DATE: Day 28 Month 07 Year 2016

SUMMARY of
2015 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, Osaka University

Research Title		**STRUCTURAL INSIGHT INTO CHAPERONE FUNCTION OF FKBP22, A PEPTIDYL PROLYL ISOMERASE FROM *Shewanella* sp. SIB1**
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Summary

The project essentially dealing with the use of nuclear magnetic resonance (NMR) to elucidate the structure of FK506-binding protein (FKBP, a member of peptidyl prolyl *cis-trans* isomerase (PPIase). For some reasons, the target of protein in this project is changed to FKBP35 from malaria parasite *Plasmodium* knowlesi. This is due to the high incidence of *Plasmodium knowlesi* infection in Malaysia accompanied with evidence of antimalarial drug resistance urge serious attempts on the development of antimalarial drugs. FK506 displayed antimalarial activity with no resistance effect, yet not feasible for further application due to its immunosuppressive effect. FK506 binds to FKBP35, the peptidyl prolyl cis-trans isomerase (PPIase) of Plasmodium parasite and inihibits its activity. Further structural-based drug discovery targeting this protein identified a domain named FK506-binding domain/FKBD). In this study, structural studies of FKBD of *P. knowlesi* (Pk-FKBD) and high throughput screening of potential inhibitor compounds were performed using Nuclear Magnetic Resonance (NMR). The result showed that Pk-FKBD has similar structural folds like the canonical FKBP folds. High throughput screening towards flourinated-compounds library shown that 3-Fluoro-N-(piperidin-4-yl)benzenesulfonamide hydrochloride apparently bound to Pk-FKBD. NMR titration experiment revealed that the *KD* value of this compound was 470 µM with the residues of K67, D76, I95, C126 and E139, located at the substrate binding cavity, were involved in the binding. We proposed that fluorine-NMR approach is a promising method to further elucidate the antimalarial drug.

***Deadline: July 31, 2016**
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