Live Cell Imaging and *in situ* analysis of cellular responses to DNA double-strand breaks in mammalian cells.

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The integrity of the human genome is constantly threatened by internal as well as external factors with the propensity to cause DNA damage. Of the various types of DNA damage that can occur within the mammalian cell nucleus, the DNA double strand break (DSB) is perhaps the most dangerous. Estimates put the number of endogenous DSBs anywhere between 10-100 per nucleus per day. A direct link between DSBs and cancer has been surmised by researchers based upon the fact that many cancer-predisposition syndromes in humans are caused by mutations in DSB-responsive genes. Our laboratory has been focused on the molecular and cellular responses to DNA DSBs induced by low and high LET radiation in mammalian cells. Especially, we are interested in DNA-dependent protein kinase (DNA-PK). DNA-PK complex consisting Ku70 and Ku80 heterodimer and DNA-PK catalytic subunit (DNA-PKcs), is the key component of the non-homologous end-joining (NHEJ) pathway of DNA double strand breaks (DSBs) repair. It is believed that Ku heterodimer first binds to DSBs and then recruits DNA-PKcs to form the complex and activate DNA-PKcs. Evidence has suggested that the kinase activity as well as the phosphorylation status of DNA-PKcs are required for NHEJ. However, it is unclear whether Ku is required for the initial localization of DNA-PKcs to DSBs site in vivo, and whether kinase activity of DNA-PKcs is indispensable for the localization of DNA-PKcs. To answer these questions, we carried out live cell imaging experiments to understand the fundamental issues of how DNA-PK complex in response to DSBs *in vivo* and to determine the dynamics of DNA-PK complex at DNA DSBs in live cells. In addition, I'll discuss the recent approaches to visualize DNA DSBs and other type DNA lesions *in situ* and in live cells induced by ionizing radiation and UV laser.