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Ionizing Radiation Resistance in Deinococcus Radiodurans

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Abstract
Deinococcus radiodurans is unmatched among all known species in its ability to resist ionizing radiation and other DNA-damaging factors. It is considered a model organism in the study of DNA damage and repair. Treatment of D. radiodurans with an acute dose of 5,000 Gy of ionizing radiation with almost no loss of viability, and an acute dose of 15,000 Gy with 37% viability. The extreme radiation resistance of this bacterium is due to efficient DNA repair capacity, high antioxidant activities, and unique cell structure. Based on the latest findings, the general characteristics and ionizing radiation resistance mechanisms of D. radiodurans are reviewed and discussed in this paper.

Key words: Ionizing radiation; Deinococcus radiodurans; DNA repair; Reactive oxygen species

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INTRODUCTION
D. radiodurans is unmatched among all known species in its ability to resist ionizing radiation (Cox & Battista, 2005). It was first described by Anderson in 1956 (Anderson, Nordon, Cain, Parrish, & Duggan, 1956). Treatment of D. radiodurans with an acute dose of 5,000 Gy of ionizing radiation with almost no loss of viability, and an acute dose of 15,000 Gy with 37% viability (Daly, 2009; Ito, Watanabe, Takeshia, & Iizuka, 1983; Moseley & Mattingly, 1971). In contrast, 5 Gy of ionizing radiation can kill a human, 200-800 Gy of ionizing radiation will kill E. coli, and more than 4,000 Gy of ionizing radiation will kill the radiation-resistant tardigrade. D. radiodurans can survive 5,000 to 30,000 Gy of ionizing radiation, which breaks its genome into hundreds of fragments (Daly & Minton, 1995; Minton, 1994; Slade & Radman, 2011). Surprisingly, the genome is reassembled accurately before beginning of the next cycle of cell division.

The extreme radiation resistance of this bacterium is mainly due to a powerful repair system that achieves an efficient and precise assembly of DNA fragments. The research of radiation resistance in D. radiodurans with great significance, and caused the attention of many scientists, especially the microbiologists, the radiation biologists and cancer researchers. We give a current outlook on D. radiodurans strategies of combating ionizing radiation in this review.

1. GENERAL CHARACTERISTICS OF DEINOCOCCUS RADIODURANS

1.1. Classification and Name
Initially, D. radiodurans was placed in the genus Micrococcus, mainly due to its morpha similarity to members of the genus Micrococcus. After research on M. radiodurans over 30 years, based on evaluation of ribosomal RNA sequences and other evidences, this species was reclassified and placed in its own genus Deinococcus; which is closely related to the genus Thermus of heat-resistant bacteria (Battista, 1997; Hensel, Demharter, Kandler, Kroppenstedt, & Stackebrandt, 1986; Omelchenko et al., 2005; Rainey, Nobre, Schumann,

Stackebrandt, & da Costa, 1997; Weisburg, Giovannoni, & Woese, 1989; Woese, 1987; Woese, Stackebrandt, Macke, & Fox, 1985). Deinococcus from the Greek words 'deinos', meaning strange or unusual, and 'coccus', meaning a grain or berry. The Deinococcus include D.proteolyticus, D. radiopugnans, D. grandis, D. radiophilus, D. geothermalis, D. murrayi, D. indicus, D. frigens, D. saxicola, D. marmoris (Cox & Battista, 2005).

D. radiodurans is divided into two subtypes of D. radiodurans R1 and D. radiodurans Sark. The former with the ability to easily chromosomal transformation and plasmid transfer, it is preferred to the best model organism for the study of bioremediation.

1.2 Physiological Features

D. radiodurans is a Gram-positive, nonsporulating, nonmotile, nonpathogenic, red-pigmented bacterium (Cox & Battista, 2005; Slade & Radman, 2011). It exists as single cells, diads and tetrads with an average cell diameter of 1μm(range, 0.5 to 3.5 μm) in liquid culture(Cox & Battista, 2005; Slade & Radman, 2011). Each D. radiodurans cell has two perpendicular furrows that result in a tetrad morphology. The four compartments contain an equal amount of DNA and it adopted a distinctive toroidal shape (Levin-Zaidman et al., 2003; Minsky, Shimoni, & Englander, 2006). The cell envelope of D. radiodurans consists of the plasma and outer membranes, which include at least five layers with a total thickness of 150 nm (Work & Griffiths, 1968). The first layer is the cytoplasmic membrane; the next layer is a rigid peptidoglycan-containing holey layer, containing glucose, galactose, rhamnose and mannose, but no heptose; the third layer is the compartmentalized layer and appears to be divided into many fine compartments; the fourth layer is the interior layer and the fifth layer is the fragile soft layer, consists of regularly packed hexagonal protein subunits (S-layer), containing carotenoids, lipids, proteins, and polysaccharides (Kubler & Baumeister, 1978; Slade & Radman, 2011; Work & Griffiths, 1968). D. radiodurans is generally grown at 30°C in rich TGY medium (0.5% tryptone , 0.1% glucose, 0.15% yeast extract) with aeration, where cell doubling spends 1.5 to 3h (Venkateswaran et al., 2000).

1.3 Features of the Genome

The genome of D. radiodurans R1 (ATCC BAA-816) has been sequenced by the United States Department of Energy, and the results published in "Science" magazine (White, 1999). The D. radiodurans chromosome is 3,284,156 bp, with an average GC content of 66.6% and protein coding region accounted for 90.9%. The genome composed of four replicons: two chromosomes (chromosome I: 2,648,638 bp, chromosome II: 412,348 bp), a megaplasmid (177,466 bp) and a small plasmid (45,704 bp). There are 3,187 open reading frames (ORFs) with an average size of 937 bp in the genome. 2185 (69%) of the D. radiodurans ORFs matched sequences available in public databases, and 1 493 assigned putative function, 511 matched hypothetical proteins, 181 function unknown. The chromosome I contains 2,633 genes, the chromosome II contains 369 genes, the megaplasmid contains 145 gene, and the small plasmid contains 40 genes. Chromosome II encodes the genes for amino acid utilization, cell envelope formation, and transporters. Genes for origins of replication are encoded on chromosome I and II, such as dnaA and dnaN for chromosome I and parA for chromosome II, but chromosome I contains ParA (ParA1) homologue (Charaka & Misra, 2012). Megaplasmid and small plasmid encodes some regulators and protein kinases, such as RadR, RadS for megaplasmid (Desai, Rajpurohit, Misra, & Deobagkar, 2011) and DrC0012 for small plasmid. This unique structure of the genome may be an important factor for its superior resistance to radiation.

