Chemical & Physical Sciences
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Turning Lemons into Lemonade: Affinity Release Strategies for Therapeutic Delivery

Photo by Jenna Wakani

Controlling protein release has typically been achieved by using strategies similar to those used for drug delivery; however, the method of encapsulation in biodegradable polymeric nanospheres is inherently limited in the amount and bioavailability of the released proteins.Typically, less than 0.1% by mass of protein is encapsulated and the exposure to shear and organic solvents impacts protein activity. While working in this area, we discovered encapsulation-free protein release – that is proteins do not have to be encapsulated, but rather their release can be controlled by electrostatic affinity interactions [1, 2]. The mechanism for this will be described as will the affinity release based on discrete protein-peptide binding partners.

For the latter, we express fusion proteins with Src homology 3 (SH3) and modify of hydrogel delivery vehicle with SH3-binding peptides, thereby controlling release of our protein of interest through the affinity of SH3 and its binding peptides [3]. More recently, we have advanced this to finding novel binding partners for each protein by manipulating yeast surface display [4]. We demonstrate the benefit of these methods in animal models of spinal cord injury, stroke and blindness.

References:

[1] Pakulska, M.M.; Elliott Donaghue, I.; Obermeyer, J.; Tuladhar, A.; McLaughlin, C.K.; Shoichet, M.S. 2016 “Encapsulation-free controlled release: electrostatic interactions eliminate the need for protein encapsulation in PLGA nanoparticles,” Science Advances, 2, e1600519 doi:10.1126/sciadv.1600519

[2] Ho, E.; Deng, Y.; Akbar, D.; Da, K.; Létourneau, M.; Morshead, C.M.; Chatenet, D.; Shoichet, M.S. 2023 “Tunable surface charge enables the electrostatic adsorption-controlled release of neuroprotective peptides from a hydrogel-nanoparticle drug delivery system”, ACS Applied Materials & Interfaces, 15: 91-105 doi: 10.1021/acsami.2c17631

[3] Pakulska M.M.; Miersch, S.; Shoichet, M.S. 2016 “Designer protein delivery: from natural occurring to engineered affinity controlled release systems,” Science, 351(6279):aac4750; doi: 10.1126/science.aac4750

[4] Teal, C.J.; Hettiaratchi, M.H.; Ho, M.T.; Ortin-Martinez, A.; Ganesh, A.N.; Pickering, A.J.; Golinski, A.W.; Hackel, B.J.; Wallace, V.A.; Shoichet, M.S. 2022 “Directed evolution enables simultaneous controlled release of multiple therapeutic proteins from biopolymer-based hydrogels”, Advanced Materials, e2202612: 1-14; doi: 10.1002/adma.202202612