Invitation seminar　分子生命開発学セミナー

Understanding the effect of copper on bacterial physiology and the potential to exploit its toxicity in antimicrobial strategies

Prof. Alastair McEwan

School of Chemistry and Molecular Biosciences
The University of Queensland
Australia

Date　12th Feb. 2019 (Tue)
Venue　15:00 – 16:00
C308, Graduate School of Biosphere Science

Copper is an important element in aerobic living organisms where it plays a key role in oxidases and oxygenases, particularly those associated with the respiratory chain, and it is also found in respiratory enzymes associated with nitrite and nitrous oxide reduction. However, copper ions in excess are toxic since the Cu(I) ion is able to displace other transition metal ions from enzymes and also destroy iron-sulfur clusters, leading to release of iron. To avoid the toxic effects of Cu bacteria have evolved homeostatic systems that allow them to detect and remove excess Cu from the cytoplasm and such systems are found even in bacteria that do not use this trace element as part of their physiology.

The way in which Cu exerts its toxic effects is dependent on the physiological characteristics of the bacterium. In *Neisseria gonorrhoeae* we have identified the heme biosynthetic pathway and the respiratory chain as being particularly susceptible to Cu toxicity, while in *Escherichia coli* we observed that the GOGAT system is affected, leading to an overlap between Cu toxicity and acid stress.

Although aqueous Cu is used to control microbial growth (e.g. algal growth) it is not sufficiently potent to be used as antibacterial agent in clinical settings. However, Cu-ionophores can be used to deliver Cu to the bacterial cytoplasm and can be used at much lower concentrations. The effect of Cu-ionophores on bacterial growth will be described and their potential as antimicrobial agents will be discussed.

References

Djoko KY, Phan MD, Peters KM, Walker MJ, Schembri MA and McEwan AG (2017) Interplay between tolerance mechanisms to copper and acid stress in *Escherichia coli*. *Proc. Nat, Acad. Sci.* (USA) 114, 6818-6823.

Djoko KY, Goytia MM, Donnelly PS, Schembri MA, Shafer WM and McEwan AG (2015) Copper(II)-Bis(Thiosemicarbazonato) complexes as antibacterial agents: Insights into their mode of action and potential as therapeutics. *Antimicrob Agents Chemother.* 59, 6444-53.

Organizer: Sotaro FUJII, Hiroshima Univ. (4045)
※ 5研究科の共同セミナーとして認められます。