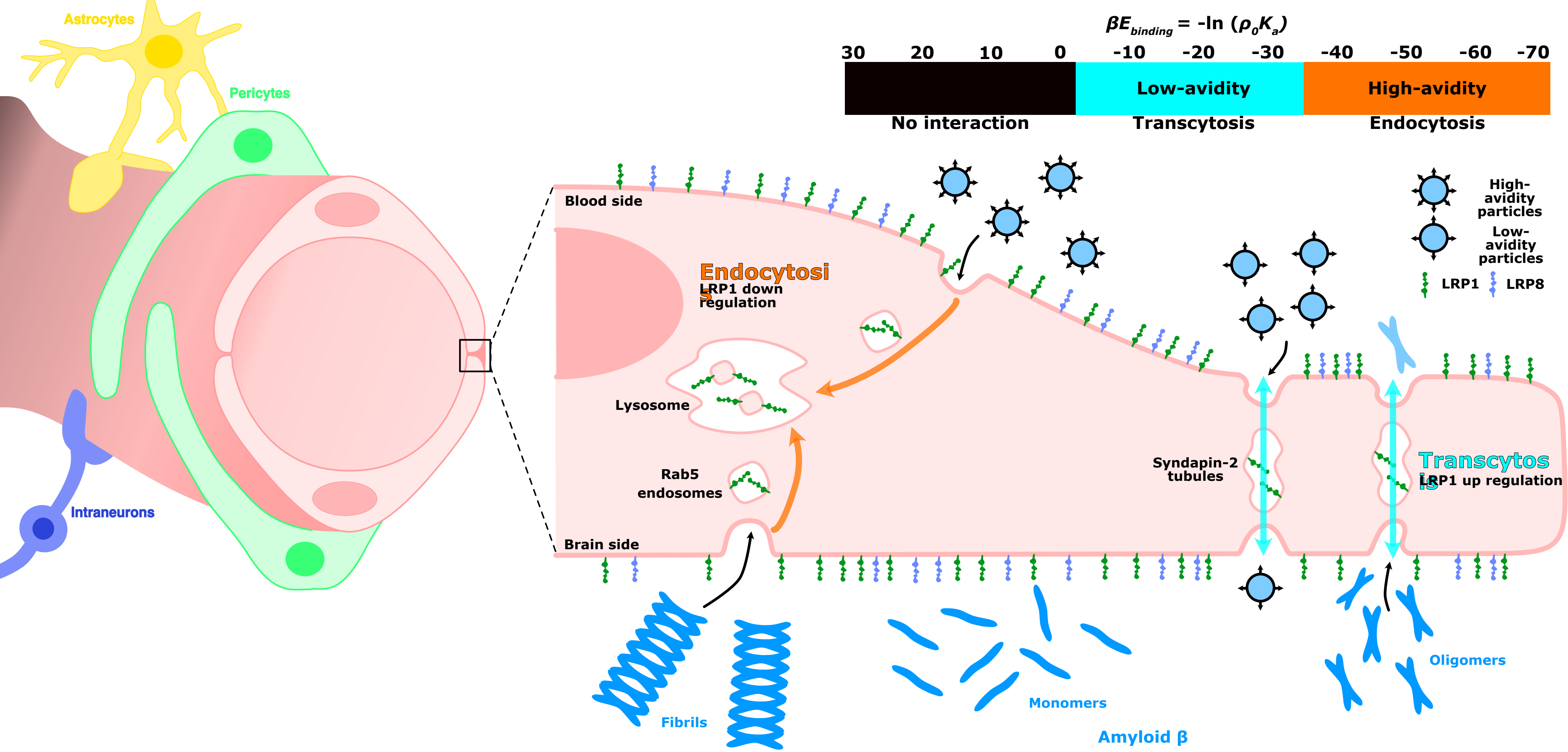


On the Amyloid- β transcytosis across the blood-brain barrier

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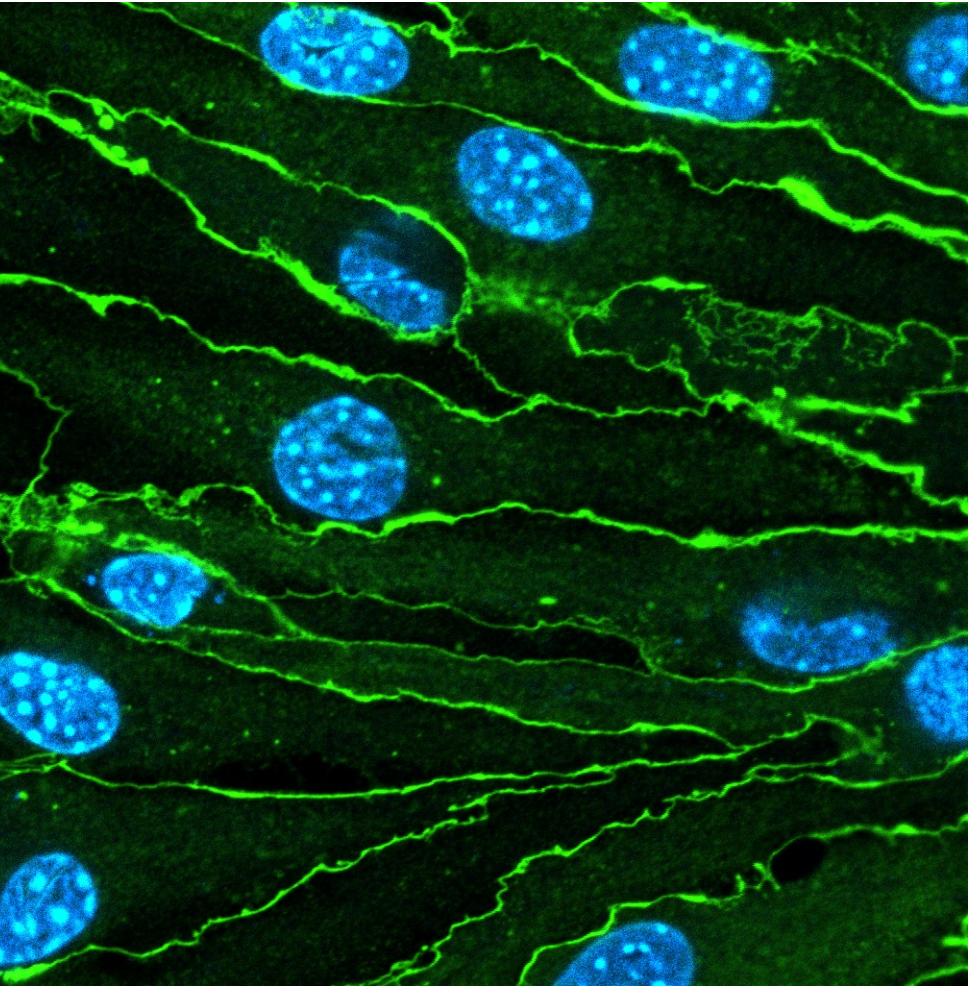


