ACS 2022 Abstract

**Designing supramolecular hydrogels for long-term subcutaneous antibody delivery**

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While HIV treatments have improved, there is still not an effective HIV vaccine available to prevent the spread of the virus. Broadly neutralizing antibodies (bNAbs) against HIV have been developed, but passively-transferred immunity only lasts for as long as the bNAbs persist in the body, which is typically on the order of weeks to a few months. To address this challenge, we have developed an injectable, supramolecular polymer-nanoparticle (PNP) hydrogel to serve as a subcutaneous antibody delivery depot to extend antibody pharmacokinetics (PK). In order to tailor this platform to deliver antibodies with different PK profiles, it is critical to understand how the underlying supramolecular network structure and dynamics affect the rate of release of cargo encapsulated in the hydrogel network. We report the measured rheological properties of various PNP hydrogel formulations as well as the diffusion of both the polymeric hydrogel components and encapsulated antibodies measured using fluorescence recovery after photobleaching (FRAP). A combination of X-ray and neutron small angle scattering experiments provides further insight into the structure of our system. Furthermore, we have conducted preliminary in vivo studies and applied compartment modeling to quantify the contribution of the depot to the overall PK profile of an antibody drug. The robust structural and dynamic understanding of the PNP hydrogels developed from our results will allow us to design next-generation biomaterials to effectively extend the delivery of antibodies against HIV as well as other viruses and infectious diseases.