2. IONIZING RADIATION RESISTANCE MECHANISMS OF DEINOCOCCUS RADIODURANS

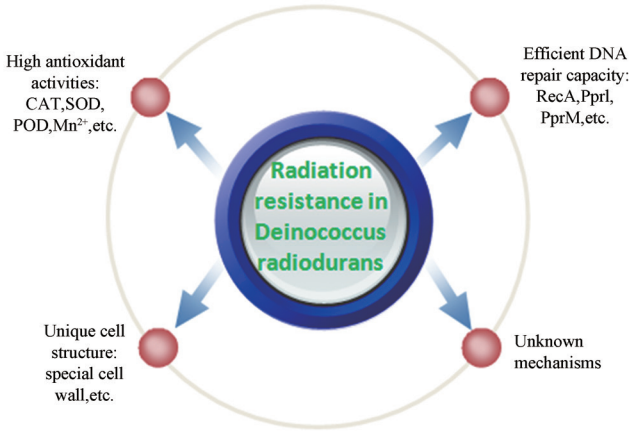

Figure 1
Radiation-Resistance Mechanisms of Deinococcus Radiodurans

Note. The high antioxidant activities, efficient DNA repair capacity and unique cell structure are contributed to the extreme radiation resistance of D. radiodurans.

Ionizing radiation is generated by the decay of radioactive elements. The cells are exposed to ionizing radiation will cause ionization and excitation of the biological molecules, so that the DNA or RNA strand breaks, the peptide strand breaks and loss of biological function. D. radiodurans with extreme radiation resistance and the exponentially grown cells can endure 15,000 Gy of ionizing radiation. D. radiodurans is the only survivor exposed to 20 kGy irradiation on earth. It is reported that

the maximum tolerated dose of ionizing radiation is 50 kGy in D.radiodurans (Ghosal et al., 2005). The extreme radiation resistance of this bacterium is due to many factors (Figure 1).

2.1 DNA Repair Mechanisms

DSBs are the most lethal damage caused by ionizing radiation. D. radiodurans can survive high doses of ionizing radiation, not because it can prevent the generation of DSBs, but it has a highly accurate and effective ability to repair DNA damage. Both of D. radiodurans and E. coli exposed to high levels of ionizing radiation can produce hundreds of genomic double-strand breaks, but the former usually repairs 100 ~ 200 DSBs in its chromosomes within 12–24 hours and the latter can only repairs 2 to 3 DSBs. DNA damage withstood by D. radiodurans is due to the diversity of DNA repair pathways: direct damage reversal, base and nucleotide excision repair, mismatch repair, and recombinational repair. The recombinational repair pathway is the main way to repair DNA damage.

2.1.1 The RecF Pathway

Homologous recombination (HR) between a resident plasmid and the chromosome following irradiation in D. radiodurans is widespread (Daly & Minton, 1997). It is carried out by the RecBCD or the RecFOR pathway in bacteria (Rocha, Cornet, & Michel, 2005). D. radiodurans does not encode RecB and RecC homologs, or SbcB, but it contains all components of the RecFOR pathway, RecF (DR_1089), RecO (DR_0819), RecR (DR_0 198), and RecJ (DR_1126) (Bentchikou, Servant, Coste, & Sommer, 2010; Khairnar, Kamble, & Misra, 2008; Venkateswaran et al., 2000). It is suggested that the RecFOR pathway plays a key role in homologous recombination repair of D. radiodurans. Recently, Katsuya Satoh and his colleagues suggested that the RecF protein is involved in the RecA activation and RecR protein contribution to the stability of incoming DNA during RecA-mediated homologous recombination processes that initiated the ESDSA pathway in D. radiodurans (Satoh et al., 2012). RecO is essential for DNA Damage Repair and plays a vital role in extreme radiation resistance of Deinococcus radiodurans (Xu et al., 2008).The RecJ is the only 5'–3'exonuclease in D. radiodurans, and it is considered to process broken DNA ends for the RecF pathway (Bentchikou et al., 2010; Cao, Mueller, & Julin, 2010).In addition to these four proteins, the RecF pathway also requires other proteins, such as RecA (DR_2340), RecN (DR_1477), RuvA (DR_1274), RuvB (DR_0596), RuvC(DR_0440), SbcC(DR_1922), SbcD (DR_1921) (Cox & Battista, 2005). RecN is an SMC family member which stimulates the intermolecular ligation of linear DNA molecules in the presence of DNA ligase and prevents the separation of DNA fragments (Reyes, Patidar, Uranga, Bortoletto, & Lusetti, 2010).

2.1.2 The PprI Pathway

There is an important pathway of homologous recombination repair in the D. radiodurans. This repair pathway is controlled by the pprI, and contains several important radiation damage repair related genes (or their products), such as pprI, pprA, recA, pprM. PprI is a protection switch gene, and its expression product PprI is a peculiar protein to D. radiodurans (Hua et al., 2003). PprI plays a central regulatory role in multiple pathways, including oxidative stress, energy metabolism, transcriptional regulation, signal transduction, protein folding and assembly (Gao et al., 2003; Hua et al., 2003). PprI can significantly and specifically induce the genes expression of recA and pprA to enhance the ability to repair DNA damage caused by ionizing radiation.

RecA is a helicase, which can control the double-stranded DNA molecule unwinds and open the double-stranded structure, thereby providing single-stranded DNA template for recombination repair. RecA plays a crucial role in DNA recombination repair and chain exchange process (Repar et al., 2010).

The D. radiodurans RecA protein (RecADr) is 57% identical (72% similar) to the E. coli RecA protein (RecAEc) (Cox & Battista, 2005; Makarova et al., 2001). RecADr forms filaments on DNA that are similar to those formed by the RecAEc , it hydrolyzes ATP, dATP and promotes DNA strand-exchange reactions (J. I. Kim, 2006; J. I. Kim et al., 2002). However, the RecADr shows its own unique features. The E. coli RecA protein and other hitherto known filament-forming homologues first combine with the DNA single strand in DNA strand-exchange reaction, while the D. radiodurans RecA protein is the exact inverse of this established pathway, binding the duplex DNA first and the homologous single-stranded DNA substrate second (Cox & Battista, 2005; J.I. Kim & Cox, 2002). It suggests that RecADr may play a unique role in DSBs repair. RecA with a high level of transient expression following exposure to ionizing radiation (Lipton et al., 2002), such as RecA gene expression is induced 8 times following 15 kGy of ionizing radiation (Liu et al., 2003). The recA deletion mutant cell is highly sensitive to ultraviolet and ionizing radiation (Gutman, Carroll, Masters, & Minton, 1994).