Background

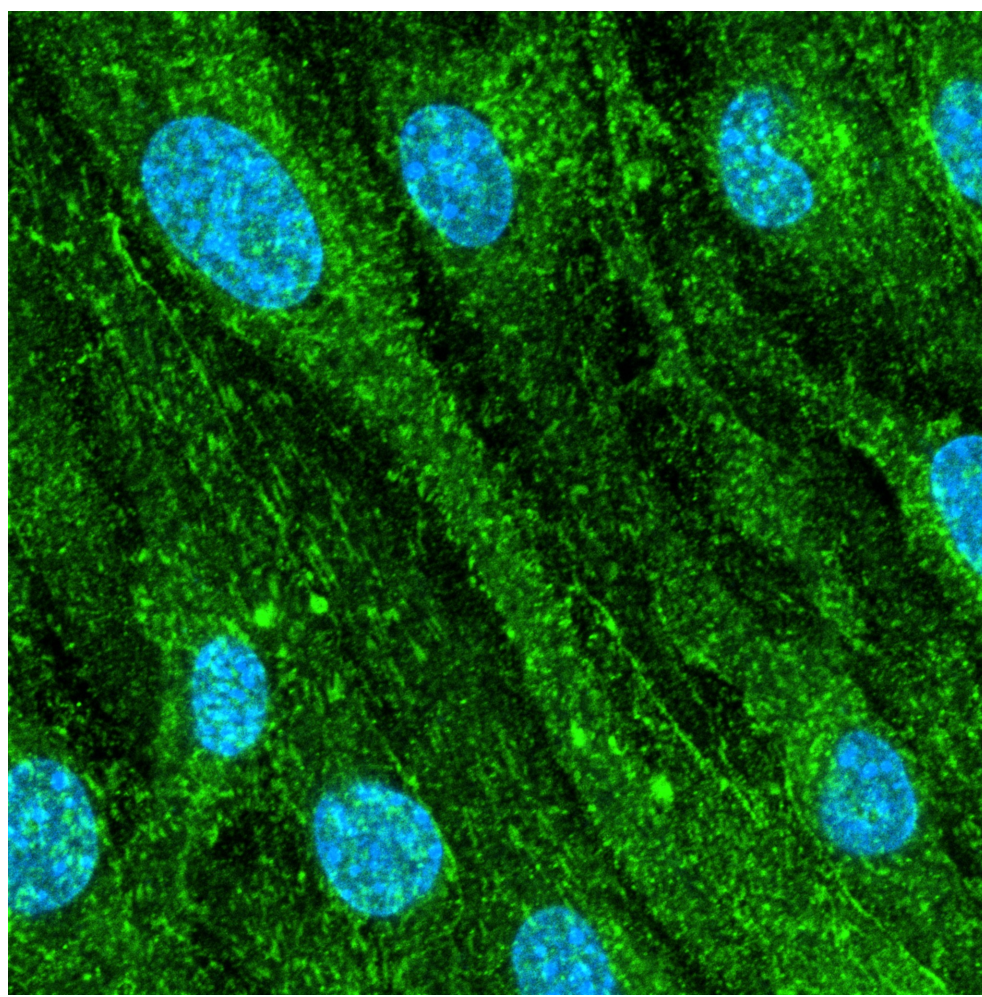
Our group has discovered that the blood-brain barrier (BBB) plays a crucial role in regulating the transport of misfolded proteins to and from the Central Nervous System (CNS). We have found that the BBB controls the trafficking of macromolecular cargo by its affinity towards receptors like the low-density lipoprotein receptor-related protein 1 (LRP1) and the low-density lipoprotein receptor-related protein 8 (LRP8). LRP1 primarily transfers amyloid- β (A β) across the BBB, while LRP8 requires further studies. We have developed functionalised polymeric nanoparticles that mimic the in vivo process by having multiple ligand-receptor affinities to encourage this process. These investigations are essential in determining how polymeric nanoparticles can enhance the clearance of A β from the CNS, which could lead to the development of novel therapies.

