Poster Presentation

BM.P14

Ubiquitin recognition by UBZ and UMI domains for DNA damage response

A. Toma[1,2], T. Takahashi[1,2], Y. Sato[1,2], S. Goto-Ito[1,2], A. Yamagata[1,2], S. Fukai[1,2]

[1]The University of Tokyo, Synchrotron Radiation Research Organization, Tokyo, Japan, [2]The University of Tokyo, Institute of Molecular and Cellular Biosciences, Tokyo, Japan

Double-strand break (DSB) and interstrand crosslink (ICL) are serious damages in DNA. Responses to these DNA damages include ubiquitination of damaged chromatin and other substrates, which recruit protein complexes required for DNA repair. Therefore, many proteins involved in DNA damage response contain ubiquitin-binding modules. For instance, a ubiquitin ligase RNF168, which catalyzes K63-linked polyubiquitination of histone H2A, contains two types of ubiquitin binding motifs, MIU (motif interacting with ubiquitin) and UIM (UIM and MIU-related Ub-binding domain). FAAP20, which recruits Fanconi anemia proteins (crosslink-repair factors), contains a UBZ (ubiquitin-binding zinc finger) domain. To date, mechanisms for ubiquitin recognition by UMI and UBZ domains have remained unclear. In this study, we determined crystal structures of RNF168 UMI and FAAP20 UBZ in complex with ubiquitin at 1.9 Å resolutions, respectively. SPR analyses using UMI and UBZ mutants, which were designed to disrupt Ub binding, confirmed that the observed interactions between Ub and UMI or UBZ are critical for binding. Our structure and the accompanying in-vitro structure-based mutagenesis experiments reveal the structural basis of these important recognition events.

Keywords: Ubiquitin, DNA damage response, Protein-protein interaction