PprA (DR_A0346) is an essential repair gene and contributes to the extreme resistance of this bacterium to a variety of genotoxic assaults (Kota, Charaka, Ringgaard, Waldor, & Misra, 2014; Narumi et al., 2004). PprA is necessary for accurate cell division of γ-irradiated D. radiodurans (Devigne, Mersaoui, Bouthier-de-la-Tour, Sommer, & Servant, 2013), and may participate in a RecA-dependent process during recovery from radiation damage (Tanaka et al., 2004). PprA protein preferentially binds to double-stranded DSBs, and inhibit the activity of exonuclease III to promote DNA end-joining by DNA ligase (Narumi et al., 2004). These results suggested

that PprA plays a key role in non-homologous end-joining (NHEJ) of this species. PprA expression level was upregulated obviously after ionizing radiation and desiccation (Liu et al., 2003; Tanaka et al., 2004), and pprA mutant D. radiodurans strain was significantly sensitive to ionizing radiation, MMC (Narumi et al., 2004). Besides, PprA also contributes to maintain the integrity of the damaged D. radiodurans genome by interacting with topoisomerases (Kota et al., 2014).

PprI, recA, and pprA are the critical component of the PprI pathway in D. radiodurans. Studies have shown that these three genes for resistance to ultraviolet of D. radiodurans are indispensable (Bauermeister, Bentchikou, Moeller, & Rettberg, 2009). Inactivation of pprA promoter and up-regulation of pprA expression by the PprI protein is triggered at the transcription innitiation level (Ohba, Satoh, Yanagisawa, & Narumi, 2005). But PprI doesn't directly bind to promoter regions of pprA and cinA-recA. It shows that PprI itself does not directly regulate the expression of pprA and recA. So there may be hitherto unknown components of PprI-mediated signal transduction pathway in D. radiodurans. Ohba and colleagues identified PprM protein was a novel component of the PprI pathway (Ohba, Satoh, Sghaier, Yanagisawa, & Narumi, 2009). The pprM mutant D. radiodurans strain was significantly sensitive to ionizing radiation, and the pprA/pprM double deletion mutant strain showed higher sensitivity than pprA or pprM single mutant strain, which suggested that PprM regulates PprA and other unknown protein(s) important for radiation resistance. However, Hua and colleagues identified the PprI protein could directly combine with the promoter region of recA and pprA (Lu, Chen, Xu, Shah, & Hua, 2012). PprI and DrRRA may work together in response to extreme ionizing radiation in D. radiodurans (Wang et al., 2012). In summary, the PprI pathway is an enormously complex DNA repair regulatory network, which is worthy of further study.

2.1.3 Novel Deinococcal DNA Repair Genes

In addition to the RecF and PprI pathway, there are many other genes involved in DNA repair of D. radiodurans. RecX could inhibit the expression of DNA repair proteins RecA, SSB, PprA and facilitate the expression of some metabolism-related proteins in D. radiodurans (Sheng, Jao, Li, Xu, & Zhang, 2009), which suggesting RecX is a DNA damage stress switch. DR_0171 mutant strain is highly sensitive to ionizing radiation and DR_0171 serves as a regulator of the transcriptional response to radiation damage in D. radiodurans (Lu et al., 2011). Besides, DdrB is a novel single-stranded DNA binding protein (SSB) that contains a novel fold (Sugiman-Marangos & Junop, 2010). Recently, a novel protein encoded by the DR_1245 gene was identified as an interacting partner of DdrB (Norais et al., 2013). Further studies show the structure of the DR_1245 protein is similar to YbjN and numerous type III secretion chaperones. It suggests that the DR_1245 protein with chaperone activity towards DdrB and possibly other substrates. Interestingly, there are many insertion sequences (IS) in the D. radiodurans genome, but only ISDra2 is strongly induced by γirradiation and provides the major source of induced mutations, and TnpB regulate the transposition of ISDra2 (Pasternak et al., 2013). Moreover, Onodera T and colleagues identified D. radiodurans ygjD (DR_0382) and yeaZ (DR_0756) genes play a role in the repair of DNA cross-links (Onodera, Satoh, Ohta, & Narumi, 2013) In conclusion, Deinococcus radiodurans DNA damage repair mechanism will be a research hotspot in the future.

2.2 High Antioxidant Activities

2.2.1 Catalases and Superoxide Dismutases

Although many studies have shown that the radiation resistance of D. radiodurans is due to its efficient DNA repair ability, however, ionizing radiation will produce large amounts of free radicals, which indirectly cause DNA, RNA and protein damage. In general, the D. radiodurans cells possess high antioxidant activity to scavenge free radicals. The catalase activity during exponential phases is 127 times and stationary phases are 32 times higher it in E. coli (P. Wang & Schellhorn, 1995). In addition, Tian and colleagues' research showed the catalase activity is 15 folds in D. radiodurans higher in E. coli (Tian et al., 2004). Catalases and peroxidases can remove H_2O_2, which is the byproduct of superoxide dismutases (SOD) eliminate superoxide free radicals from the cells (Abreu et al., 2008). There are three catalases (katE catalases DR_1998 and DR_A0259 and eukaryotic-type DR_A0146), four superoxide dismutases (Mn-dependent DR_1279 and Cu/Zn-dependent DR_1546, DR_A0202, and DR_0644), a cytochrome c peroxidase (DR_A0301), and an iron-dependent peroxidase (DR_A0145) in D. radiodurans (Lipton et al., 2002; Slade & Radman, 2011). DR_1279 is constitutively expressed, and its product can be efficient removal of superoxide radicals(Abreu et al., 2008) . Recently, Hua et al. identified extracellular dGMP induced catalase (DR_1988) activity, and enhanced D. radiodurans tolerance to H_2O_2 and gamma-radiation significantly (Li et al., 2013). These results suggest that catalases and SODs protect macromolecules from ROS-mediated damage in vivo of D. radiodurans.