BBB characterisation

Tight junctions

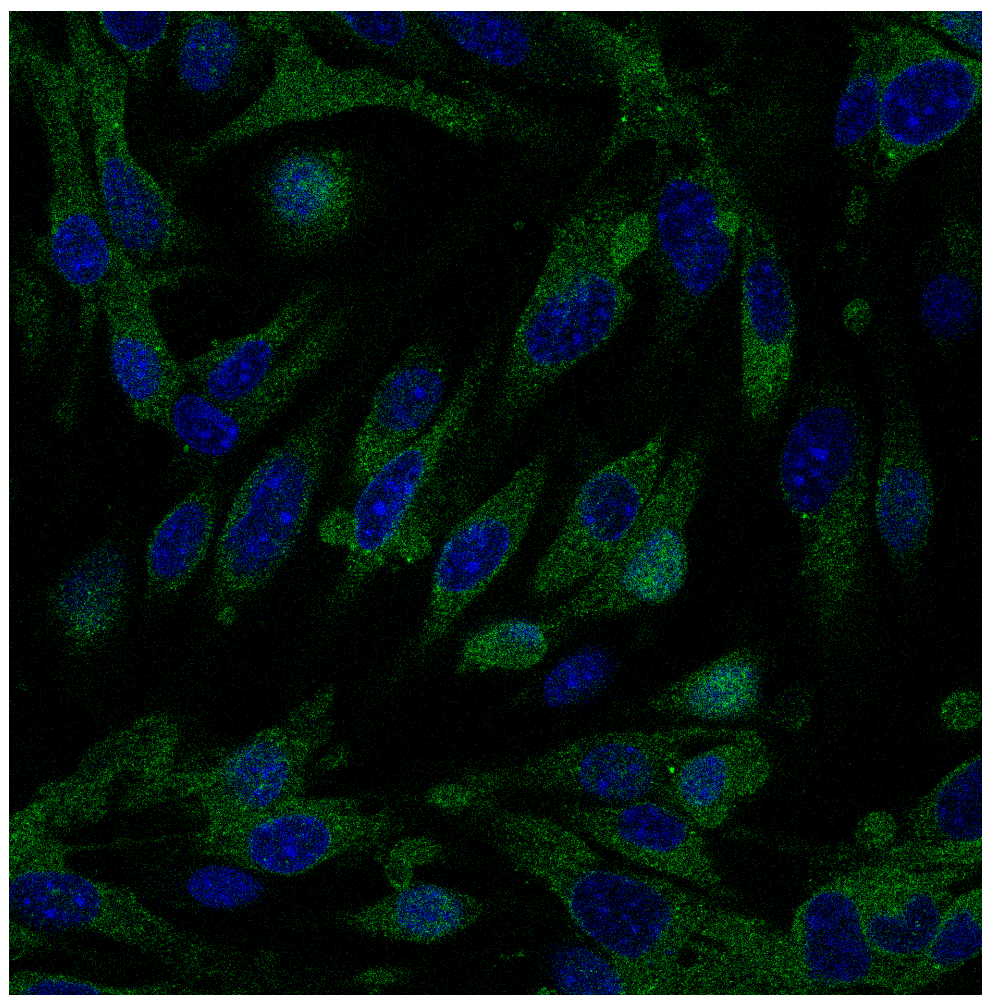


ZO-1

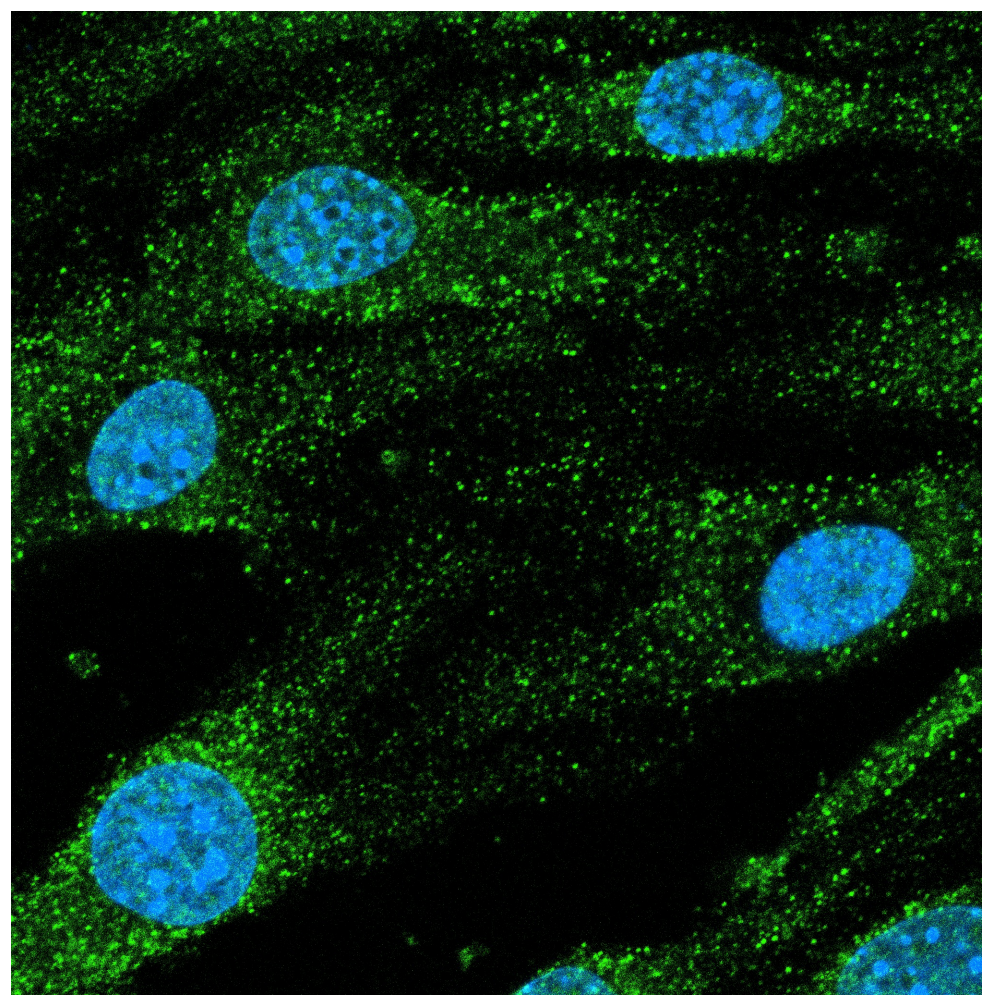


Occludin

Receptors

