

Structure-based anti-viral research

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Emerging and re-emerging infectious diseases pose a significant threat to human health. Recent outbreaks of severe acute respiratory syndrome (SARS) in 2003 and influenza H1N1 in 2008 had profound social and economic impacts worldwide. There is an urgent need for effective therapeutics aimed at management, treatment or prevention of these diseases. To this end, my group has been actively focused on emerging and re-emerging diseases caused by viral infection, including SARS, influenza and HIV, and has determined the three-dimensional structures of a number of targets for anti-viral drug discovery.

To date, we have determined more than 20 protein and complex structures from the SARS coronavirus, including: the main protease, nsp5 (Yang et al., 2003; Yang et al., 2005); the nsp7-nsp8 primase super-complex (Zhai et al., 2005; Li et al., 2010); the zinc-finger protein nsp10 (Su et al., 2006); and the endonuclease nsp15 (Xu et al., 2006). From the influenza H5N1 virus polymerase heterotrimer, we have determined the structure of the C-terminal domain of PA (PA_C) in complex with an inhibitory N-terminal peptide from PB1 (PB1_N) (He et al., 2008), the structure of the N-terminal endonuclease domain of PA (PA_N) (Yuan et al., 2009), and the systematic complex structures of the PA endonuclease domain with with adenosine, uridine, and thymidine nucleoside monophosphates (NMPs) (Zhao et al., 2009).

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