2.2.2 Carotenoids

D. radiodurans also contains other oxidative defense components, such as glutaredoxin, thioredoxin, thioredoxin reductase, alkyl hydroperoxide reductase, and carotenoids (Slade & Radman, 2011; White, 1999). Carotenoids are efficient scavengers of reactive oxygen species (ROS) and belong to the group of lipophilic antioxidants (Tian & Hua, 2010). Carotenoids are able to detoxify various forms of ROS, which protect DNA from oxidative damage, proteins from carbonylation, and

membranes from lipid peroxidation (Slade & Radman, 2011; Tian et al., 2009). D. radiodurans carotenoids can eliminate all types of reactive oxygen species in vitro, such as hydroxyl radicals, superoxide radicals, hydrogen peroxide and singlet oxygen (Zhang et al., 2007). Furthermore, D. radiodurans carotenoids also remove RNS (reactive nitrogen species) such as 2,2-diphenyl-1-picrylhydrazyl (DPPH•) (Tian et al., 2009). D. radiodurans possess 13 genes involved in carotenoids biosynthesis, and with a perfect biosynthetic pathway(Tian & Hua, 2010). Deinoxanthin as a major product in the carotenoid synthetic process of D. radiodurans, which has a stronger eliminate capabilities than two carotenes (lycopene, β-carotenoids) and two xanthophylls (zeaxanthin, lutein) to remove hydrogen peroxide and singlet oxygen(Tian, Xu, Sun, Lin, & Hua, 2007). However, carotenoids seems to have little effect on the radiation resistance, block carotenoid biosynthesis pathway (knockout crtB) only a weak increase in Deinococcus to ionizing radiation, drying and UV radiation sensitivity (Luan et al., 2014; Tian et al., 2007; Zhang et al., 2007). It suggests that carotenoids may not be the main ROS scavengers in vivo of D. radiodurans.

2.2.3 Manganese Complexes

The D. radiodurans ultrafiltrate is enriched in Mn, phosphate, peptides, nucleosides and bases, which protect proteins from ionizing radiation-induced ROS damage (Daly et al., 2010; Daly et al., 2004). D. radiodurans cells have unusually high manganese content, which up to 0.2 ~ 4.0 mmol/L (15-150 times higher than radiosensitive bacteria) (Daly et al., 2007; Daly et al., 2004).The majority of cellular Mn in D.radiodurans is present as small complexes with orthophosphate and amino acids or peptides, and Mn-peptide complexes are the most protective (Daly et al., 2010; Daly et al., 2007). Mn^{2+} metabolite defenses are key to preserving the activity of repair enzymes in Deinococcus radiodurans exposed to ionizing radiation (Culotta & Daly, 2013),which by scavenging O_2•−and H_2O_2, specifically protect proteins against oxidative damage(Daly et al., 2010; Daly et al., 2007). The nucleotide residues (e.g., uridine) also form complexes with Mn^{2+} and orthophosphate, which with a higher ability to eliminate ROS than Mn^{2+}-orthophosphate alone (Daly et al., 2010). Further research shows, as much as 40% of the total Mn^{2+} is in manganese superoxide dismutase, which is the most effective for regulating superoxide in Deinococcus radiodurans (Tabares & Un, 2013). In vitro, the superoxide free radical scavenging relies on manganese threshold concentration (Barnese, Gralla, Cabelli, & Valentine, 2008; Daly et al., 2010; Daly et al., 2007) . Divalent manganese ions (Mn^{2+}) scavenge superoxide radicals by binding phosphate(Barnese et al., 2008), and hydrogen peroxide in combination with bicarbonate salts, amino acid or polypeptide in the extracellular (Berlett, Chock, Yim, & Stadtman, 1990).

Manganese may not only be a chemical scavenger but may also replace Fe in Fe-loaded enzymes, thereby preventing the iron in the Fenton reaction to cause oxidative damage to the protein (Anjem, Varghese, & Imlay, 2009). D. radiodurans has a high intracellular manganese-to-iron (Mn/Fe) ratio of 0.24(Daly et al., 2004), which contribution to extreme ionizing radiation resistance (Daly et al., 2004; Sun et al., 2012), desiccation resistance (Fredrickson et al., 2008) and low levels of protein oxidative damage (Daly et al., 2007). There is more than one regulator of Mn/Fe homeostasis that involves its high intracellular Mn/Fe ratio in D. radiodurans (Sun et al., 2012).

2.3 Unique Cell Structure

D. radiodurans cell is divided into four compartments by two perpendicular furrows, and each compartment contains an equal amount of DNA and it adopted a distinctive toroidal shape. This rare DNA compartments and the ringlike shape of the chromatin contribute to its extremely radiation-resistant (Levin-Zaidman et al., 2003; Minsky et al., 2006). D. radiodurans is gram-positive bacteria, but its cell wall is similar to gram-negative bacteria. This cell wall includes a plurality of layers as thick as 150 nm (Work & Griffiths, 1968), which play an important role in its extremely radiation-resistant. The fragile soft layer is tightly to cell walls in D. radiodurans that consists of regularly packed hexagonal protein subunits (S-layer or HPI-layer), containing carotenoids, lipids, proteins, and polysaccharides (Baumeister et al., 1986; Kubler & Baumeister, 1978; Work & Griffiths, 1968). The S-layer with a number of functions, include cell adhesion, enzyme attachment, prevention of adsorption of macromolecules and cellular rigidity, which contribute to the extremely radiation-resistant of D. radiodurans (Rothfuss, Lara, Schmid, & Lidstrom, 2006). Many genes are involved in building the S-layer and maintain the integrity of the cell envelope in D. radiodurans (Farci et al., 2014; Rothfuss et al., 2006). Besides, membrane proteins are important structural components and function in many physiological processes. Tian and colleagues did a proteomic analysis of membrane proteins from Deinococcus geothermalis, identified the special protein composition and functions in the cell membrane of Deinococcus (Tian et al., 2010). DR_2518 is a DNA damage-responsive membrane protein kinase plays an important role in radiation resistance and DNA strand break repair in D. radiodurans (Rajpurohit & Misra, 2010). These results suggest that the particular membrane proteins are involved in the extreme radiation resistance of D. radiodurans.

3. CONCLUSION

In summary, recent researches have shown that the tolerance of D. radiodurans to radiation is owe to efficient DNA repair capacity, high antioxidant activities, and unique cell structure. The high DNA repair rates make D.

radiodurans with a powerful repair system that achieves an efficient and precise assembly of DNA fragments. The high antioxidant activities can scavenge free radicals and protect macromolecules from ROS-mediated damage in vivo of D. radiodurans. The unique cell structure of D. radiodurans also contributes to its extreme radiation resistance. All of above show that D. radiodurans have a complex network system contains many genes, proteins and other substances to cope with its DNA damage and repair, which can help D. radiodurans survive in extreme levels of ionizing radiation.

Researches on the molecular mechanisms of DNA repair not only has important theoretical significance, but also has extensive practical application prospects. Aging and cancer are tightly associated with DNA, RNA and protein oxidative damage due to ROS generation (Choudhari, Chaudhary, Gadbail, Sharma, & Tekade, 2014; Kryston, Georgiev, Pissis, & Georgakilas, 2011; Lee & Wei, 2007), it suggests that the radioresistance mechanism of D. radiodurans help us to understand the formation mechanism of cancer and aging. Engineering of D. radiodurans with good application prospects in environmental remediation (Appukuttan, Rao, & Apte, 2006; Appukuttan, Seetharam, Padma, Rao, & Apte, 2011; Brim et al., 2000; Chaturvedi & Archana, 2014). Moreover, some functional genes of D. radiodurans are used to plant breeding for disease resistance and desiccation tolerance(J. Battista, Park, & McLemore, 2001; Sun et al., 2012) Therefore, we have every reason to believe that with further research of D. radiodurans will show more attractive prospects.

