

Konrapob Klaywong 2011: Analysis of Targets for Antiviral Drug on NS1 Protein of Avian Influenza Virus. Master of Science (Genetic Engineering), Major Field: Genetic Engineering, Interdisciplinary Graduate Program. Thesis Advisor: Associate Professor Porn Tippa Lekcharoensuk, Ph.D. 101 pages.

The use of antiviral drugs will create pressure on the influenza A virus to escape from drug inhibition. Therefore, the analysis of new drug targeting protein is essential. Influenza A virus non-structural 1 (NS1) protein is a virulence protein since it antagonizes host innate immune responses and inhibits host protein synthesis but enhances viral gene expression. Thus, NS1 may be one of antiviral drug targeting candidates. Recombinant RBD-NS1 protein of an avian influenza virus H5N1, A/chicken/Thailand/KU14/04, was produced. The three dimensional structure of our RBD-NS1 protein was built based on that of A/crow/Kyoto/T1/2004. The structure positions 3  $\alpha$  helices in which Arginine 38 and Lysine 41 of the 2<sup>nd</sup> helix involve in dsRNA binding. A virtual screening was performed using Auto Dock 3.0.5 for high throughput screening compounds from the National Cancer Institute (NCI) database. The lead compounds with binding energy lower than -16.05 Kcal/mol were selected for further assay. An RNA binding assay technique was developed to test the RNA binding function of RBD-NS1 protein and the inhibitory effect of the selected lead compounds and 34 herbal extracts. Virtual screening demonstrated 5 lead compounds that bound within the RBD groove with binding energy less than -16.05 Kcal/mol. Two compounds with low binding energy, Estradiol (NCI0035) and Veratridine (NCI0082), were found to have no inhibitory effect on the RBD-NS1. However, the extracts from 5 herbs, *Curcuma xanthorrhiza*, *Terminalia belirica*, *Salacia chinensis*, *Zingiber montanum* and *Peltophorum pterocarpum*, could inhibit the binding between the dsRNA and RBD-NS1 protein. The results show that RNA binding assay was successfully developed to test compounds that can inhibit function of RBD-NS1 protein. NS1 protein may be a new target of antiviral drug for avian influenza virus.

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