DNA damage and tumorigenesis

As a complex pathologic process, tumorigenesis has involved various regulating mechanisms at molecular and cellular levels, particularly closely related to DNA damage. In previous issues of *JMCB*, we have published several papers highlighting the relationship between tumorigenesis and DNA damage. As a guest editor, Dr. Shen has organized a special issue on genomic instability and cancer (*Shen, 2011*). In addition, two related *JMCB* collections were published in last year (*Wu, 2012*) and early this year (*Wu, 2013*). The collection of four papers published in this issue will add more data and insights into this area.

It is well known that epigenetic dysfunction such as the inhibition of different DNA repair components might play a role in human cancer development (*Lahtz and Pfeifer, 2011*). In the first article of this issue, Dr. Hsiao and Mizzen analyzed the regulation of epigenetic modification of histones under DNA damage signaling. It is known that 53BP1 as a DNA damage response protein is involved in the foci formation at DNA double-strand breaks (DSBs) (also see a related review in *JMCB* by Aly and Ganesan, 2011), which could promote their repair by non-homologous end joining. The authors first showed that 53BP1 foci assemble primarily on dimethylated lysine 20 in histone H4 (H4K20me2) established prior to DNA damage by methyltransferases. They further defined a novel role for H4K16 acetylation in regulating 53BP1 foci dynamics. These findings uncovered that rapid induction of H4 deacetylation by DSBs affected multiple aspects of DNA damage response, suggesting that the inhibition of 53BP1 binding to H4K20me2 by H4K16 hyperacetylation may contribute to cancer therapy.

In the second paper, Dr. Li and colleagues reported that CyclinB1/Cdk1, which normally plays important regulating role in mitosis of mammalian cell cycle, was involved in response to radiation stress. The authors showed that a substantial amount of CyclinB1/Cdk1 was translocated to the mitochondrion under irradiation condition, and then phosphorylated manganese superoxide dismutase (MnSOD), a major antioxidant enzyme within the mitochondria. The authors further indicated that the phosphorylation of MnSOD generated by CyclinB1/Cdk1 resulted in increased MnSOD activity and stability, as well as the suppression of radiation-induced apoptosis. Their studies demonstrate a unique pro-survival mechanism involving CyclinB1/Cdk1-mediated MnSOD activation under genotoxic stress conditions.

It is reported that sarcoma lesions could up-regulate collagen type VI (Col VI), a putative extracellular matrix ligand of chondroitin sulfate proteoglycan 4 (CSPG4)/NG2, and contribute to prognostic impact of NG2. Dr. Perris and colleagues showed, in this issue, that the NG2-mediated binding to Col VI activated the convergent cell survival- and cell adhesion/migration-promoting signal transduction pathways, by analyzing the cells with modified expression of NG2 diverged in their interaction with Col VI under different microenvironmental conditions. The authors suggest that the interaction between NG2 and Col VI plays a role in the regulation of the cancer cell/host microenvironment interactions for sustaining sarcoma progression.

Translesion synthesis (TLS) allows the DNA replication machinery to bypass an unrepaired DNA damage site using special TLS polymerases such as polymerases κ, η, ι. Therefore, it is very important to understand how the TLS polymerases are tightly regulated for DNA damage tolerance. In this issue, Dr. Choi and colleagues performed structural studies on the polymerase-interacting domain of a human Rev1 protein that regulates the activities of TLS polymerases. The authors indicate that Rev1 uses a tertiary structure and two surfaces to recruit TLS polymerases, with one site for polymerases κ, η, ι, and the other for polymerase δ.

We think that these research papers will provide new information for better revealing the molecular regulation of tumorigenesis and thus contributing to the efficacy of cancer therapy.
References