REFERENCES

Abreu, I. A., Hearn, A., An, H., Nick, H. S., Silverman, D. N., & Cabelli, D. E. (2008). The kinetic mechanism of manganese-containing superoxide dismutase from Deinococcus radiodurans: A specialized enzyme for the elimination of high superoxide concentrations. *Biochemistry, 47*(8), 2350-2356. doi: 10.1021/bi7016206

Anderson, A. W., Nordon, H. C., Cain, R. F., Parrish, G., & Duggan, D. (1956). Studies on a radioresistant Micrococcus. I. Isolation, morphology, cultural characteristics, and resistance to gamma radiation. *Food Technology, 10*(1), 575–578.

Anjem, A., Varghese, S., & Imlay, J. A. (2009). Manganese import is a key element of the OxyR response to hydrogen peroxide in Escherichia coli. *Mol Microbiol, 72*(4), 844-858. doi: 10.1111/j.1365-2958.2009.06699.x

Appukuttan, D., Rao, A. S., & Apte, S. K. (2006). Engineering of deinococcus radiodurans R1 for bioprecipitation of uranium from dilute nuclear waste. *Appl Environ Microbiol, 72*(12), 7873-7878. doi: 10.1128/AEM.01362-06

Appukuttan, D., Seetharam, C., Padma, N., Rao, A. S., & Apte, S. K. (2011). PhoN-expressing, lyophilized, recombinant Deinococcus radiodurans cells for uranium bioprecipitation. *J Biotechnol, 154*(4), 285-290. doi: 10.1016/j.jbiotec.2011.05.002

Barnese, K., Gralla, E. B., Cabelli, D. E., & Valentine, J. S. (2008). Manganous phosphate acts as a superoxide dismutase. *J Am Chem Soc, 130*(4), 4604-4606. doi: 10.1021/ja710162n

Battista, J., Park, M. J., & McLemore, A. E. (2001). Inactivation of two homologues of proteins presumed to be involved in the desiccation tolerance of plants sensitizes Deinococcus radiodurans R1 to desiccation. *Cryobiology, 43*(2), 133-139. doi: 10.1006/cryo.2001.2357

Battista, J. R. (1997). Against all odds: the survival strategies of Deinococcus radiodurans. *Annual Review of Microbiology, 51*, 203–224. doi: 10.1146/annurev.micro.51.1.203

Bauermeister, A., Bentchikou, E., Moeller, R., & Rettberg, P. (2009). Roles of PprA, IrrE, and RecA in the resistance of Deinococcus radiodurans to germicidal and environmentally relevant UV radiation. *Arch Microbiol, 191*(12), 913-918. doi: 10.1007/s00203-009-0522-7

Baumeister, W., Barth, M., Hegerl, R., Guckenberger, R., Hahn, M., & Saxton, W. O. (1986). Three-dimensional structure of the regular surface layer (HPI layer) of Deinococcus radiodurans. *J Mol Biol, 187*(2), 241-250.

Bentchikou, E., Servant, P., Coste, G., & Sommer, S. (2010). A major role of the RecFOR pathway in DNA double-strand-break repair through ESDSA in Deinococcus radiodurans. *PLoS Genet, 6*(1), e1000774. doi: 10.1371/journal.pgen.1000774

Berlett, B. S., Chock, P. B., Yim, M. B., & Stadtman, E. R. (1990). Manganese(II) catalyzes the bicarbonate-dependent oxidation of amino acids by hydrogen peroxide and the amino acid-facilitated dismutation of hydrogen peroxide. *Proc Natl Acad Sci USA, 87*(1), 389-393.

Brim, H., McFarlan, S. C., Fredrickson, J. K., Minton, K. W., Zhai, M., Wackett, L. P., & Daly, M. J. (2000). Engineering Deinococcus radiodurans for metal remediation in radioactive mixed waste environments. *Nat Biotechnol, 18*(1), 85-90. doi: 10.1038/71986

Cao, Z., Mueller, C. W., & Julin, D. A. (2010). Analysis of the recJ gene and protein from Deinococcus radiodurans. *DNA Repair (Amst), 9*(1), 66-75. doi: 10.1016/j.dnarep.2009.10.009

Charaka, V. K., & Misra, H. S. (2012). Functional characterization of the role of the chromosome I partitioning system in genome segregation in Deinococcus radiodurans. *J Bacteriol, 194*(21), 5739-5748. doi: 10.1128/JB.00610-12

Chaturvedi, R., & Archana, G. (2014). Cytosolic expression of synthetic phytochelatin and bacterial metallothionein genes in Deinococcus radiodurans R1 for enhanced tolerance and bioaccumulation of cadmium. *Biometals, 27*(3), 471-482. doi: 10.1007/s10534-014-9721-z

Choudhari, S. K., Chaudhary, M., Gadbail, A. R., Sharma, A., &

Tekade, S. (2014). Oxidative and antioxidative mechanisms in oral cancer and precancer: A review. *Oral Oncol, 50*(1), 10-18. doi: 10.1016/j.oraloncology.2013.09.011

Cox, M. M., & Battista, J. R. (2005). Deinococcus radiodurans - the consummate survivor. *Nat Rev Microbiol, 3*(11), 882-892. doi: 10.1038/nrmicro1264

Culotta, V. C., & Daly, M. J. (2013). Manganese complexes: diverse metabolic routes to oxidative stress resistance in prokaryotes and yeast. *Antioxid Redox Signal, 19*(9), 933-944. doi: 10.1089/ars.2012.5093

Daly, M. J. (2009). A new perspective on radiation resistance based on Deinococcus radiodurans. *Nat Rev Microbiol, 7*(3), 237-245. doi: 10.1038/nrmicro2073

Daly, M. J., Gaidamakova, E. K., Matrosova, V. Y., Kiang, J. G., Fukumoto, R., Lee, D. Y., . . . Levine, R. L. (2010). Small-molecule antioxidant proteome-shields in Deinococcus radiodurans. *PLoS One, 5*(9), e12570. doi: 10.1371/journal.pone.0012570

Daly, M. J., Gaidamakova, E. K., Matrosova, V. Y., Vasilenko, A., Zhai, M., Leapman, R. D., . . . Fredrickson, J. K. (2007). Protein oxidation implicated as the primary determinant of bacterial radioresistance. *PLoS Biol, 5*(5), e92. doi: 10.1371/journal.pbio.0050092

