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Discovery of Inhibitors Against 3C Proteases of SARS Coronavirus,Enteroviruses 71, and Coxsackievirus B3

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A chymotrypsin-like protease (called 3C protease) found in piconaviruses is responsible for processing the poly-proteins translated from RNA genomes into functional enzymes and structural proteins essential for viral replication, so it represents a good anti-viral drug target.Enterovirus 71 and coxsackievirus B3 are piconaviruses, which cause hand, foot, and mouse diseases in human, and meningitis and mycocarditis leading to heart failure in young adults and congestive heart failure, respectively. In late 2002, an emerging infectious disease caused by a novel human coronavirus induced severe acute respiratory syndrome (SARS). It rapidly spread from its origin in southern China to more than 25 countries in 2003, affecting almost 8000 patients resulting in about 800 fatalities, a high mortality rate. The SARS virus also requires a 3C-like protease in the life cycle. We have identified several groups of inhibitors against the 3C-like and 3C proteases through high throughput screening and rational drug design. Some inhibitors are common for the two types of proteases, although they share no sequence homology.

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