DATE: Day 19 Month July Year 2019

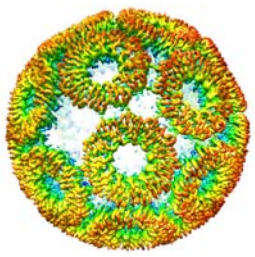
SUMMARY of
2018 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, Osaka University

Research Title		**An ultra-stable gold-coordinated protein cage displaying reversible assembly and paradoxical geometry.**
Applicant	**Name**	**HEDDLE JONATHAN GARDINER**
	Affiliation	**Malopolska Centre of Biotechnology, Jagiellonian University**
	Present Title	**Extraordinary Professor**
Research Collaborator (Host PI)		**Junichi Takagi**

Summary

Artificial protein cages are a topic of great research interest as they can potentially be designed for a variety of novel uses such as drug delivery. Designing and producing such cages is however challenging because,. In natural systems, the protein building blocks of the cage are held together my multiple hydrogen bonds an hydrophobic packing interactions. These are very difficult to design and simulate and are often interdependent making the effect of changing one part on the whole very difficult to predict. It would therefore be advantageous if a new system of holding together such protein subunits in a cage could be demonstrated. One attractive possibility is using metal ions to link together protein subunits via simple coordination bonds instead of protein-protein interactions. This could simplify the design process but had not previously been demonstrated for an artificial protein cage,

Our work was based upon previous observations of a mutant version of TRAP protein, which is normally a ring made from 11 identical protein monomers. In the mutant, the lysine at position 35 was replaced with a cysteine. These mutant rings looked identical to the wild type but upon addition of gold(I) they assembled into large, capsid-like cages, called TRAP-cage. This presented a number of puzzles such as what the role of gold was and how it was possible that an apparently regular convex polyhedron could be made from protein faces that were 11-sided in nature (which is mathematically forbidden). We were able to answer these questions including using cryo-EM to solve the structure of the TRAP-cage: It is an approx. 2.2 MDa protein cage made from 24 copies of the TRAP ring. It is highly stable, resistant to extreme temperatures (>100 °C) and high levels of chaotropic agents (e.g. 7M urea). However it falls apart readily on exposure to mild concentrations of reducing agent. The structure shows that each ring is surrounded by five neigbours and is held together not by protein-protein interaction by coordination bonds where a single gold(I) bridges opposing cysteines with 10 cysteines form each ring bridged in this way, these being -S-Au-S- “staples”.



***Deadline: May 17, 2019**
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