Daly, M. J., Gaidamakova, E. K., Matrosova, V. Y., Vasilenko, A., Zhai, M., Venkateswaran, A., . . . Ghosal, D. (2004). Accumulation of Mn(II) in Deinococcus radiodurans facilitates gamma-radiation resistance. *Science, 306*(5698), 1025-1028. doi: 10.1126/science.1103185

Daly, M. J., & Minton, K. W. (1995). Resistance to radiation. *Science, 270*(5240), 1318. doi: 10.1126/science.270.5240.1318

Daly, M. J., & Minton, K. W. (1997). Recombination between a resident plasmid and the chromosome following irradiation of the radioresistant bacterium Deinococcus radiodurans. *Gene., 187*(2), 225-229. doi: 10.1016/S0378-1119(96)00755-X

Desai, S. S., Rajpurohit, Y. S., Misra, H. S., & Deobagkar, D. N. (2011). Characterization of the role of the RadS/RadR two-component system in the radiation resistance of Deinococcus radiodurans. *Microbiology, 157*(Pt 10), 2974-2982. doi: 10.1099/mic.0.049361-0

Devigne, A., Mersaoui, S., Bouthier-de-la-Tour, C., Sommer, S., & Servant, P. (2013). The PprA protein is required for accurate cell division of gamma-irradiated Deinococcus radiodurans bacteria. *DNA Repair (Amst), 12*(4), 265-272. doi: 10.1016/j.dnarep.2013.01.004

Farci, D., Bowler, M. W., Kirkpatrick, J., McSweeney, S., Tramontano, E., & Piano, D. (2014). New features of the cell wall of the radio-resistant bacterium Deinococcus radiodurans. *Biochim Biophys Acta, 1838*(7), 1978-1984. doi: 10.1016/j.bbamem.2014.02.014

Fredrickson, J. K., Li, S. M., Gaidamakova, E. K., Matrosova, V. Y., Zhai, M., Sulloway, H. M., . . . Daly, M. J. (2008). Protein oxidation: key to bacterial desiccation resistance? *ISME J, 2*(4), 393-403. doi: 10.1038/ismej.2007.116

Gao, G., Tian, B., Liu, L., Sheng, D., Shen, B., & Hua, Y. (2003). Expression of Deinococcus radiodurans PprI enhances the radioresistance of Escherichia coli. *DNA Repair (Amst), 2*(12), 1419-1427.

Ghosal, D., Omelchenko, M. V., Gaidamakova, E. K., Matrosova, V. Y., Vasilenko, A., Venkateswaran, A., . . . Daly, M. J. (2005). How radiation kills cells: survival of Deinococcus radiodurans and Shewanella oneidensis under oxidative stress. *FEMS Microbiol Rev, 29*(2), 361-375. doi: 10.1016/j.femsre.2004.12.007

Gutman, P. D., Carroll, J. D., Masters, C. I., & Minton, K. W. (1994). Sequencing, targeted mutagenesis and expression of a recA gene required for the extreme radioresistance of Deinococcus radiodurans. *Gene, 141*(1), 31-37.

Hensel, R., Demharter, W., Kandler, O., Kroppenstedt, R. M., & Stackebrandt, E. (1986). Chemotaxonomic and moleculargenetic studies of the genus Thermus: evidence for a phylogenetic relationship of Thermus aquaticus and Thermus ruber to the genus Deinococcus. *Int. J. Syst. Bacteriol, 36*(3), 444–453. doi: 10.1099/00207713-36-3-444

Hua, Y., Narumi, I., Gao, G., Tian, B., Satoh, K., Kitayama, S., & Shen, B. (2003). PprI: a general switch responsible for extreme radioresistance of Deinococcus radiodurans. *Biochem Biophys Res Commun, 306*(2), 354-360.

Ito, H., Watanabe, H., Takeshia, M., & Iizuka, H. (1983). Isolation and Identification of Radiation-Resistant Cocci Belonging to the Genus Deinococcus from Sewage Sludges and Animal Feeds. *Agric. Biol. Chem, 47*(6), 1239–1247.

Khairnar, N. P., Kamble, V. A., & Misra, H. S. (2008). RecBC enzyme overproduction affects UV and gamma radiation survival of Deinococcus radiodurans. *DNA Repair (Amst), 7*(1), 40-47. doi: 10.1016/j.dnarep.2007.07.007

Kim, J. I. (2006). Analysis of double stranded DNA-dependent activities of Deinococcus radiodurans RecA protein. *J Microbiol, 44*(5), 508-514.

Kim, J. I., & Cox, M. M. (2002). The RecA proteins of Deinococcus radiodurans and Escherichia coli promote DNA strand exchange via inverse pathways. *Proc Natl Acad Sci USA, 99*(12), 7917-7921. doi: 10.1073/pnas.122218499

Kim, J. I., Sharma, A. K., Abbott, S. N., Wood, E. A., Dwyer, D. W., Jambura, A., . . . Cox, M. M. (2002). RecA Protein from the extremely radioresistant bacterium Deinococcus radiodurans: expression, purification, and characterization. *J Bacteriol, 184*(6), 1649-1660.

Kota, S., Charaka, V. K., Ringgaard, S., Waldor, M. K., & Misra, H. S. (2014). PprA contributes to Deinococcus radiodurans resistance to nalidixic acid, genome maintenance after DNA damage and interacts with deinococcal topoisomerases. *PLoS One, 9*(1), e85288. doi: 10.1371/journal.pone.0085288

Kryston, T. B., Georgiev, A. B., Pissis, P., & Georgakilas, A. G. (2011). Role of oxidative stress and DNA damage in human carcinogenesis. *Mutat Res, 711*(1-2), 193-201. doi: 10.1016/j.mrfmmm.2010.12.016

Kubler, O., & Baumeister, W. (1978). The structure of a

periodic cell wall component (HPI-layer of Micrococcus radiodurans). *Cytobiologie, 17*(1), 1-9.

Lee, H. C., & Wei, Y. H. (2007). Oxidative stress, mitochondrial DNA mutation, and apoptosis in aging. *Exp Biol Med (Maywood), 232*(5), 592-606.

