Bojian Zheng et al., Pharm Anal Acta 2016, 7:1 (Suppl)
http://dx.doi.org/10.4172/2153-2435.C1.028

OMICS International
conferenceseries.com

8th International Conference and Exhibition on

Pharmaceutics & Novel Drug Delivery Systems

March 07-09, 2016 Madrid, Spain

Identification of a small-molecule inhibitor of influenza virus via disrupting the PA and PB1 interaction of the viral polymerase

Bojian Zheng and **Shuofeng Yuan**
The University of Hong Kong, Hong Kong

Assembly of the heterotrimeric influenza virus polymerase complex from the individual subunits PB1, PA, and PB2 is a prerequisite for viral replication, in which the interaction between the N-terminal of PB1 (PB1N) and the C terminal of PA (PAC) may be a desired target for antiviral development. In this study, we first compared the feasibility of high throughput screening by Enzyme-Linked Immunosorbent Assay (ELISA) and Fluorescence Polarization (FP) assay. Among the two, ELISA was demonstrated to own broader dynamic range so that it was used for screening inhibitors which blocked PA and PB1 interaction. Several binding inhibitors of PAC-PB1N were identified and subsequently tested for the antiviral efficacy. Apparently, 3-(2-chlorophenyl)-6-ethyl-7-methyl[1,2,4]triazolo[4,3-a]pyrimidin-5-ol, designated ANA-1, was found to be a strong inhibitor of PAC-PB1N interaction and act as a potent antiviral agent against the infections of multiple subtypes of influenza A virus, including H1N1, H3N2, H5N1, H7N7, H7N9 and H9N2 subtypes, in cell cultures. Intranasal administration of ANA-1 protected mice from lethal challenge and reduced lung viral loads in H1N1 virus infected BALB/c mice. Docking analyses predicted that ANA-1 bound to an allosteric site of PAC, which would cause conformational changes thereby disrupting the PAC-PB1N interaction. Overall, our study has identified a novel compound with potential to be developed as an anti-influenza drug.

Biography

Bojian Zheng has completed his PhD at The University of Hong Kong and Postdoctoral studies from McMaster University in Canada. He is a Professor currently working in Department of Microbiology, The University of Hong Kong. He has published more than 180 papers in reputed journals and has been serving as an Editorial Board Member of several international journals.

bzheng@hkucc.hku.hk

Notes: