DATE: Day 23 Month 04 Year 2024

SUMMARY of
FY2023 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, Osaka University

Research Title		Structural analysis of Immune System Proteins based on Ligand recognition
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	Present Title	**Professor**
Research Collaborator (Host PI)		**Atsushi Nakagawa**

Summary

1. First, we solved the NOD1 complex with small molecules using BL44XU beamline. We showed the binding sites of some ligands to LRR motif proteins with crystallography and modular engineering techniques. Firstly, we determined the crystal structures of prototype-dNOD1, D711S-dNOD1, and D711S-R877S-dNOD1, respectively (Fig.1). Interestingly, we can improve gradually the electron density map of tri-DAP, the ligand of NOD. Finally, we found the clear electron density of tri-DAP in D711S-R877S-dNOD1. Secondly, by using this approach, we can also show the binding site of the other important ligand of NOD2, MDP, in the crystal structure of dNOD2. In addition, we also determined the crystal structure of protype-NOD3, further searching the unknown ligands. Overall, we successfully showed how to identify the binding sites with module engineering and crystallography.

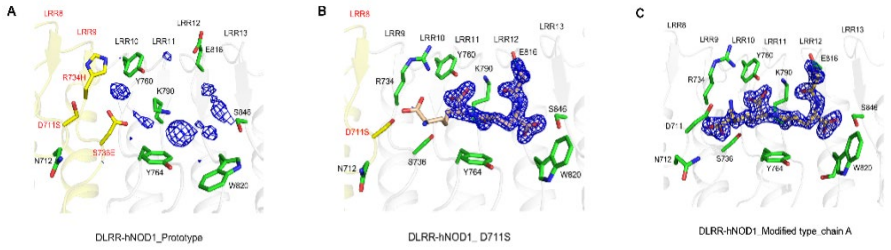

Fig.1. Electron density map of tri-DAP in prototype-dNOD1, D711S-dNOD1, and D711S-R877S-dNOD1

2. Second, we also solved the crystal structure of glutamyl-tRNA synthetase (QARS) with Gln-AMS was determined to a resolution of 2.8 Å (Fig.2). Analysis of the crystal structure revealed that QARS is composed of two N-terminal subdomains, catalytic domain, acceptor binding domain, and helical subdomain. The catalytic domain contains an active site that binds glutamine and ATP. Also, we found the electron density map of the glutamine near the acceptor binding domain. Through this, we propose that glutamine is not only involved in the translational procedure but plays a critical role in the non-translational process by participating in MSC regulation.

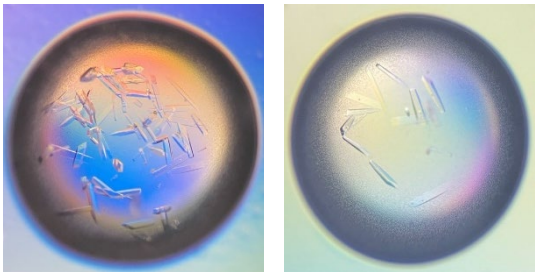

Fig.2. The crystal fo QARS-Gln-ATP

3.Schistosomiasis, also known as bilharzia, stands as one of the leading causes of death globally among parasitic diseases, following closely after malaria. The affliction manifests a range of symptoms in humans, including indigestion, abdominal fullness, loss of appetite, epigastric discomfort irrespective of meals, diarrhea, edema, hepatomegaly, and toxemia resulting from liver dysfunction. The crystals were diffracted to about 1.6 Å resolution at best. We could achieve structures of SmTAL with calmodulin antagonists W7 compounds. The systematic absences indicated that the space group was $P2_12_12_1$, with unit cell dimensions of a=51.442 Å, b=61.462 Å, c=74.978 Å, α=90.000, β=90.000, γ=90.000