Mirror Image Biology: Pushing the Envelope in Designing Biological Systems- A Workshop

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NASEM

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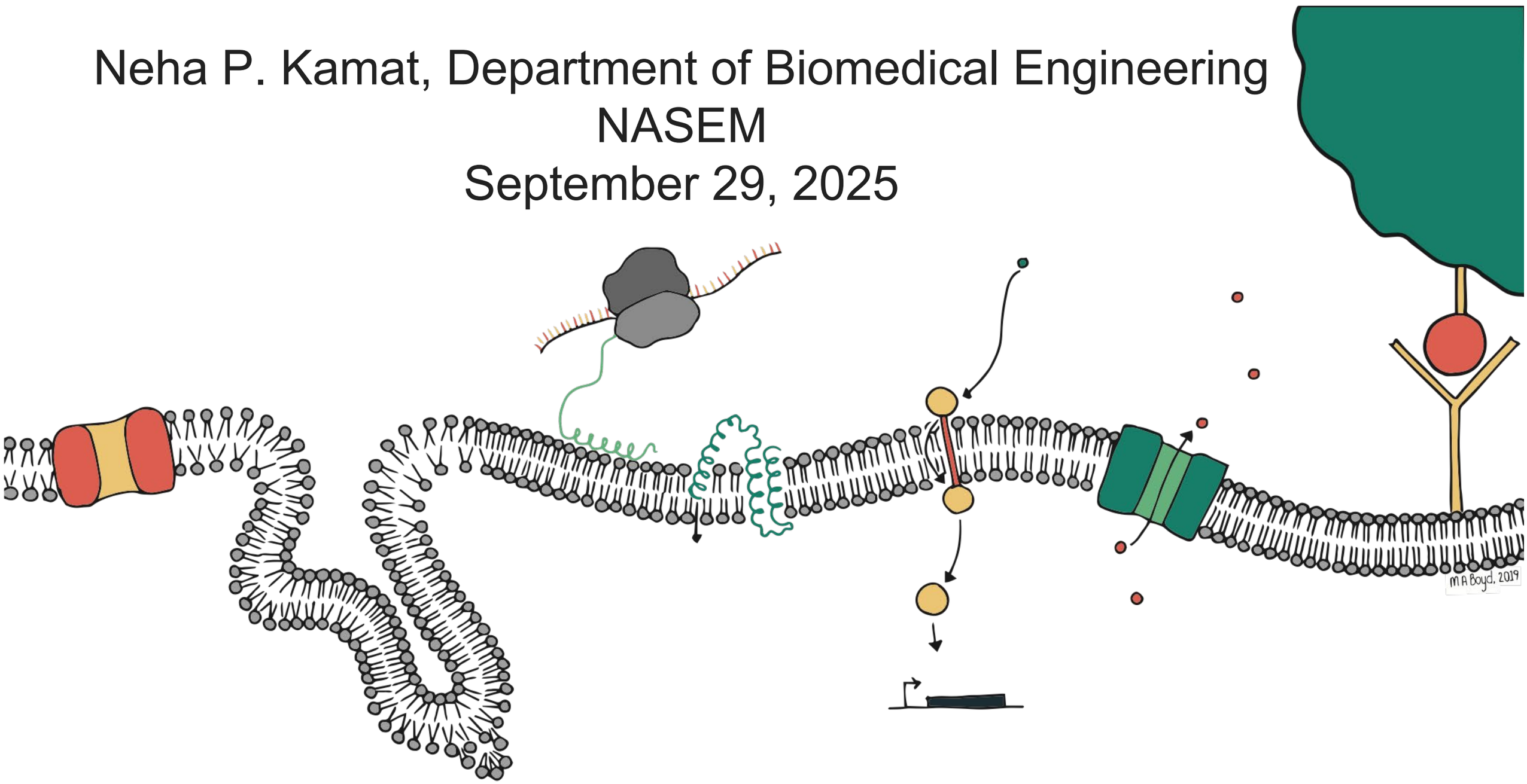

