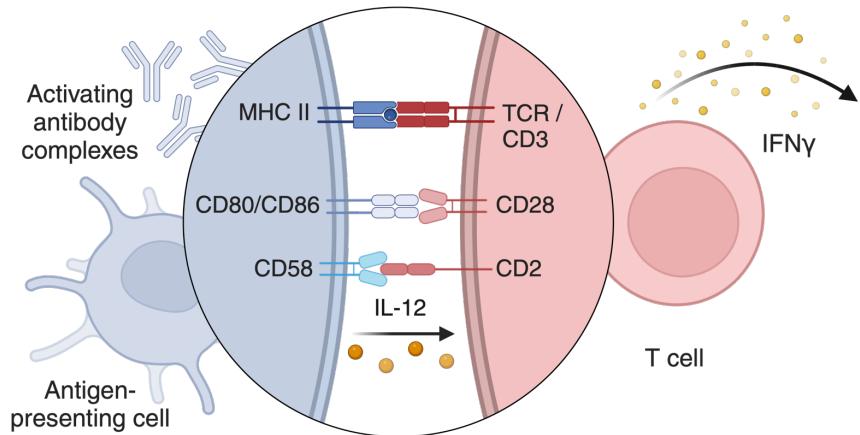
Protein-protein binding & interfacial crowding
(BSA + incubation)



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hIL-12 released from stabilized particles maintains bioactivity in PBMCs

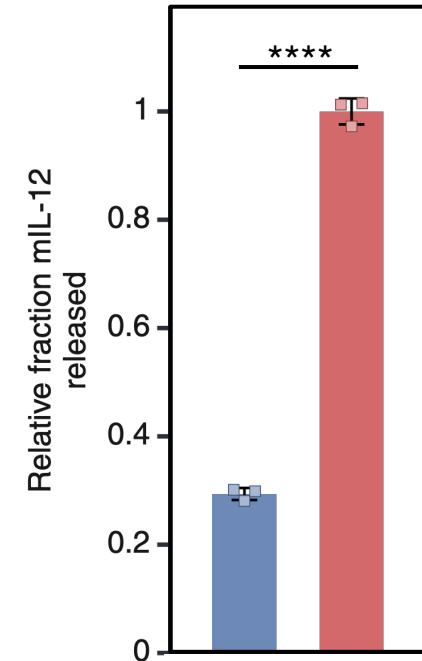
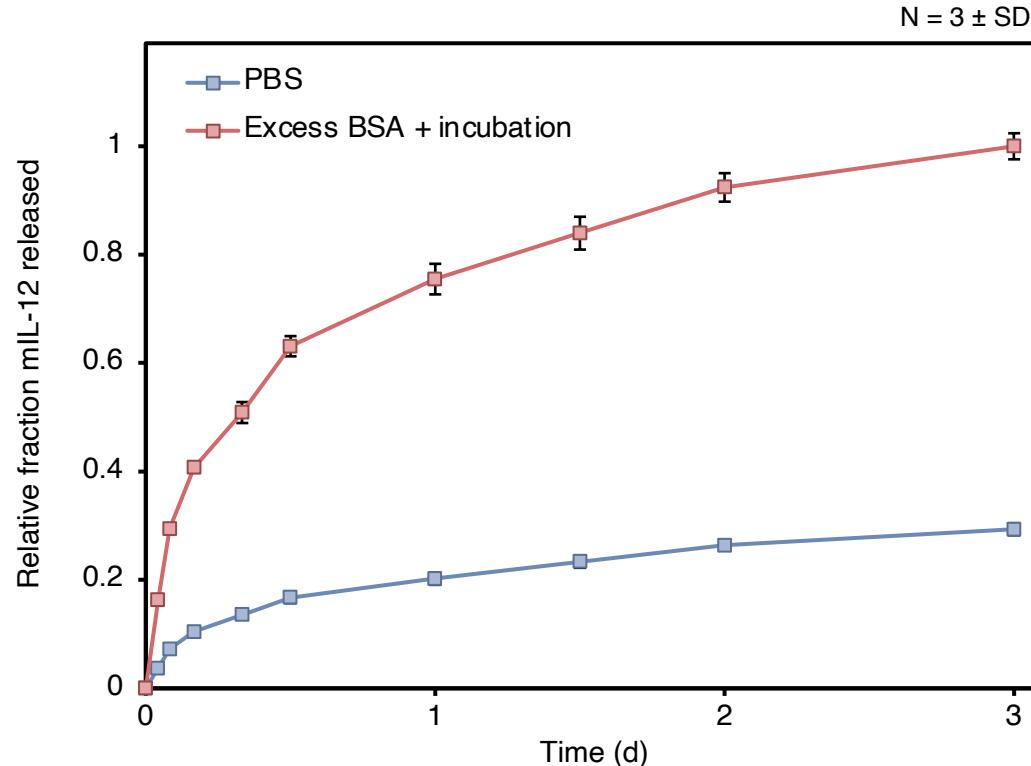
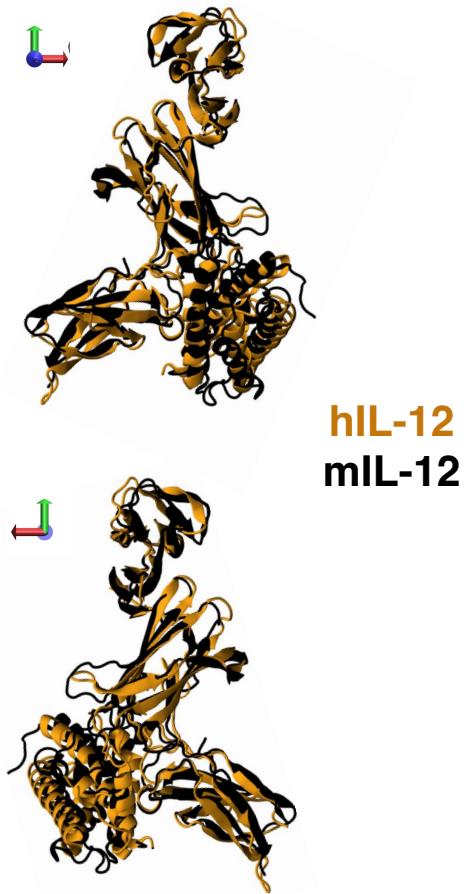