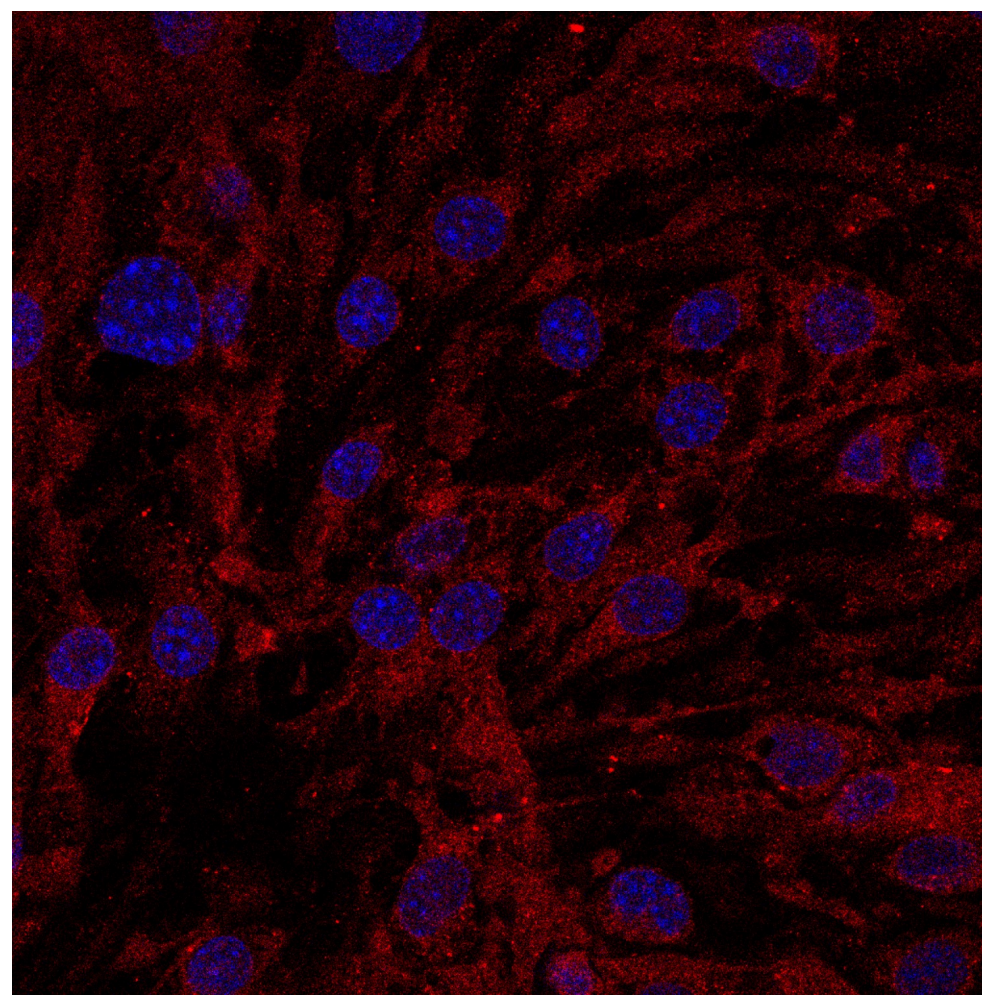


LRP8

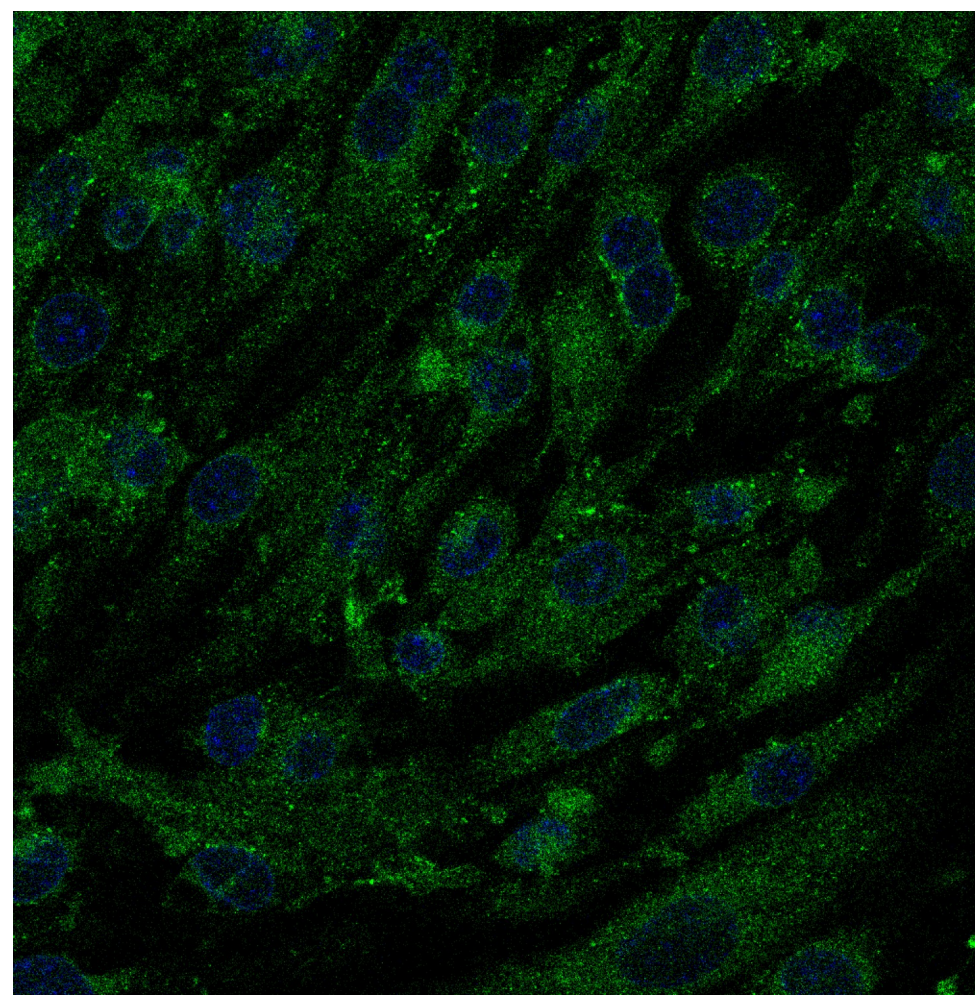


LRP1

Intracellular proteins



PACSIN2

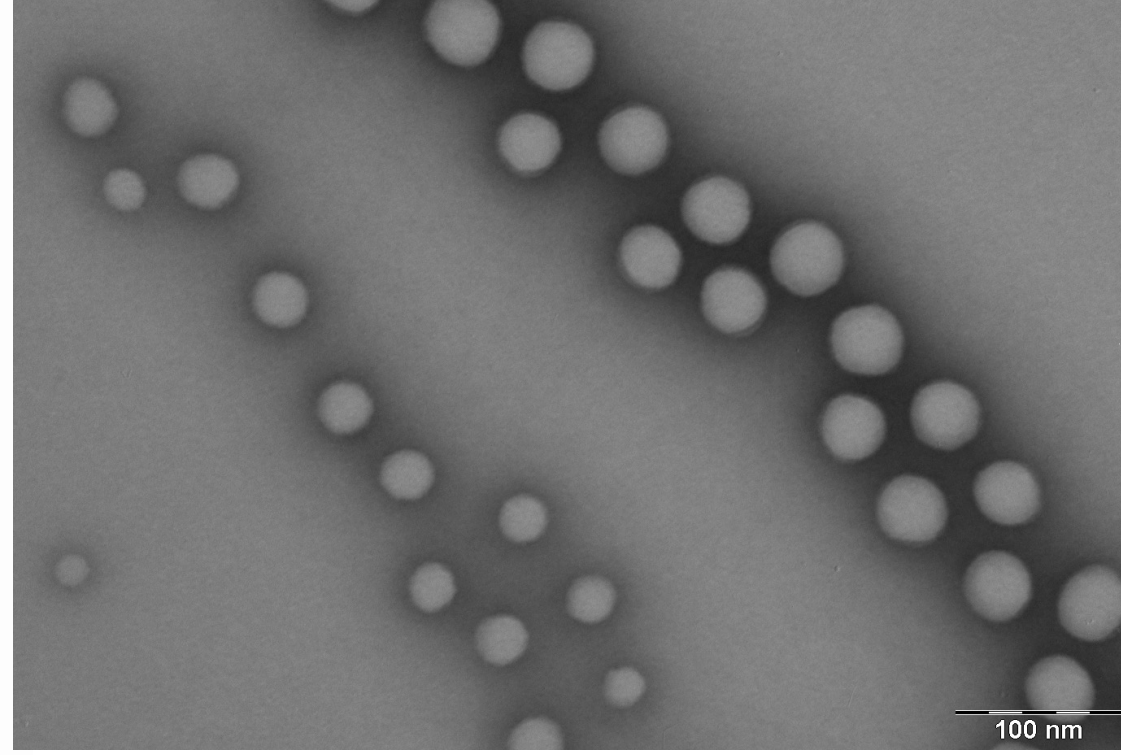
