DATE: Day 7 Month May Year 2025

SUMMARY of
FY2024 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, Osaka University

Research Title		Structural and Functional Roles of cis-Proline in Intrinsically Disordered Proteins
Applicant	**Name**	Basu Gautam
	Affiliation	Indian Institute of Science Education and Research (IISER) Kolkata
	Present Title	Adjunct Professor
Research Collaborator (Host PI)		Kenji Mizuguchi

Summary

Intrinsically disordered proteins (IDP), with a high content of charged residues and low content of hydrophobic residues than natively folded proteins, exist as an ensemble of fast interconverting structures. The presence of a single proline in IDP results in two ensembles of fast interconverting structures that convert between each other slowly, limited by the *cis/trans* proline isomerization rate (tens of seconds). The presence of multiple (N) proline residues can potentially result in 2^N slowly interconverting structural ensembles. By analyzing some realistic examples of IDPs (sequence and NMR data) we discuss the structural and possibly functional consequences of multiple prolines in IDP. We also present preliminary molecular simulations data on a 16-residue (GILEDM^{117}**P**VD^{120}**P**DNEAYE) fragment from the C-terminal IDP domain of α-synuclein that contain two proline residues ^{117}**P** and ^{120}**P**, in three proline *cis/trans* conformational combinations (*trans-trans*, *cis-trans* and *trans-cis*). Our analysis suggests that minor ensembles of IDP containing one or more proline residues in *cis* conformation(s) should not be ignored since their cumulative populations can be significant.

***Deadline: May 9, 2025**
***Please submit it to E-mail: tanpakuken-kyoten@office.osaka-u.ac.jp.**
***Please describe this summary within 1 sheet. Please DON'T add some sheets.**
***This summary will be published on the web.**