MS04-2-1 Structural investigation of HER2 specific protein binder
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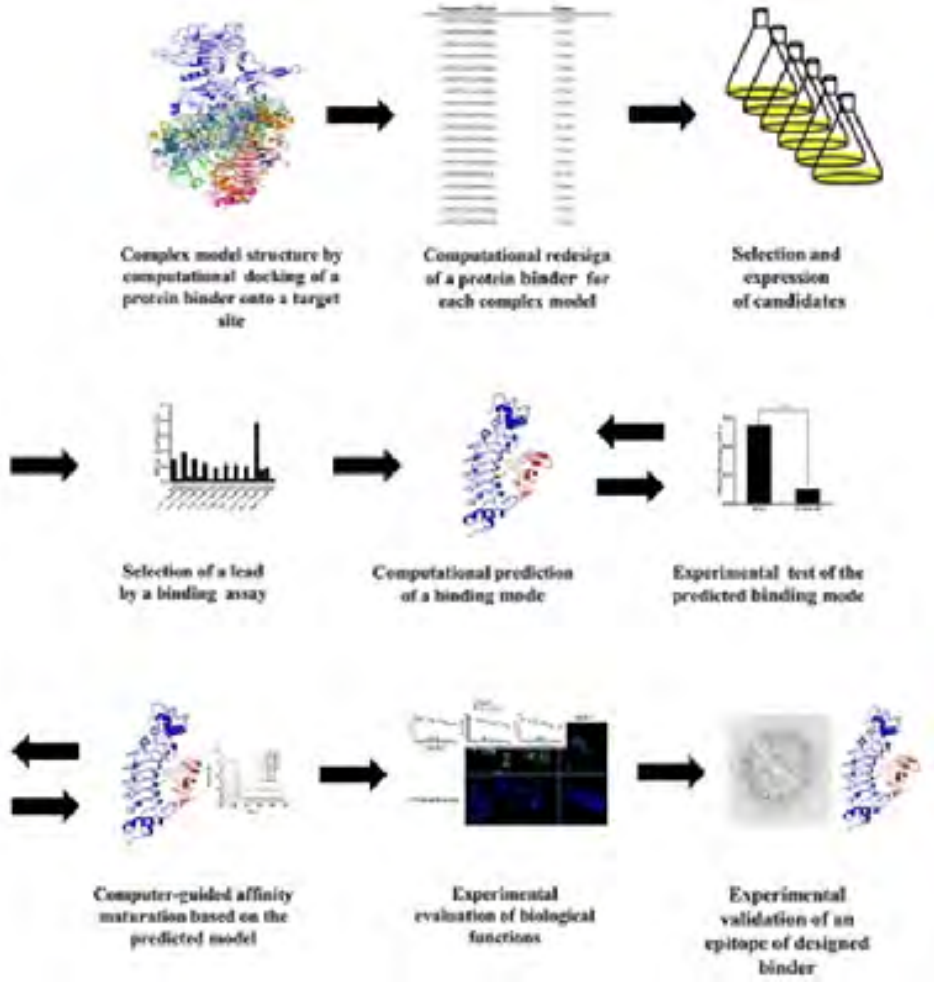
Abstract
A protein binder with a desired epitope and binding affinity is critical to the development of therapeutic agents. Here we present computationally- guided design and affinity improvement of a protein binder recognizing a specific site on domain IV of human epidermal growth factor receptor 2 (HER2). As a model, a protein scaffold composed of Leucine-rich repeat (LRR) modules was used. We designed protein binders which appear to bind a target site on domain IV using a computational method. Top 10 designs were expressed and tested with binding assays, and a lead with a low micro-molar binding affinity was selected. Binding affinity of the selected lead was further increased by two-orders of magnitude through mutual feedback between computational and experimental methods. The utility and potential of our approach was demonstrated by determining the binding interface of the developed protein binder through its crystal structure in complex with the HER2 domain IV.

References
Tae Yoon Kim#, Jeong Seok Cha#, Hoyoung Kim, Yoonjoo Choi*, Hyun-Soo Cho* and Hak- Sung Kim* “Computationally-guided design and affinity improvement of a protein binder targeting a specific site on HER2.” Computational and Structural Biotechnology Journal, Volume 19, 1325-1334, 2021.03.

overall workflow of repebody development



Structure of Rb-H2 in complex with HER2 domain IV