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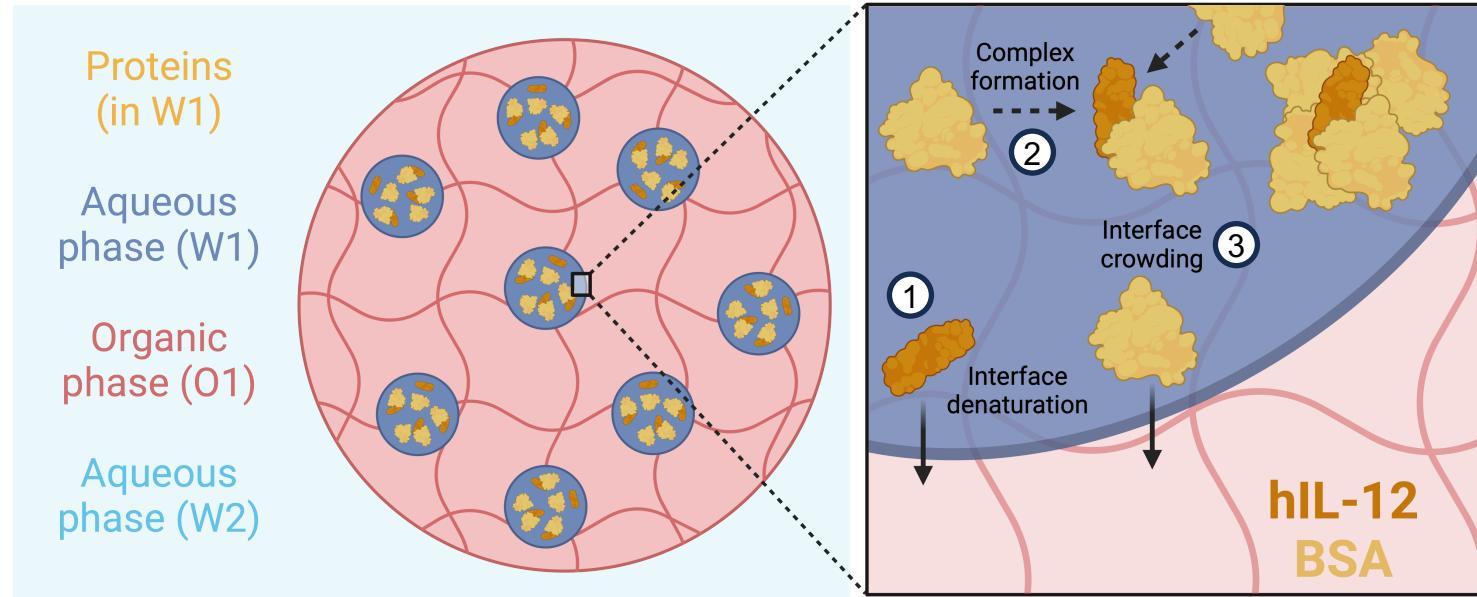


