Structural and functional studies on proteins as potential drug discovery targets

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Structural biology teaches us about the fundamental nature of biological molecules. Drug design is the most immediate medical application of structural biology. Therefore, our studies have been focused on structural and functional studies of human disease-related proteins and proteins essential for growth and development of pathogenic organisms. A summary of achievements is outlined below.

1. Structural biological studies of human autocrine motility factor (AMF)

AMF, a tumor-secreted cytokine, stimulates cell migration *in vitro* and metastasis *in vivo*. We determined the crystal structure of human AMF and proposed a recognition mechanism of AMF by its receptor, AMFR. The structure provides an insight into the lead compound design of more effective AMF inhibitors.

2. Structural biological studies of human ribonuclease L (RNase L)

An interferon-induced ribonuclease, RNase L, is implicated in the molecular mechanism of interferon action. We determined the crystal structure of the N-terminal ankyrin repeat domain (ANK) of human RNase L complexed with its activator 2’,5’-linked oligoadenylate (2-5A). The structural basis for 2-5A recognition by ANK is essential for designing stable 2-5As with a high likelihood of activating RNase L.

3. Structural biological studies of *Plasmodium falciparum* *S*-adenosyl-L-homocysteine hydrolase (PfSAHH)

The human malaria parasite *Plasmodium falciparum* is responsible for the death of more than a million people each year. PfSAHH inhibitors are expected to provide a new type of chemotherapeutic agent against malaria. We determined the crystal structure of PfSAHH complexed with the reaction product adenosine. The structure provides opportunities to design potent and selective PfSAHH inhibitors.