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DNA is continuously subjected to various exogenous damaging agents such as ultraviolet light as well as endogenous agents such as reactive oxygen species. To avoid the deleterious effects of such damage, living organisms acquired various repair mechanisms. However, with so many types and numbers of damage it is impossible for cells to repair all of them before replication or transcription takes place. As a result, the mechanisms for replication and transcription often encounter damage. Recently, it has been found that cells have special means to tolerate these situations, so-called translesion DNA synthesis and transcription-coupled repair. In this mini symposium, we will deal with the mechanisms by which cells detect and repair various lesions, how the replication apparatus bypasses DNA blocks to maintain replication, and how lesions are detected and repaired when transcription machinery encounters them. We will also touch upon how these mechanisms play roles in avoiding apoptosis, carcinogenesis, aging, and genetic diseases.