Volume 50(3-4):179, 2006
Acta Biologica Szegediensis
http://www.sci.u-szeged.hu/ABS

DISSERTATION SUMMARY

Role of the posttranslational modification in the DNA repair

Valeria Szukacsov

Institute of Genetics, Biological Research Center, Hungarian Academy of Sciences, Szeged, Hungary

DNA damage is a relatively common event in the life of a cell and may lead to mutation, cancer, and cellular or organismic death. Damages to DNA induce several cellular responses that enable the cell either to eliminate or cope with the damage or to activate programmed cell death process.

Postreplication repair is the mechanisms that assure the replication of the damaged DNA. One of the postreplication repair pathways is the translesion synthesis. This process comes into the play, when the replicative DNA polymerase can not incorporate nucleotide opposite the damaged bases and the moving of the replication fork is blocked. In this case switching of the replicative polymerase and translesion polymerases occurs. The TLS polymerases can incorporate nucleotides opposite the damaged bases. This process can be error–free or error–prone. The error-prone synthesis generates mutation, in contrast to the error-free pathway.

The major regulator in the polymerase switching is the Proliferating cell nuclear antigen (PCNA). PCNA has been described as a processivity factor of DNA polymerases, and it has an essential role in the DNA replication machinery. Recent studies suggest that PCNA plays an important role in polymerase switching, and PCNA could determine which polymerase gain access to the replication sites. The major unanswered question is: How could PCNA regulate the polymerase switching? The recent experiments have suggested the importance of the secondary modifications of the PCNA as well as the polymerases.

PCNA is exquisitely modulated by covalent post-translational modifications involving ubiquitin and the ubiquitin-related protein SUMO. PCNA is a target for SUMO modification, mono-ubiquitylation, and K63-linked multi-ubiquitylation. In contrast to K48-linked multi-ubiquitylation, mono-ubiquitylation and modification by K63-linked chains do not generally promote proteasomal degradation, but rather they seem to alter the function of the substrate or to mediate protein–protein interactions. Two target sites have been identified in PCNA for modification: K164, a conserved modification site that is both modified by SUMO and ubiquitin, and K127, a yeast-specific site that seems to be exclusively modified by SUMO.

Several studies have analyzed the function of the ubiquitylation of the PCNA, but the sumoylation events have not been characterised yet. The goal of our study is to understand better the switching mechanism of polymerases and shed light on role the sumoylation of the PCNA. We have reconstituted the sumoylation of PCNA in vitro, and we have started to characterize this modification. Now, we would like to purify sumoylated PCNA and closely study the major question: how PCNA can regulate the polymerase switching mechanism during the postreplication repair.

References

Haracska L, Torres-Ramos CA, Johnson RE, Prakash S, Prakash L (2004) Opposing effects of ubiquitin conjugation and SUMO modification of PCNA on replicational bypass of DNA lesions in Saccharomyces cerevisiae. Mol Cell Biol 24(10):4267-4274.

Supervisor: Lajos Haracska
E-mail: haracska@brc.hu