DNA Double-Strand Breaks—Repair and Transmission of Signals

W13–1 DNA repair network for the maintenance of genome integrity in vertebrates

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A wide range of potential insult to the genomic DNA is contributed not only by the environment, but also by cellular activities. Spontaneous damage comes in many forms and should be efficiently repaired by a variety of repair processes. If the damage is not repaired before the cell progresses to the next stage of the cell cycle, the nature of the damage may alter, resulting in the formation of secondary lesions. Some types of DNA damages are known to arrest DNA replication, causing a daughter strand gap that encompasses the damage in the template strand. These DNA lesions are thought to be repaired by either homologous recombination(HR), non-homologous end-joining, or translesion DNA synthesis. Although these repair pathways have overlapping roles in the maintenance of the genome, they can function in a competitive manner as well. While HR repair a lesion precisely by using the template DNA, the other repair pathways are error prone and often introduce mismatch nucleotides into the DNA. Consequently, genomic information gets altered, depending on the pathway used. To elucidate the independent as well as collaborative role of DNA repair pathways in vertebrates, we employ strategy to systematically knockout DNA repair genes in chicken DT40 cell.

W13–2 DNA Double-strand Break Repair and Traditional Radiation Biology

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Most of the concepts and phenomenon in traditional radiation biology were too conceptual and did not correspond to molecular events: e.g., lethal damage (LD), sublethal damage (SLD) and potentially lethal damage (PLD). Recently, two DSB repair pathways have been identified that differ in their requirements for DNA homology: homologous recombination (HR) and non-homologous end-joining (NHEJ) pathways. Rad54 participates in HR repair of DNA double-strand breaks, while Ku proteins are involved in NHEJ. Using the mutants KU70$^{-/-}$, RAD54$^{-/-}$, and KU70$^{-/-}$/RAD54$^{-/-}$ generated from the chicken B-cell line, DT40, we found that SLD recovery is due to double-strand break repair by HR, and that these breaks are SLD (1). NHEJ pathway works throughout the cell cycle but HR pathway only in S and G2 (2). I would like to discuss how most of the phenomenon could be explained by two DSB repair pathways. (1) Radiat. Res., 155, 680 (2001). (2) EMBO J., 17, 5497 (1998).