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研究課題名	Discovery of anti-influenza agents and drug targets using curated pathway map (FluMap) and high-precision molecular docking simulation
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研究報告書

With the increased availability of bioinformatics technologies, opportunities for the application of network pharmacology to predict drug effects and toxicity resulting from multi-target interactions are being created. We applied a novel screening approach which combines elaborately developed machine learning systems and the use of molecular simulation and database mining to assess binding potentials of a test compound against proteins involved in a complex molecular network. This screening approach enables systematic prediction of network-dependent effects of a test compound (e.g. lead or drug), which accelerates systems pharmacology-based prediction to address drug safety issues.

We developed two machine learning systems, including a re-scoring function to assess binding modes generated by docking tools and to rank them accordingly, and a binding mode selection function designed to identify the most predictive binding mode. We applied this method to screen a number of test compounds over Influenza A Virus Life Cycle pathway map (FluMap) for discovering anti-influenza agents.

The developed machine learning systems significantly enhance the prediction accuracy. Using the method, we have screened the compounds targeting the host proteins identified by siRNA screening, and identified those showing efficacy *in vitro*. This would contribute in reducing the number of tests for further bioassay.

Together with a curated pathway map, the proposed screening approach is able to comprehensively characterize the underlying mechanism of a drug candidate and also to interpret its cascade effects, leading a step change in the prediction of drug efficacy and safety.