The 493 th IMEG Seminar

【Title】Management of DNA repair factor action by controlling phosphorylation/dephosphorylation in FA pathway

【Date】 Feb. 21 (Wed), 2024 17:00～18:00

【Speaker】Ai Murata, Ph.D.
Postdoc, University of Oxford

【Venue】 ZOOM access will be announced through IMEG email list

【Abstract】

Interstrand crosslinks (ICLs) of the DNA helix are a deleterious form of DNA damage. DNA instability occurs in the rare genetic disease Fanconi Anemia (FA), due to the inability of the patient's cells to repair ICLs. A complex set of DNA damage response pathways handles ICLs, including the (FA)/BRCA (breast cancer genes) repair pathway, translesion synthesis (TLS), homologous recombination (HR), and nucleotide excision repair (NER) and a separate NEIL3-dependent ICL repair pathway. FA is a rare recessive disorder leading to chromosome instability, developmental abnormalities, bone marrow failure, aplastic anemia, and enhanced susceptibility to certain tumors. Unfortunately, all FA patients go through stages, from leukemia to cancer, which is an incurable disease. Currently, 23 genes have been identified to cause FA, and they all code for proteins implicated in the repair of ICLs. Mutations in several of these genes have also been linked to increased incidence of certain cancers, for example, BRCA1, BRCA2 and PALB2. Elucidation of these mechanisms of DNA instability will help us understand the processes of cancerization and developmental abnormalities.

We published that FANCD2 (FA main factor) is phosphorylated by CK2 kinase. CK2 is a serine/threonine-selective protein kinase that has been implicated in cell cycle control, DNA repair, and other cellular processes. The phosphorylated point mutations become the cluster and causes a loss of function of the FANCD2 when we mutated in FANCD2. PP2A has been identified as a potential drug target for Parkinson's and Alzheimer's diseases. PP2A is a serine/threonine-selective protein phosphatase. To verify whether PP2A is involved in FA pathway regulation, we confirmed the response of FANCD2 to DNA damage in an *in vitro* reconstitution system and *in vivo*. I will introduce about relationship between CK2 and PP2A in FA pathway.

[Contact】 Dept. of Chromosome Biology, Kei-ichiro Ishiguro (Ext. 6606)