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[Medicine] A New Approach to Developing Anti-influenza Drugs, Academia Sinica Identified New Target

[Medicine] A New Approach to Developing Anti-influenza Drugs, Academia Sinica Identified New Target (Chinese Version)

Academia Sinica Newsletter (2011/09/20) Although scientists worldwide continue to develop anti-influenza drugs, more and better drugs are still urgently needed as the virus continues to develop new strains and drug resistant strains. A research team led by Academia Sinica President Chi-Huey WONG and the director of Institute of Biological Chemistry Ming-Daw TSAI reported identification of a new anti-influenza drug target. This research has been published in the renowned US journal Proceedings of the National Academy of Sciences (PNAS) on September 19, 2011.

RNA-dependent RNA polymerase (RDRP), an enzyme from the influenza A virus, plays an essential role in viral replication. Viral replication requires the association of RDRP with the nucleoprotein (NP). NP is known to exist as trimers. The research team discovered that the "E339…R416 salt bridge" is a critical factor for trimer formation. They showed that, by disrupting the E339…R416 salt bridge of the NP protein, the trimer is disrupted. As a consequence, the interaction of NP and RDRP is impaired, and the virus is unable to replicate.

To demonstrate the feasibility of using disruption of the E339…R416 salt bridge as a target for the development of drugs to combat influenza, the team combined two types screening commonly used in drug discovery, virtual screening and high-throughput screening, to select several small molecule compounds from a library of 1.7 million compounds. They showed that the selected compounds can disrupt the NP trimer and inhibit H1N1 viral replication. Because the E339…R416 salt bridge is highly conserved in different strains of the influenza virus, they anticipate that the drugs further developed against this target will be broadly effective and less likely to develop drug resistance.

The full article entitled "The E339…R416 salt bridge of nucleoprotein as a feasible target for Influenza virus inhibitors" can be found online at the PNAS website at:
http://www.pnas.org/content/early/2011/09/15/1113107108.abstract.

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