MegaMolecules and Applications as Antibody Mimics

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This talk will describe a general strategy for synthesizing molecular architectures that combine large size (>100 nm) with precise structural definition. The approach relies on the selective reactions of engineered enzyme domains with their covalent inhibitors, enabling the rapid, modular assembly of large, highly functionalized scaffolds. By varying the number and arrangement of protein domains and linkers, this platform supports the construction of linear, cyclic, and branched structures with molecular weights exceeding 500 kDa. The talk will then present examples of megamolecule-based antibody mimics that function as a new class of nanomedicines. These constructs incorporate multiple affinity domains, small-molecule drugs, and nucleic acids, and enable targeted enzyme delivery, molecular imaging, and recruitment of immune effector cells to tumors. More broadly, this work establishes a foundation for the design of structurally precise, multifunctional protein assemblies, opening new opportunities in synthetic biology and nanomedicine.