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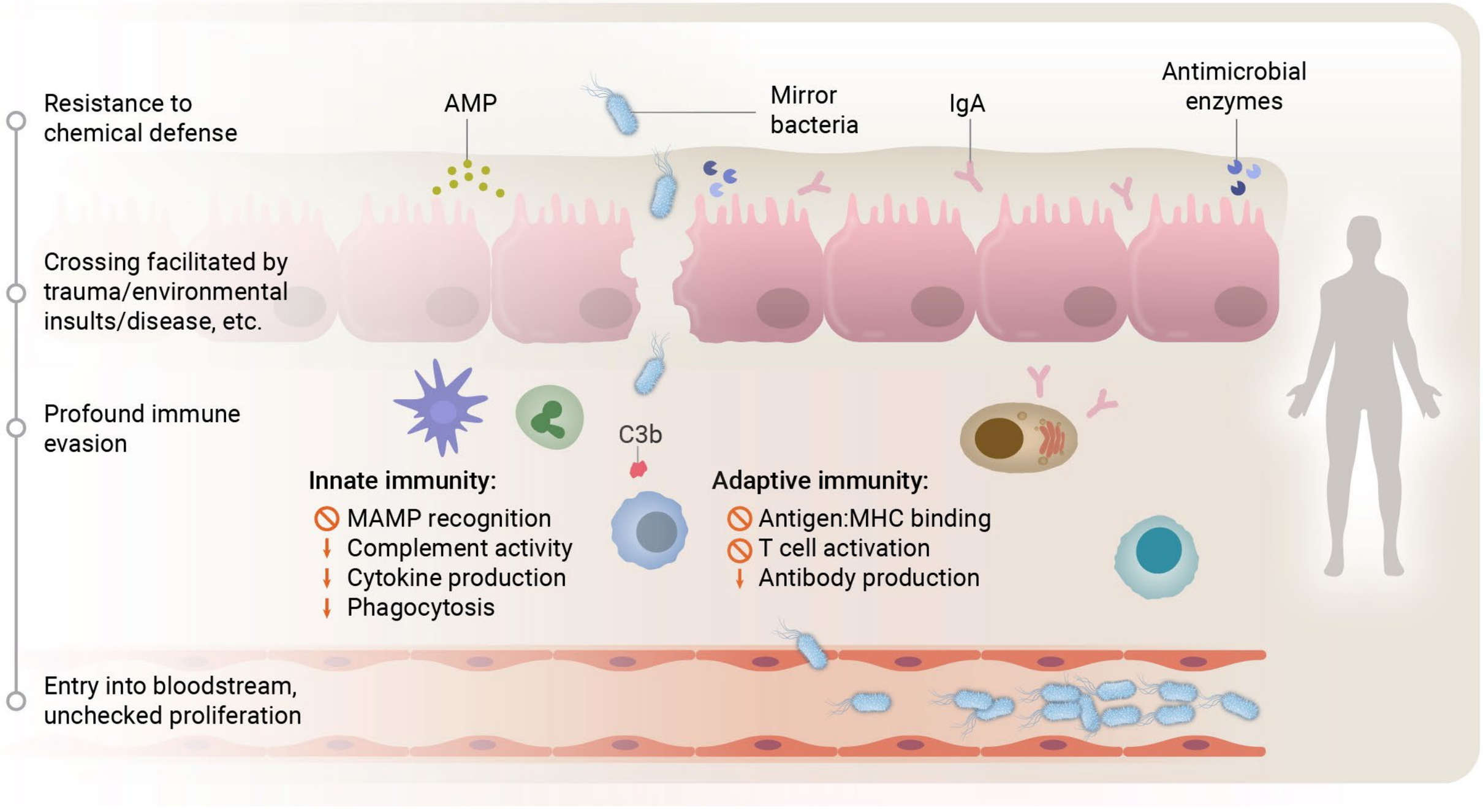
Would mirror cells/ mirror components evade the immune system?



Adamala et al. Technical Report on Mirror Bacteria: Feasibility and Risks. December 2024.