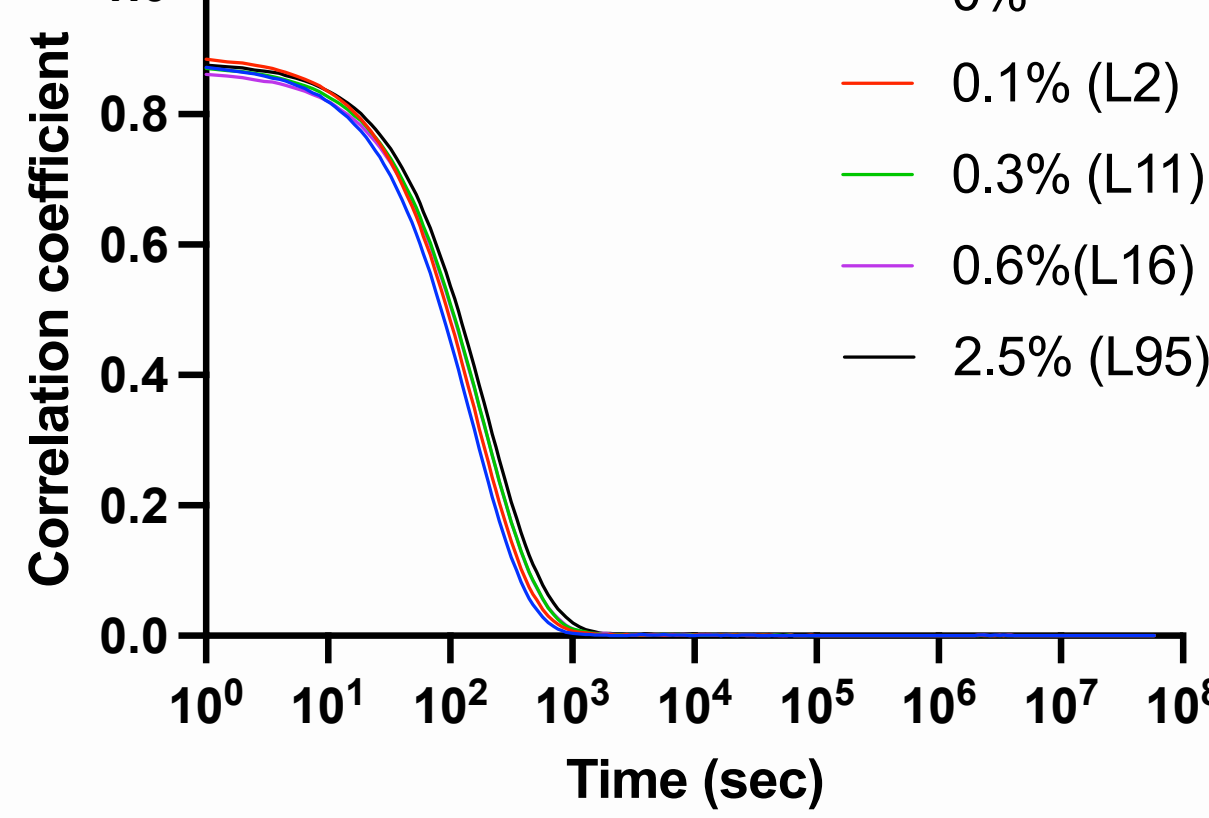
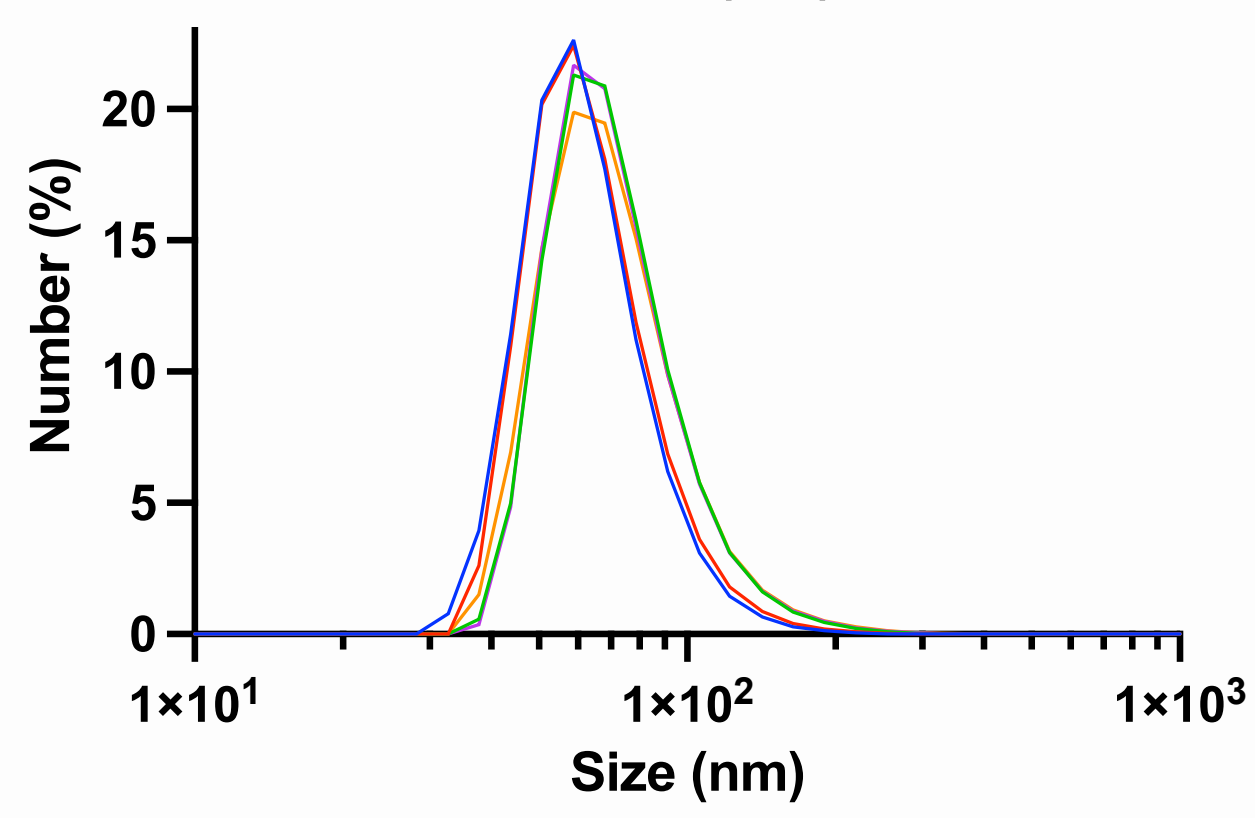
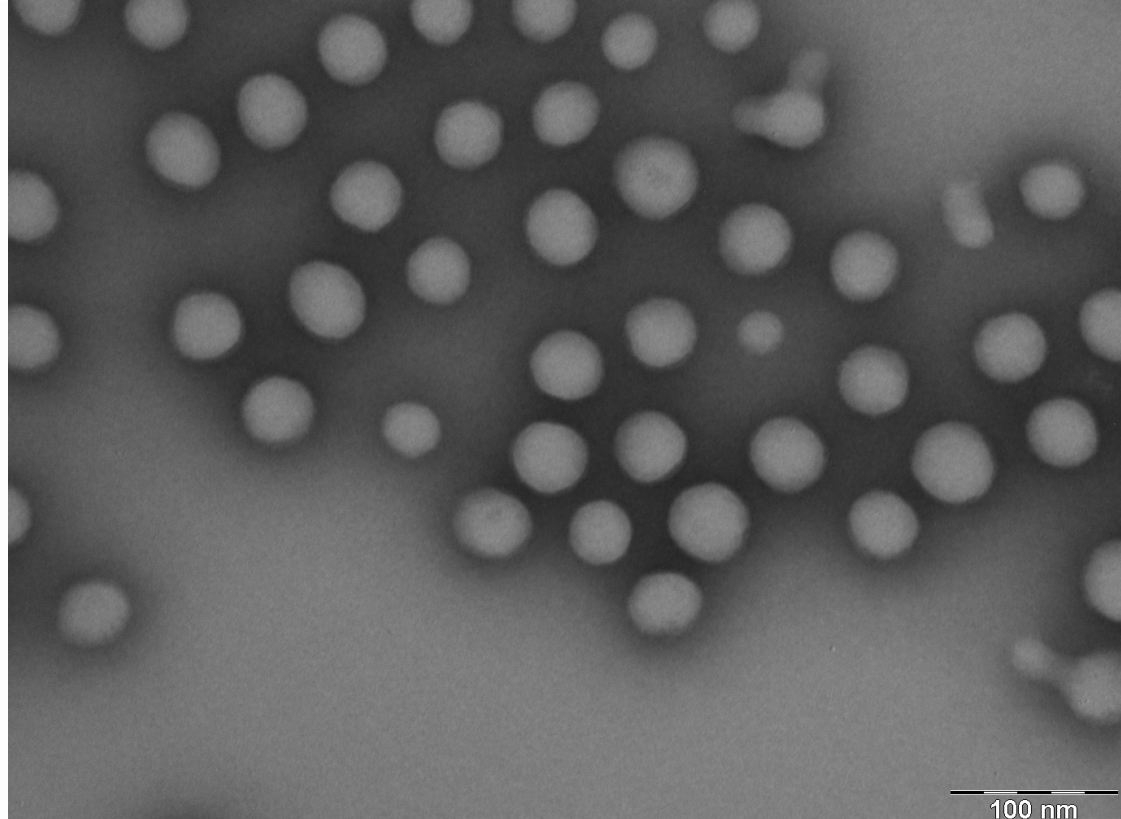
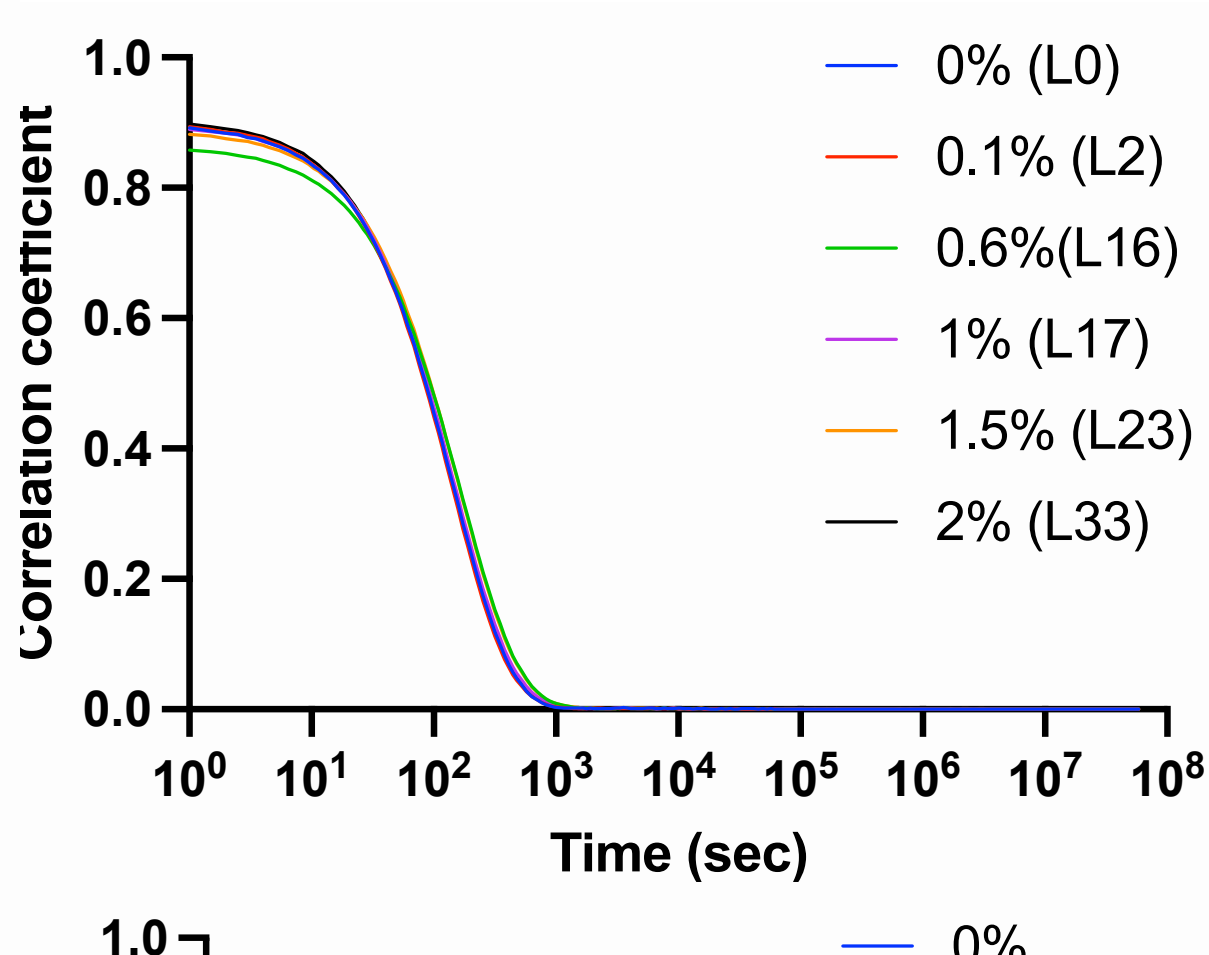
