Milan Kozisek et al., J Infect Dis Ther 2016, 4:6(Suppl)
http://dx.doi.org/10.4172/2332-0877.C1.015

Development and optimization of the assay for screening the compounds disrupting protein-protein interaction in influenza A polymerase

Milan Kozisek[1], **Hejdanek Jakub**[1, 2], **Machara Ales**[2] and **Konvalinka Jan**[1, 2]
[1]Academy of Sciences of the Czech Republic, Czech Republic
[2]Charles University, Czech Republic

Influenza virus causes severe respiratory infections in birds and mammals that are responsible for up to half a million deaths of human beings worldwide each year. Two targets of therapeutic interventions in influenza life cycle, viral neuraminidase and M2 channel are exploited in treatment. However, the recent emergence of new pandemic type along with increasing resistance against approved drugs has urged the need for a new drug target and design of its inhibitor. Recently, an interesting protein-protein interaction between two subunits of viral polymerase PA and PB1 has been identified as a new promising drug target. The fact that relatively few residues drive the binding and the binding interface is highly conserved presents an intriguing possibility to identify antiviral lead compounds effective against all subtypes of influenza A virus. In our laboratory, we have expressed and purified recombinant C-terminal part of the PA polymerase subunit with GST at its N-terminus from pandemic isolate A/California/07/2009 H1N1. The biotinylated peptide representing the N-terminal interacting part of PB1 subunit was synthesized by using a solid-phase synthesizer. The protein-protein interaction between PA and PB1 was then kinetically characterized using a surface Plasmon resonance (SPR). Finally, we developed and optimized an assay for screening the compounds disrupting the interaction between polymerase subunits, based on the AlphaScreen technology and validated the assay that has the potential to be used in drug discovery.

Biography

Milan Kozisek is a Senior Scientist at the Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague. He has completed his PhD in 2010. He is an author of 29 papers in peer-reviewed international journals and 4 patents.

milan.kozisek@uochb.cas.cz

Notes: