

# Okayama University Medical Research Updates (OU-MRU) 2019.3 Vol.65

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Okayama University research: Game changer: How do bacteria play Tag?

(Okayama, 18 March) In a recent study published in *Proteins and Proteomics researchers* at Okayama University show how bacteria attach to organisms before infecting them.

Bacteria have been long invading animals and plants. One of their most intricate but less understood mechanisms is their ability to adhere to other organisms. A research team led by Professor Takashi Tamura at Okayama University has unravelled the role of a molecule, DsbA, and how its chemical properties control this adhering function of bacteria.

Professor Tamura have previously shown that before bacteria can adhere to other living objects certain structures on the bacteria's surface must be stabilized to form a strong scaffold. Special proteins found within the bacteria are responsible for this stabilization. To understand this process better, Professor Takashi Tamura's team used a virus that attacks bacteria only (bacteriophage). This virus binds to an appendage-like structure found on the bacterial surface. DsbA is the protein responsible for stabilizing this appendage to facilitate this attachment. To decipher how DsbA does its job, the team created several mutants of bacteria, each with a different form of the DsbA protein. The code responsible for conferring DsbA a chemical charge was different in each mutant. A bacteriophage called as M13 was then introduced into these bacteria, grown on a plate.

Ideally, when M13 successfully attaches to and infects bacteria, "plaques" of viral colonies will be observed on the plate, in place of the bacterial colonies. These plaques were measured for all the different mutants. It was found that one particular mutant (DsbA [CDIC]) had 40 times more plaques than any other mutant or the unmutated bacteria. The charge on this mutant was much lower than the unmutated protein. However, another mutant, also with a low charge, did not have more plaques. This suggested that the mutated code of (DsbA [CDIC]) could be bringing about additional effects. Using structural mapping the team then found that DsbA [CDIC] had enlarged binding pockets, compared to the other variants. This could facilitate better binding of the scaffolding appendage.

Insights into these mechanisms of their attachment can help build strategies to combat bacteria. Antibiotic resistance is also spread from one bacterium to another by close contact. Designing drugs that could inactivate the factors driving DsbA function seems like one such strategy.

#### Background

**Proteins and structure:** Proteins that bind to and modulate the activity of other proteins are known as enzymes. Special regions on these proteins called active sites are responsible for

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this function. The active site consists of a 'binding site', a pocket where the partner protein actually binds and a 'catalytic site' which gives the protein a chemical charge. This charge provides the energy for the protein to undergo a chemical reaction. In the case of DsbA, codes on the catalytic site were changed to create the mutants.

**Bacteriophage:** Bacteriophage or "bacteria eaters" are viruses that attack and subsequently hijack bacteria. The first step in this process requires the bacteriophage to attach itself onto the bacterial surface. Typically, the bacteriophage does this by binding to F-pilus, an appendage-like structure found on the bacteria's surface.



# Caption

DsbA [CDIC] could generate many more viral plaques (green dots) compared to another DsbA mutant (right).

# Reference

Shinya Sutoh, Yuko Uemura, Yuko Yamaguchi, Asako Kiyotou, Rena Sugihara, Makiko Nagayasu, Mihoko Kurokawa, Koreaki Ito, Naoki Tsunekawa, Michiko Nemoto, Kenji Inagaki, Takashi Tamura. Redox-tuning of oxidizing disulfide oxidoreductase generates a potent disulfide isomerase. *Biochimica et Biophysica Acta - Proteins and Proteomics*, 1867(2019), 194-201.

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Okayama University is one of the largest comprehensive universities in Japan with roots going back to the Medical Training Place sponsored by the Lord of Okayama and established in 1870. Now with 1,300 faculty and 13,000 students, the University offers courses in specialties ranging from medicine and pharmacy to humanities and physical sciences.

Okayama University is located in the heart of Japan approximately 3 hours west of Tokyo by Shinkansen.

Website: http://www.okayama-u.ac.jp/index e.html



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Hirofumi Makino, M.D., Ph.D. President, Okayama University

