Computational protein design and its application for in silico antibody discovery

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In the endless protein fold space, nature has sampled only a "spot" of the space. Protein design with the ROSETTA software suite enables sampling of enormous protein fold space that has not been explored by nature. Since the function of a protein is determined by the three-dimensional structure of the protein, billions of new proteins with a novel function, in principle, can be generated by designing new protein folds. I will introduce a number of examples of de novo protein design and protein-protein interface design by this computational approach with aims to create novel proteins for therapy or diagnosis. In particular, I will talk about computational antibody design, which involves amino acid and protein docking and explores the amino acid sequences of the 'complementary determining regions' of antibodies. Combined with experimental validation and yeast surface display, the computational approach enabled discovering antibodies against the spike protein of all circulating SARS-CoV-2 variants with pico to femto molar binding affinity.

[References]

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