Levin-Zaidman, S., Englander, J., Shimoni, E., Sharma, A. K., Minton, K. W., & Minsky, A. (2003). Ringlike structure of the Deinococcus radiodurans genome: a key to radioresistance? *Science, 299*(5604), 254-256. doi: 10.1126/science.1077865

Li, M., Sun, H., Feng, Q., Lu, H., Zhao, Y., Zhang, H., . . . Hua, Y. (2013). Extracellular dGMP enhances Deinococcus radiodurans tolerance to oxidative stress. *PLoS One, 8*(1), e54420. doi: 10.1371/journal.pone.0054420

Lipton, M. S., Pasa-Tolic', L., Anderson, G. A., Anderson, D. J., Auberry, D. L., Battista, J. R., . . . Fredrickson, J. (2002). Global analysis of the Deinococcus radiodurans proteome by using accurate mass tags. *Proc Natl Acad Sci U S A, 99*(17), 11049–11054. doi: 10.1073/pnas.172170199

Liu, Y., Zhou, J., Omelchenko, M. V., Beliaev, A. S., Venkateswaran, A., Stair, J., . . . Daly, M. J. (2003). Transcriptome dynamics of Deinococcus radiodurans recovering from ionizing radiation. *Proc Natl Acad Sci U S A, 100*(7), 4191-4196. doi: 10.1073/pnas.0630387100

Lu, H., Chen, H., Xu, G., Shah, A. M., & Hua, Y. (2012). DNA binding is essential for PprI function in response to radiation damage in Deinococcus radiodurans. *DNA Repair (Amst), 11*(2), 139-145. doi: 10.1016/j.dnarep.2011.10.013

Lu, H., Xia, W., Chen, H., Yin, L., Zhao, X., Xu, G., & Hua, Y. (2011). Characterization of the role of DR0171 in transcriptional response to radiation in the extremely radioresistant bacterium Deinococcus radiodurans. *Arch Microbiol, 193*(10), 741-750. doi: 10.1007/s00203-011-0712-y

Luan, H., Meng, N., Fu, J., Chen, X., Xu, X., Feng, Q.,. . . Wang, J. (2014). Genome-wide transcriptome and antioxidant analyses on gamma-irradiated phases of deinococcus radiodurans R1. *PLoS One, 9*(1), e85649. doi: 10.1371/journal.pone.0085649

Makarova, K. S., Aravind, L., Wolf, Y. I., Tatusov, R. L., Minton, K. W., Koonin, E. V., & Daly, M. J. (2001). Genome of the extremely radiation-resistant bacterium Deinococcus radiodurans viewed from the perspective of comparative genomics. *Microbiol Mol Biol Rev, 65*(1), 44-79. doi: 10.1128/MMBR.65.1.44-79.2001

Minsky, A., Shimoni, E., & Englander, J. (2006). Ring-like nucleoids and DNA repair through error-free nonhomologous end joining in Deinococcus radiodurans. *J Bacteriol, 188*(17), 6047-6051. doi: 10.1128/JB.01951-05

Minton, K. W. (1994). DNA repair in the extremely radioresistant bacterium Deinococcus radiodurans. *Mol Microbiol, 13*(1), 9-15. doi: 10.1111/j.1365-2958.1994.tb00397.x

Moseley, B. E., & Mattingly, A. (1971). Repair of irradiation transforming deoxyribonucleic acid in wild type and a radiation-sensitive mutant of Micrococcus radiodurans. *J Bacteriol, 105*(3), 976-983.

Narumi, I., Satoh, K., Cui, S., Funayama, T., Kitayama, S., & Watanabe, H. (2004). PprA: A novel protein from Deinococcus radiodurans that stimulates DNA ligation. *Mol Microbiol, 54*(1), 278-285. doi: 10.1111/j.1365-2958.2004.04272.x

Norais, C., Servant, P., Bouthier-de-la-Tour, C., Coureux, P. D., Ithurbide, S., Vannier, F., . . . Sommer, S. (2013). The Deinococcus radiodurans DR1245 protein, a DdrB partner homologous to YbjN proteins and reminiscent of type III secretion system chaperones. *PLoS One, 8*(2), e56558. doi: 10.1371/journal.pone.0056558

Ohba, H., Satoh, K., Sghaier, H., Yanagisawa, T., & Narumi, I. (2009). Identification of PprM: a modulator of the PprI-dependent DNA damage response in Deinococcus radiodurans. *Extremophiles, 13*(3), 471-479. doi: 10.1007/s00792-009-0232-8

Ohba, H., Satoh, K., Yanagisawa, T., & Narumi, I. (2005). The radiation responsive promoter of the Deinococcus radiodurans pprA gene. *Gene, 363*, 133-141. doi: 10.1016/j.gene.2005.07.035

Omelchenko, M. V., Wolf, Y. I., Gaidamakova, E. K., Matrosova, V. Y., Vasilenko, A., Zhai, M., . . . Makarova, K. S. (2005). Comparative genomics of Thermus thermophilus and Deinococcus radiodurans: divergent routes of adaptation to thermophily and radiation resistance. *BMC Evol Biol, 5*, 57. doi: 10.1186/1471-2148-5-57

Onodera, T., Satoh, K., Ohta, T., & Narumi, I. (2013). Deinococcus radiodurans YgjD and YeaZ are involved in the repair of DNA cross-links. *Extremophiles, 17*(1), 171-179. doi: 10.1007/s00792-012-0506-4

Pasternak, C., Dulermo, R., Ton-Hoang, B., Debuchy, R., Siguier, P., Coste, G., . . . Sommer, S. (2013). ISDra2 transposition in Deinococcus radiodurans is downregulated by TnpB. *Mol Microbiol, 88*(2), 443-455. doi: 10.1111/mmi.12194

Rainey, F. A., Nobre, M. F., Schumann, P., Stackebrandt, E., & da Costa, M. S. (1997). Phylogenetic diversity of the deinococci as determined by 16S ribosomal DNA sequence comparison. *Int J Syst Bacteriol, 47*(2), 510-514. doi: 10.1099/00207713-47-2-510

Rajpurohit, Y. S., & Misra, H. S. (2010). Characterization of a DNA damage-inducible membrane protein kinase from deinococcus radiodurans and its role in bacterial radioresistance and DNA strand break repair. *Mol Microbiol, 77*(6), 1470-1482. doi: 10.1111/j.1365-2958.2010.07301.x

Repar, J., Cvjetan, S., Slade, D., Radman, M., Zahradka, D., & Zahradka, K. (2010). RecA protein assures fidelity of DNA repair and genome stability in Deinococcus radiodurans. *DNA Repair (Amst), 9*(11), 1151-1161. doi: 10.1016/j.dnarep.2010.08.003

Reyes, E. D., Patidar, P. L., Uranga, L. A., Bortoletto, A. S.,

& Lusetti, S. L. (2010). RecN is a cohesin-like protein that stimulates intermolecular DNA interactions in vitro. *J Biol Chem., 285*(22), 16521-16529. doi: 10.1074/jbc.M110.119164

Rocha, E. P., Cornet, E., & Michel, B. (2005). Comparative and evolutionary analysis of the bacterial homologous recombination systems. *PLoS Genet, 1*(2), e15. doi: 10.1371/journal.pgen.0010015