We have chiral and achiral strategies for molecular detection

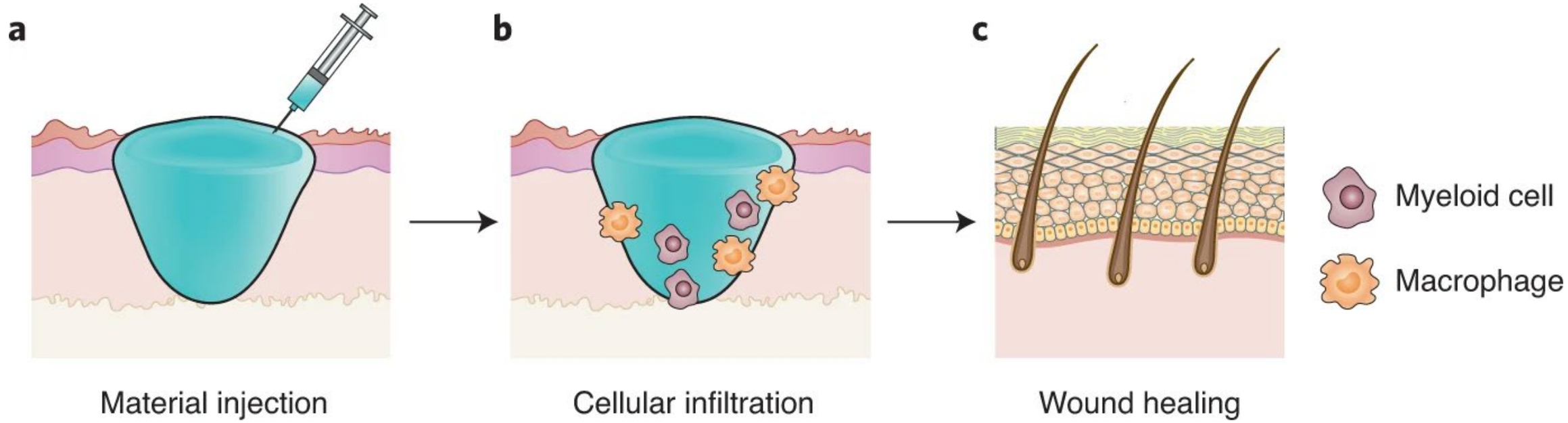
CHIRAL-more difficulty detecting mirror components

- Pattern recognition receptors (PRRs)
- Enzymes (nucleases)

ACHIRAL- remain effective against mirror life, but might be slower

- Antimicrobial peptides
- Reactive oxygen species (ROS)
- cGAS-STING pathway (senses dsDNA and works on B- and Z-DNA
- IgG antibodies (adaptive immune systems)

Microporous annealed particle (MAP) hydrogels loaded with L or D x-linking peptides



