DATE: 31 July 2016

SUMMARY of
2015 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.**
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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 were able to obtain HA variation, correlated mutation patterns, and the effect of pH levels on relative binding energy of UA CR9114 calculated directly from simulation trajectories. Understanding the binding mechanisms of CR9114 and HA provides important insights into CR9114 functions and how HA mediated pathogenesis escapes antibody binding. HA is a difficult therapeutic target because it is continually undergone positive selection process.

With suggestion from IPR, we will continue our collaboration by using virtual adapted umbrella sampling (VAUS) to investigate molecular interaction patterns between different UAs (CR9114, CR6261, CR8020, CR8043, CT149, F10, and F16v3) and their corresponding HAs. These interaction patterns will provide important insights for elucidating the molecular binding mechanism of universal influenza antibody and assisting the design of effective universal influenza vaccines.