Murine IL-12 release is enhanced by BSA stabilization



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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

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Thank you!

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Shields Lab postdocs & grad students

- Taylor Ausec
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- Collin Kemper
- Kendra Kreienbrink
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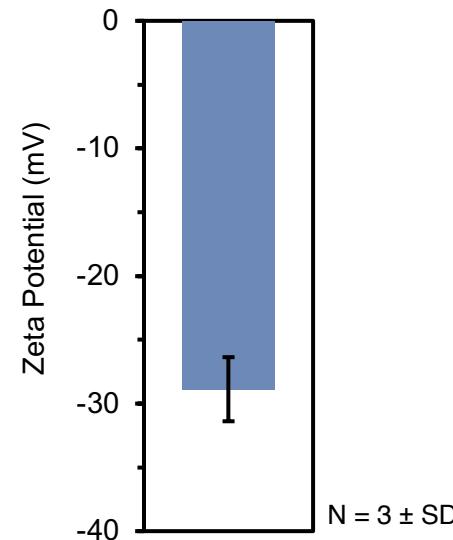
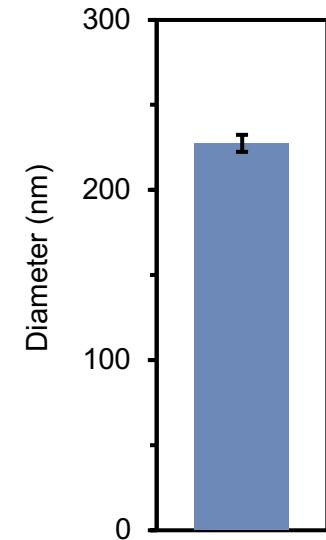
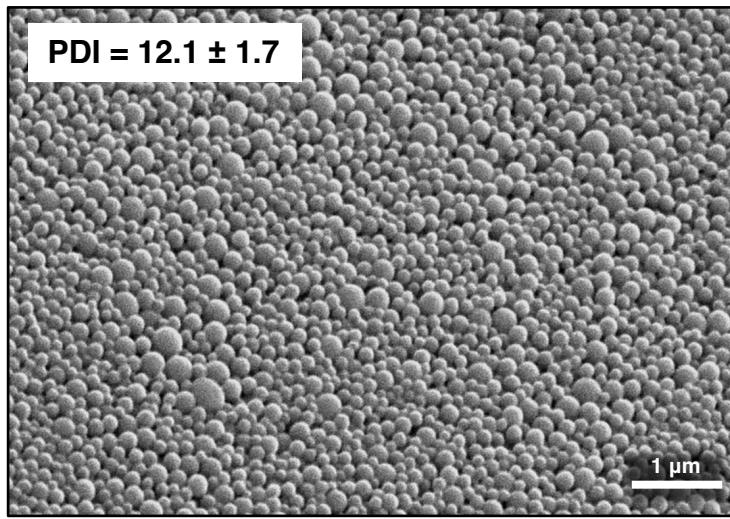