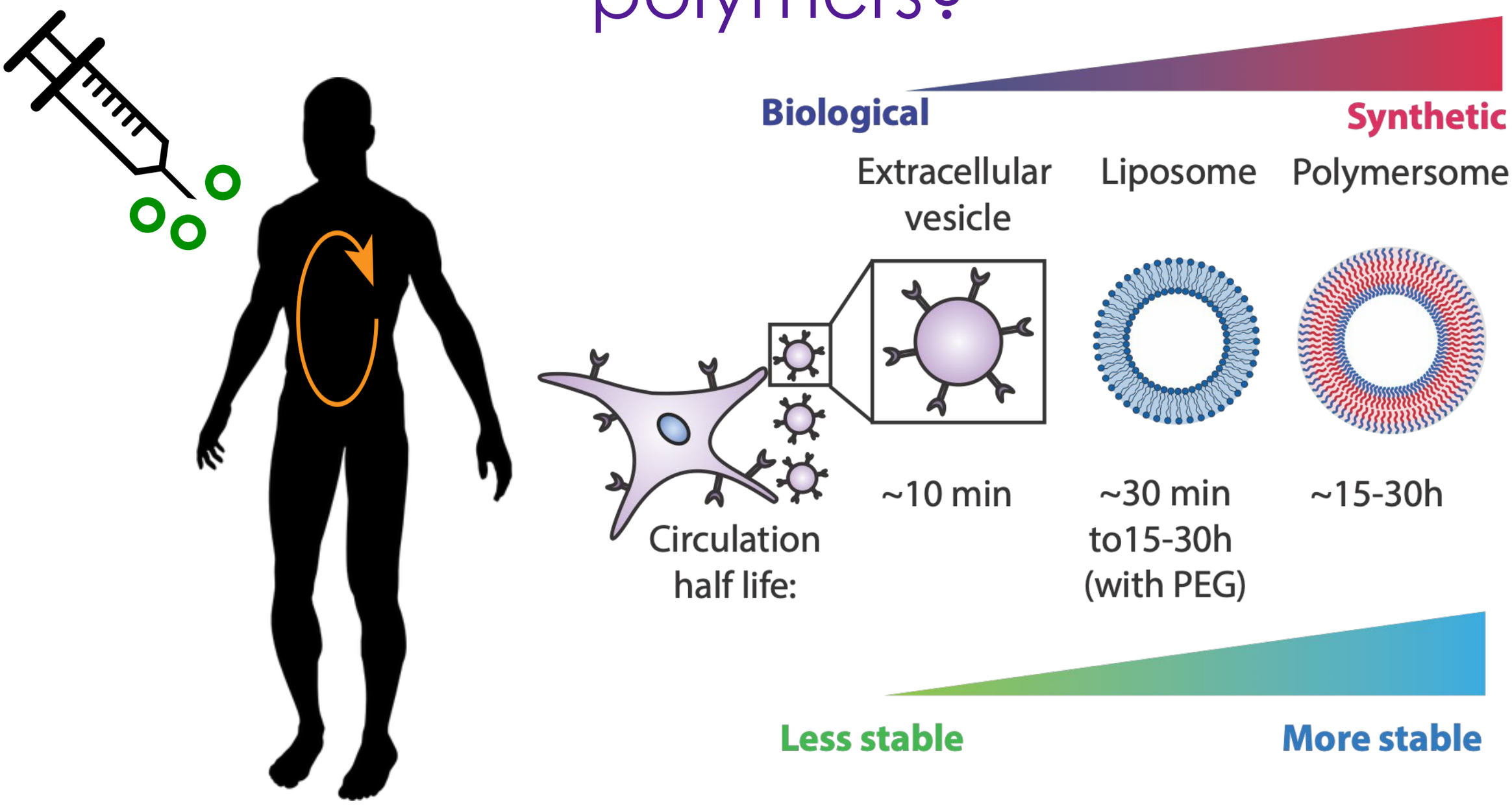
Stelzel, J.L., Doloff, J.C. *Nat. Mater.* **20**, 452–453 (2021)

Although the mirror epitopes do not trigger immediate innate inflammatory pathways, they do:

- lead to a robust T cell-dependent response characterized by the recruitment of CD11b+ F4/80+ macrophages
- production of interleukin-33 (IL-33)
- generation of specific IgG subclasses

Griffin DR, … Segura T, Scumpia PO. Nat Mater. 2021

What can we learn from synthetic polymers?



"We have determined the prevalence of anti-PEG antibodies in the German population to be 83% positive for either anti-PEG IgG or IgM. Interestingly, the prevalence inversely correlated with age. This high prevalence might well be due to casual exposure to PEG compounds in everyday products."

Deuker et al. Nanoscale Horiz. 2023
#s from Yunxi et al. Sci Adv. 2025

So then what might be areas of biological risk for mirror cells/mirror components?

- Replication competence: what does it mean to replicate? Is DNA replication enough? How long must something replicate to be considered a risk? If a cell, are there mechanisms for sustained nutrient uptake to enable adaptation?

- Autoimmune therapies: Biological systems that learn NOT to EVADE, but to WORK WITH the immune system might present more serious concerns (e.g. self tolerance)

Next steps

- Define replication (what components, duration or cycle # that dictates capability of escape)

- Look for/ develop methods to monitor and detect immune cell TOLERANCE vs. evasion

- What does mirror “creep” look like

- Use biohybrid materials to help guide regulatory policies for mirror cells and molecules

- Study immune cell interactions with mirror molecules