Rothfuss, H., Lara, J. C., Schmid, A. K., & Lidstrom, M. E. (2006). Involvement of the S-layer proteins Hpi and SlpA in the maintenance of cell envelope integrity in Deinococcus radiodurans R1. *Microbiology, 152*(Pt 9), 2779-2787. doi: 10.1099/mic.0.28971-0

Satoh, K., Kikuchi, M., Ishaque, A. M., Ohba, H., Yamada, M., Tejima, K., . . . Narumi, I. (2012). The role of Deinococcus radiodurans RecFOR proteins in homologous recombination. *DNA Repair (Amst), 11*(4), 410-418. doi: 10.1016/j.dnarep.2012.01.008

Sheng, D., Jao, J., Li, M., Xu, P., & Zhang, J. (2009). RecX is involved in the switch between DNA damage response and normal metabolism in D. radiodurans. *J Biochem, 146*(3), 337-342. doi: 10.1093/jb/mvp072

Slade, D., & Radman, M. (2011). Oxidative stress resistance in deinococcus radiodurans. *Microbiol Mol Biol Rev, 75*(1), 133-191. doi: 10.1128/MMBR.00015-10

Sugiman-Marangos, S., & Junop, M. S. (2010). The structure of DdrB from Deinococcus: a new fold for single-stranded DNA binding proteins. *Nucleic Acids Res, 38*(10), 3432-3440. doi: 10.1093/nar/gkq036

Sun, H., Li, M., Xu, G., Chen, H., Jiao, J., Tian, B., . . . Hua, Y. (2012). Regulation of MntH by a dual Mn(II)- and Fe(II)-dependent transcriptional repressor (DR2539) in Deinococcus radiodurans. *PLoS One, 7*(4), e35057. doi: 10.1371/journal.pone.0035057

Tabares, L. C., & Un, S. (2013). In situ determination of manganese(II) speciation in Deinococcus radiodurans by high magnetic field EPR: Detection of high levels of Mn(II) bound to proteins. *J Biol Chem, 288*(7), 5050-5055. doi: 10.1074/jbc.C112.444992

Tanaka, M., Earl, A. M., Howell, H. A., Park, M. J., Eisen, J. A., Peterson, S. N., & Battista, J. R. (2004). Analysis of Deinococcus radiodurans's transcriptional response to ionizing radiation and desiccation reveals novel proteins that contribute to extreme radioresistance. *Genetics, 168*(1), 21-33. doi: 10.1534/genetics.104.029249

Tian, B., & Hua, Y. (2010). Carotenoid biosynthesis in extremophilic Deinococcus-Thermus bacteria. *Trends Microbiol, 18*(11), 512-520. doi: 10.1016/j.tim.2010.07.007

Tian, B., Sun, Z., Shen, S., Wang, H., Jiao, J., Wang, L., . . . Hua, Y. (2009). Effects of carotenoids from Deinococcus radiodurans on protein oxidation. *Lett Appl Microbiol, 49*(6), 689-694. doi: 10.1111/j.1472-765X.2009.02727.x

Tian, B., Wang, H., Ma, X., Hu, Y., Sun, Z., Shen, S., . . . Hua, Y. (2010). Proteomic analysis of membrane proteins from a radioresistant and moderate thermophilic bacterium Deinococcus geothermalis. *Mol Biosyst, 6*(10), 2068-2077. doi: 10.1039/c004875e

Tian, B., Wu, Y., Sheng, D., Zheng, Z., Gao, G., & Hua, Y. (2004). Chemiluminescence assay for reactive oxygen species scavenging activities and inhibition on oxidative damage of DNA in Deinococcus radiodurans. *Luminescence, 19*(2), 78-84. doi: 10.1002/bio.761

Tian, B., Xu, Z., Sun, Z., Lin, J., & Hua, Y. (2007). Evaluation of the antioxidant effects of carotenoids from Deinococcus radiodurans through targeted mutagenesis, chemiluminescence, and DNA damage analyses. *Biochim Biophys Acta, 1770*(6), 902-911. doi: 10.1016/j.bbagen.2007.01.016

Venkateswaran, A., McFarlan, S. C., Ghosal, D., Minton, K. W., Vasilenko, A., Makarova, K., . . . Daly, M. J. (2000). Physiologic determinants of radiation resistance in Deinococcus radiodurans. *Appl Environ Microbiol, 66*(6), 2620-2626.

Wang, L. Y., Yin, L. F., Xu, G. Z., Li, M. F., Zhang, H., Tian, B., & Hua, Y. (2012). Cooperation of PprI and DrRRA in response to extreme ionizing radiation in Deinococcus radiodurans. *Chinese Science Bulletin, 57*(1), 98-104. doi: 10.1007/s11434-011-4790-7

Wang, P., & Schellhorn, H. E. (1995). Induction of resistance to hydrogen peroxide and radiation in Deinococcus radiodurans. *Can J Microbiol, 41*(2), 170-176.

Weisburg, W. G., Giovannoni, S. J., & Woese, C. R. (1989). The Deinococcus-Thermus phylum and the effect of rRNA composition on phylogenetic tree construction. *Syst Appl Microbiol, 11*, 128-134. doi: 10.1016/S0723-2020(89)80051-7

White, O. (1999). Genome sequence of the radioresistant bacterium deinococcus radiodurans R1. *Science, 286*(5444), 1571-1577. doi: 10.1126/science.286.5444.1571

Woese, C. R. (1987). Bacterial evolution. *Microbiol Rev, 51*(2), 221-271.

Woese, C. R., Stackebrandt, E., Macke, T. J., & Fox, G. E. (1985). A phylogenetic definition of the major eubacterial taxa. *Syst Appl Microbiol, 6*(2), 143-151. doi: 10.1016/S0723-2020(85)80047-3

Work, E., & Griffiths, H. (1968). Morphology and chemistry of cell walls of Micrococcus radiodurans. *J Bacteriol, 95*(2), 641-657.

Xu, G., Wang, L., Chen, H., Lu, H., Ying, N., Tian, B., & Hua, Y. (2008). RecO is essential for DNA damage repair in Deinococcus radiodurans. *J Bacteriol, 190*(7), 2624-2628. doi: 10.1128/JB.01851-07

Zhang, L., Yang, Q., Luo, X., Fang, C., Zhang, Q., & Tang, Y. (2007). Knockout of crtB or crtI gene blocks the carotenoid biosynthetic pathway in Deinococcus radiodurans R1 and influences its resistance to oxidative DNA-damaging agents due to change of free radicals scavenging abilit. *Arch Microbiol, 188*(4), 411-419. doi: 10.1007/s00203-007-0262-5