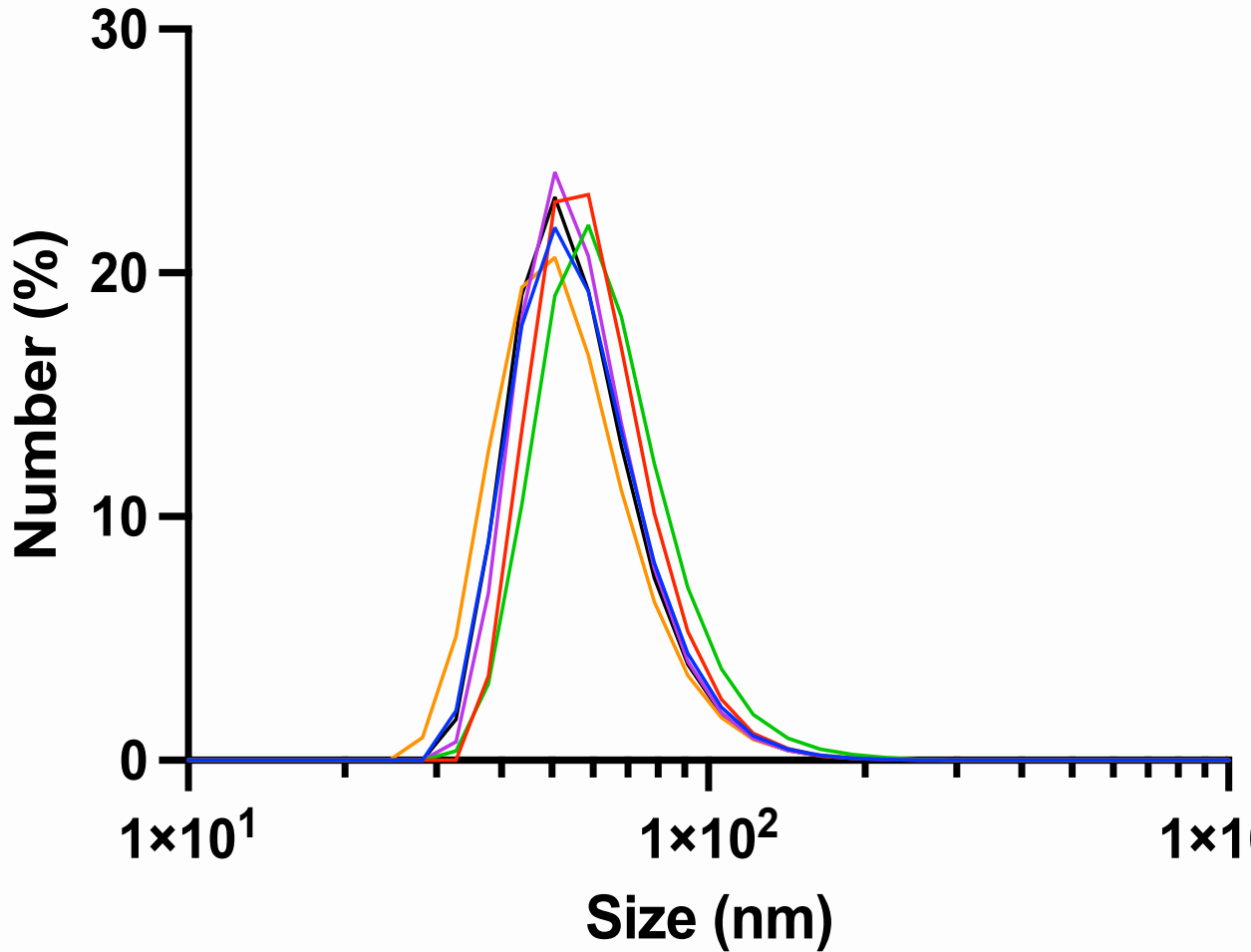
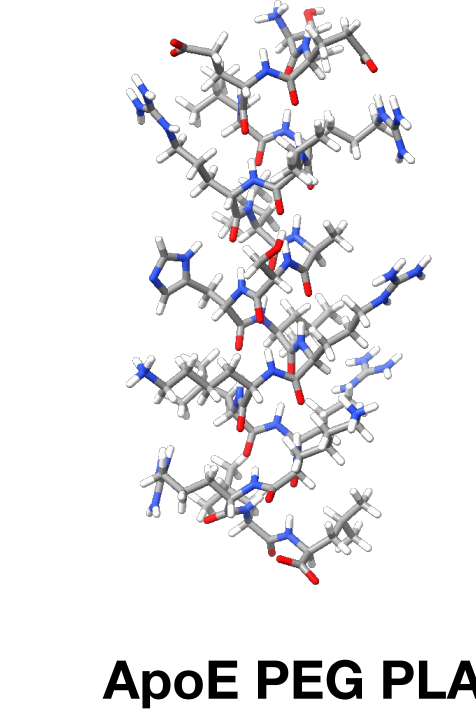
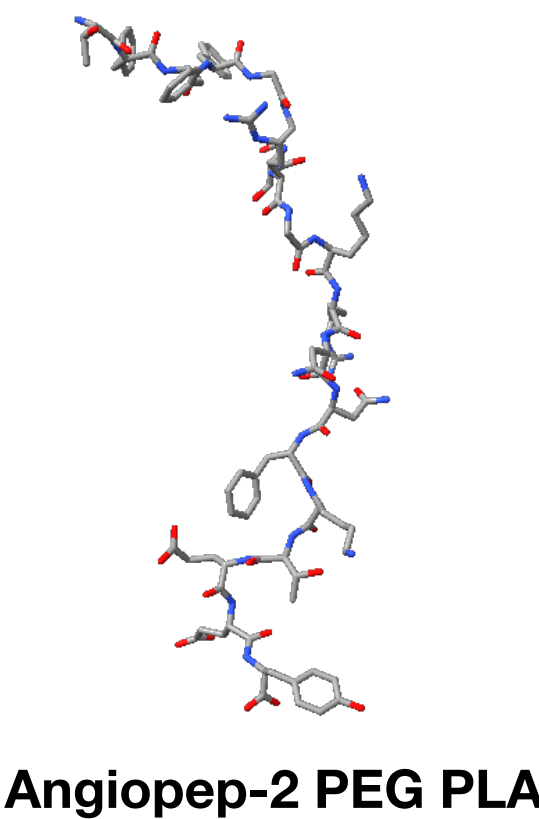
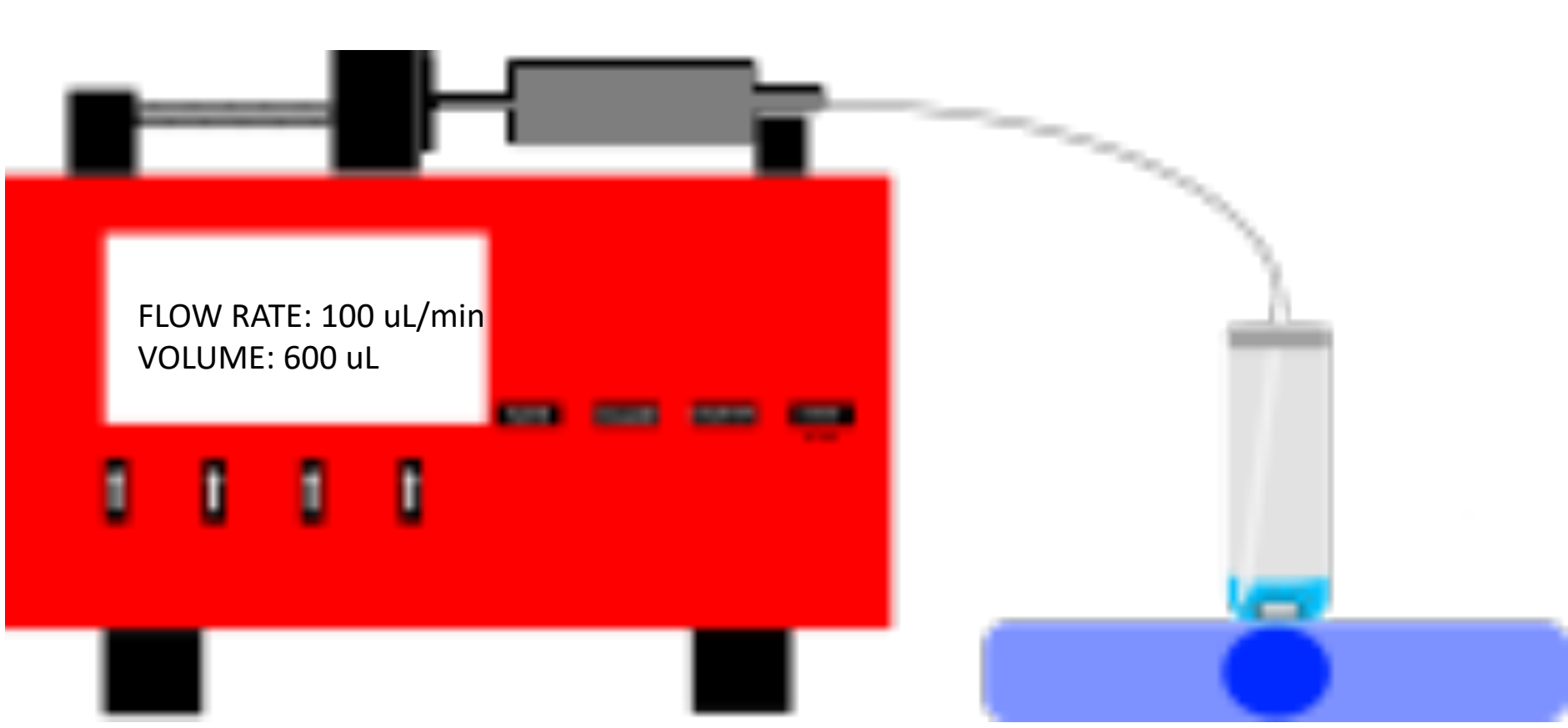


