DATE: 26/03/2017

SUMMARY of
2016 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, Osaka University

Research Title		**Investigation on universal influenza antibody interaction with hemagglutinin (HA) protein using virtual system coupled adaptive umbrella sampling.**
Applicant	**Name**	**Le Thi Ly**
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Research Collaborator (Host PI)		**Professor Haruki Nakamura**

Summary:

The ability of influenza A virus (IVA) hemagglutinin (HA) receptor to acquire mutations that confer host immunity evasion has obstructed the design of rational vaccine against IVA. HA has been targeted for universal antibody (UA) development to block a broad spectrum of IVA. However, the evolution of HA receptor and molecular binding mechanism of UA to this receptor is not completely understood.

From our previous study, the protein sequences of HA receptor were thoroughly studied using bioinformatics tools to identify co-evolution patterns and conserved epitopes. In addition, we also investigated on the binding mechanism of UA CR9114 which binds conserved H5N1 HA stalk domain using molecular dynamics simulation.

Under collaboration with IPR, we studied the protein sequences from representative HA subtypes and universal HAabs to identify important phylogenetic variations, co-evolution patterns and conserved epitopes. The sequence evolution result was then mapped on 3D structure of HA and HAabs to analyze the sequence - structure -function relationship in their relative molecular recognitions. Molecular dynamics simulations using the 7 representative complexes of HA-HAabs (H1_CR6261, H3_CR8020, H5_CR9114, H3_CT149, H5_F10, and H1_F16v3) were carried out to quantitatively measure the contributions of the HAabs to the binding to HA. We were able to investigate molecular interaction patterns between different UAs (CR9114, CR6261, CR8020, CR8043, CT149, F10, F16v3) and their corresponding HAs. These interaction patterns is currently being calculated by using molecular mechanics – Poisson Boltzmann Surface Area method in order to obtain the molecular binding mechanism of universal influenza antibody and assist the design of novel effective universal influenza vaccines.

We further obtained protein sequence variations, correlated mutation patterns, and structural changes of HA and HAabs. Understanding the relationship between sequence-structure-function relationships of HA and HAabs provides important insights into molecular recognition patterns of HA-HAabs and how HAabs bind to HA under various epitopic variations. The simulation results were quantified to examine the contribution of unique features of HAab.

We are at this time summarizing our results and performing experimental data validation on binding energy and hope that the results are publishable.

***Deadline: July 31, 2016**
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