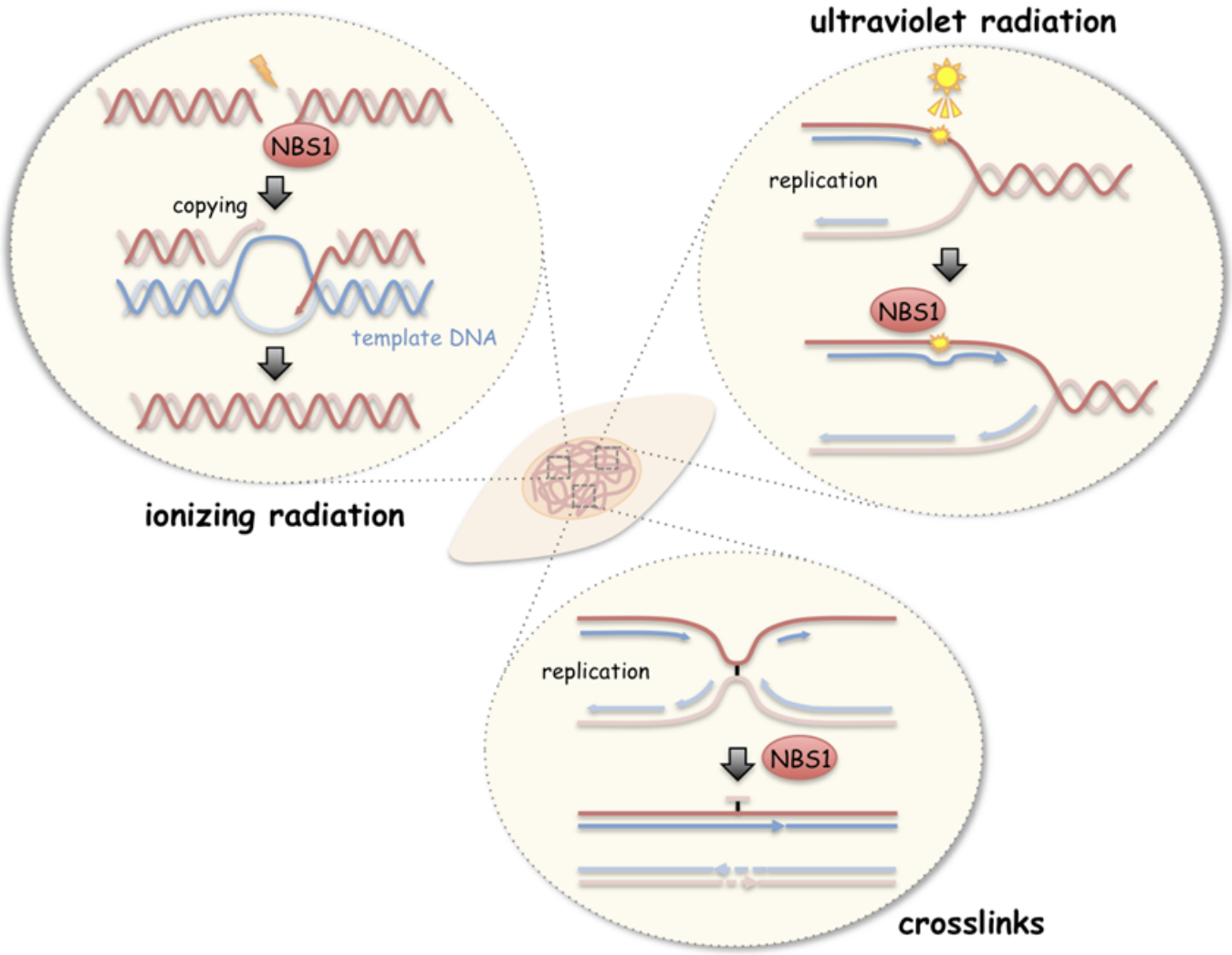
What does a guardian protect genomic DNA from?

Living organisms can achieve their propagation through copying (replicating) the genetic information, coded in DNA sequence, and dividing them to each daughter cell. DNA sequence is a basic element and its conservation is essential for individual life and stable continuation of species. However, the sequence has been changed in huge numbers of generations (so-called “evolution”). The major driving forces for this phenomenon are mistakes of replicating DNA and/or repairing damaged DNA regions induced by various types of stresses such as environmental radiations and byproducts of cellular metabolism.

DNA damage, due to various types of stresses, occurs at a rate of ~500,000 regions per cell per day. Because only an unrepaired region can be harmful for living cells, these regions should be repaired by the DNA repair systems, in which specified proteins (enzymes) recognize the damaged regions and repair them. Living cells have many kinds of DNA repair systems to repair any kind of damages. 1) Ubiquitous DNA damage induced by ultraviolet radiation from the sun inhibits DNA replication. Translesion DNA synthesis can bypass these regions and maintain the replication progression. 2) Ionizing radiation and reactive oxygen species break both strands in the double helix. These breaks are considered to be among the most lethal forms of DNA damage because one unrepaired break is sufficient to elicit cell death and can lead carcinogenesis. These regions are firstly recognized and repaired by the following steps. Enzymes make the DNA sequence of damaged regions by using homolog sequence as a template, and to complete the repair, the end of the new strand are sealed to the exiting strand. 3) Some anticancer drugs and aldehydes contained in alcohol and diet induce crosslinks in the double strands, which block the progression of DNA replication.



NBS1 acts as a guardian to protect genomic DNA from various types of stresses, including ionizing radiation, ultraviolet radiation, and crosslinks.

Nijmegen breakage syndrome (NBS), reported by Weemaes C.M. in 1981, is a genetic disorder characterized by immunodeficiency, microcephary, growth retardation and a high frequency of malignancies. We had successfully identified the responsible gene, *NBS1* and its functions, which respond against the various types of DNA damages induced by ultraviolet radiation, ionizing radiation, and also crosslinks. Thus, we have concluded that NBS1 seems to orchestrate the following proteins and coordinate the response to protect genomic DNA from a vast range of toxic agents (illustrated in figure). NBS1 is implicated in the maintenance of genome integrity after many insults to prevent malignancy, particularly lymphoma. Therefore, it is important to further reveal the

functions of NBS1 for an investigation into the cause of these diseases.

Yuichiro Saito

Publication

Functional Role of NBS1 in Radiation Damage Response and Translesion DNA Synthesis.
Saito Y, Komatsu K
Biomolecules. 2015 Aug 20/i>