RAB5

PEG PLA polymersomes

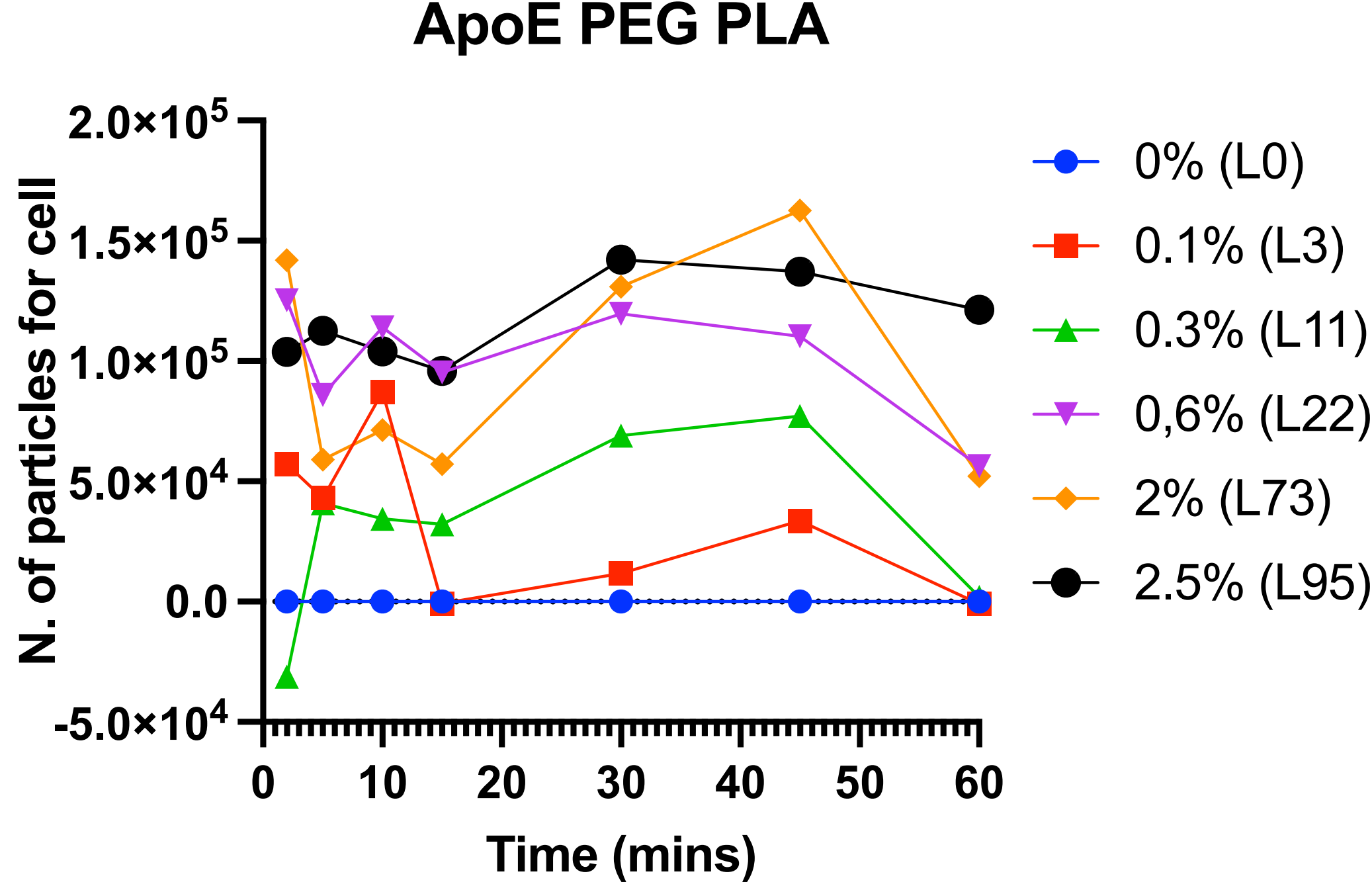
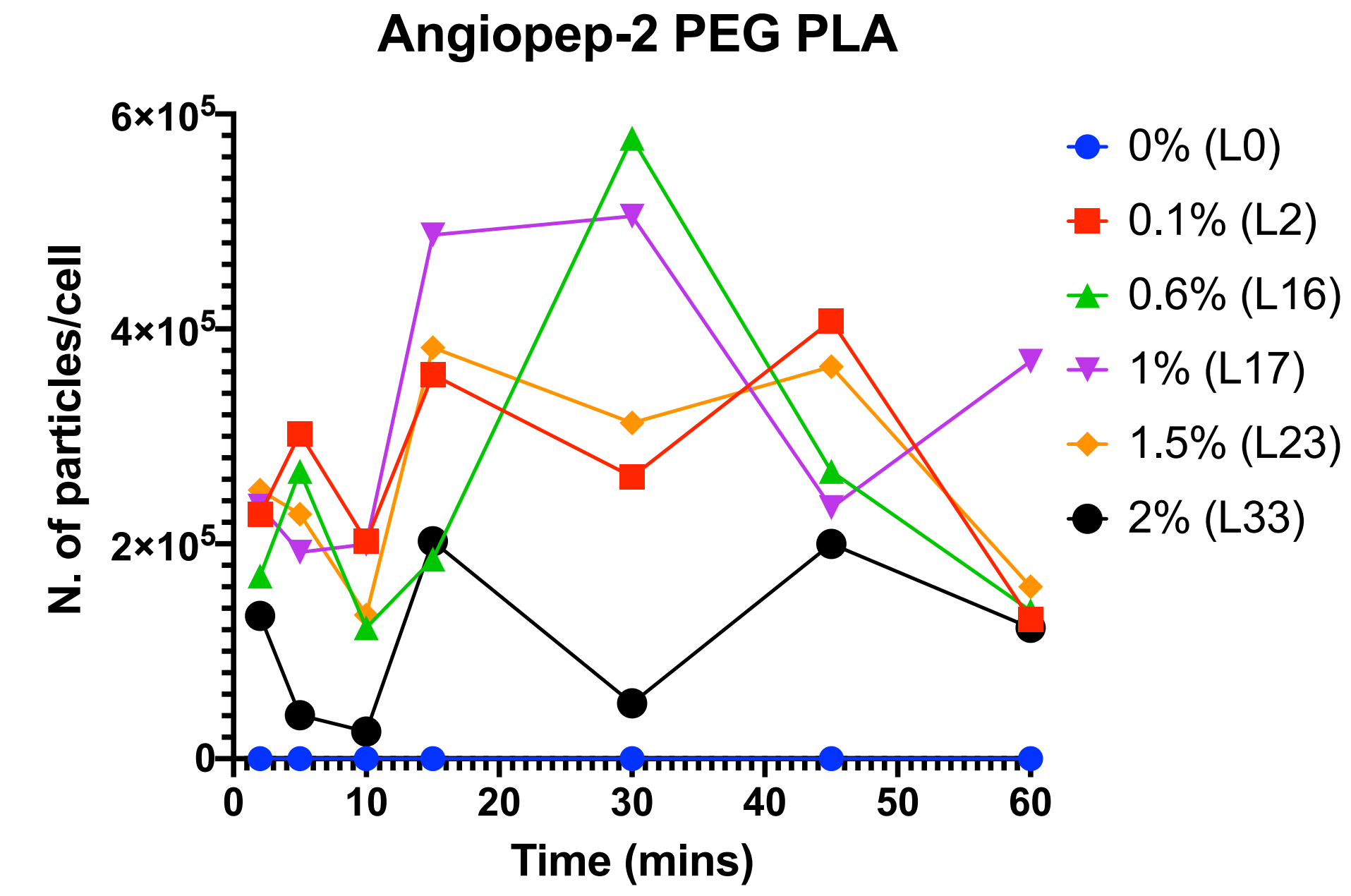
Solvent switch approach