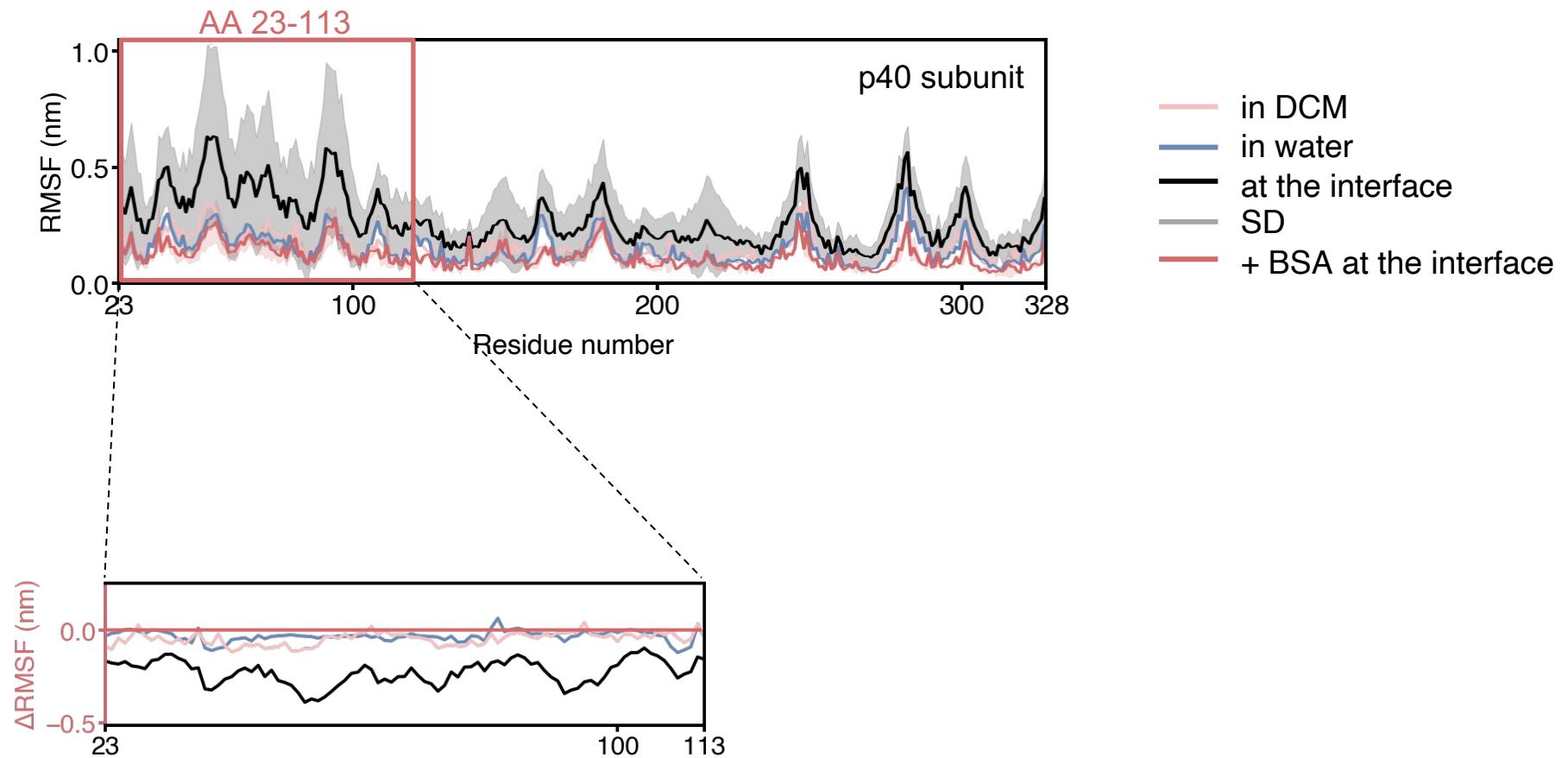
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