Injection of the organic copolymer solution into water



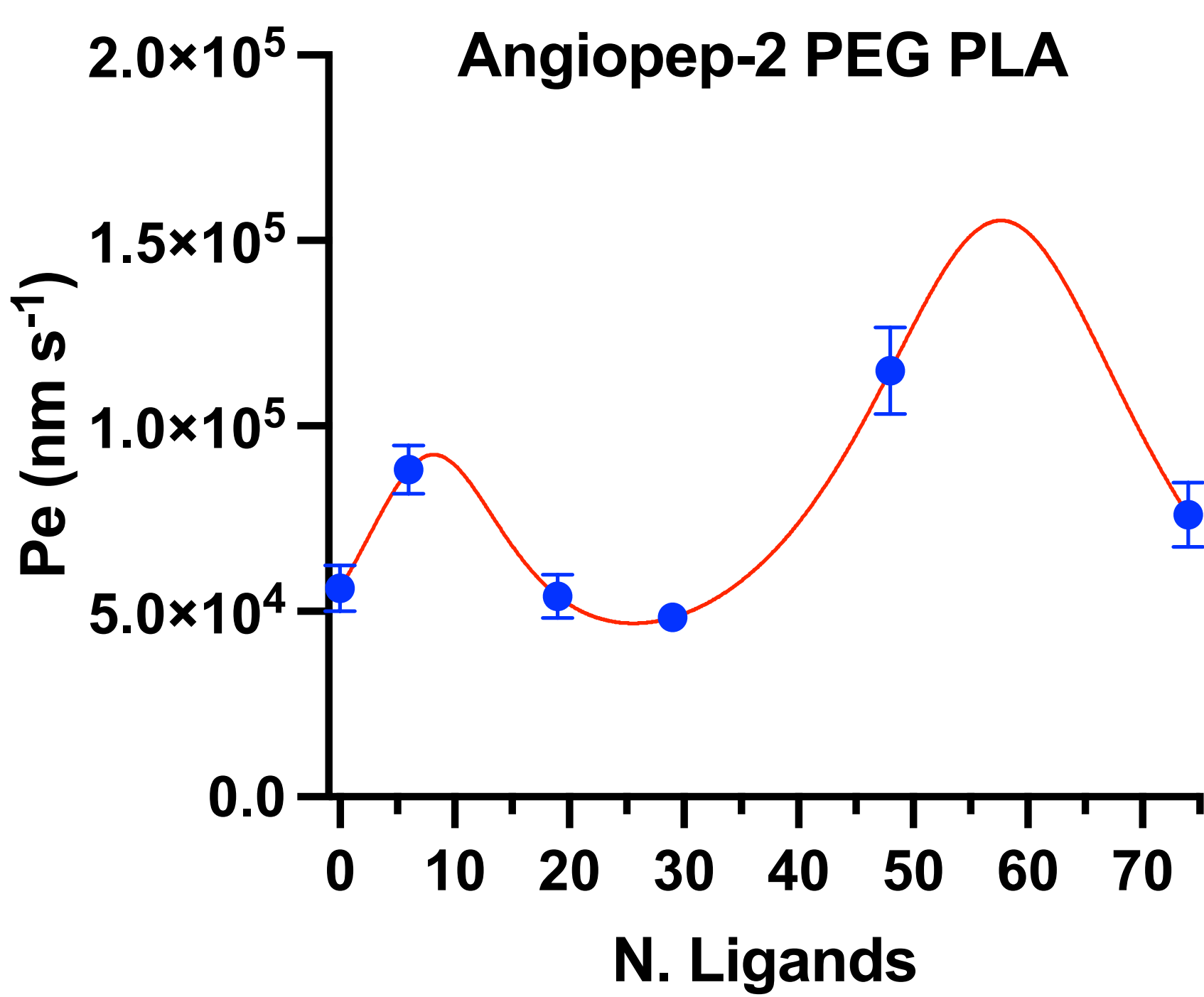
Binding assays

Studying the nanoparticles' affinity



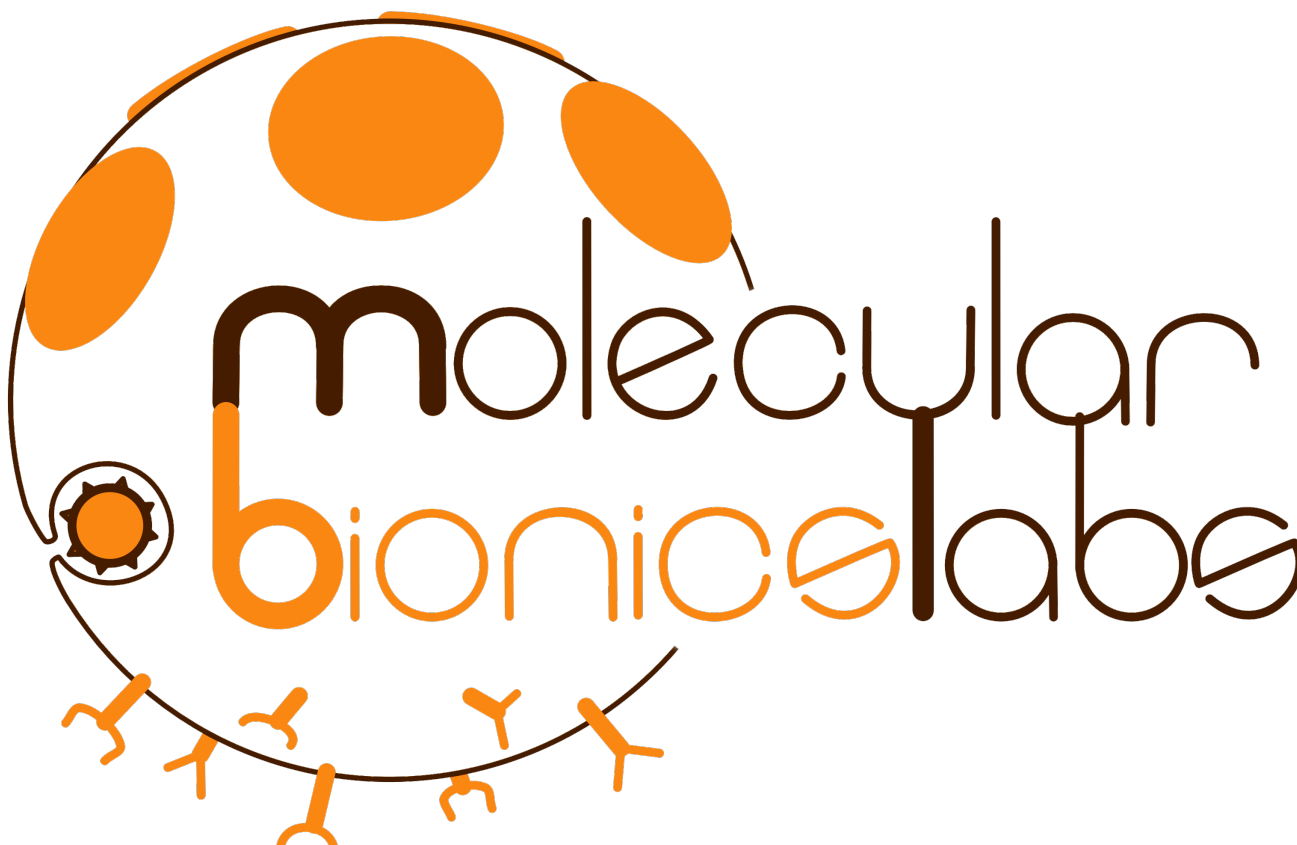
Permeability assay

Evaluating the nanoparticles' transcytosis



Future prospective

These findings have opened the door for more in-depth investigations into the gene and protein expression of LRP1 and LRP8, as well as for a deeper exploration of the molecular mechanisms underlying the transcytosis of these receptors.



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"la Caixa" Foundation

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