DdrA, DdrD, and PprA: Components of UV and Mitomycin C Resistance in Deinococcus radiodurans R1

Kathiresan Selvam1, Jana R. Duncan1, Masashi Tanaka2, John R. Battista1*

1 Department of Biological Sciences, Louisiana State University and A & M College, Baton Rouge, Louisiana, United States of America, 2 Department of Molecular Immunology and Inflammation, National Center for Global Health and Medicine, Tokyo, Japan

Abstract

Mutants created by deleting the ddrA, ddrB, ddrC, ddrD, and pprA loci of Deinococcus radiodurans R1 alone and in all possible combinations of pairs revealed that the encoded gene products contribute to this species’ resistance to UV light and/or mitomycin C. Deleting pprA from an otherwise wild type cell sensitizes the resulting strain to UV irradiation, reducing viability by as much as eight fold relative to R1. If this deletion is introduced into a ΔddrA or ΔddrD background, the resulting strains become profoundly sensitive to the lethal effects of UV light. At a fluence of 1000 Jm^{-2}, the ΔddrA ΔpprA and ΔddrD ΔpprA strains are 100- and 1000-fold more sensitive to UV relative to the strain that has only lost pprA. Deletion of ddrA results in a 100 fold increase in strain sensitivity to mitomycin C, but in backgrounds that combine a deletion of ddrA with deletions of either ddrC or ddrD, mitomycin resistance is restored to wild type levels. Inactivation of ddrB also increases D. radiodurans sensitivity to mitomycin, but unlike the ddrA mutant deleting ddrC or ddrD from a ΔddrB background further increases that sensitivity. Despite the effect that loss of these gene products has on DNA damage resistance, none appear to directly affect either excision repair or homologous recombination suggesting that they participate in novel processes that facilitate tolerance to UV light and interstrand crosslinks in this species.

Introduction

Deinococcus radiodurans R1 is the type species for the Deinococcaceae, a family of bacteria [1,2] exhibiting extraordinary resistance to the lethal effects of many DNA damaging agents, including ionizing radiation (IR), ultraviolet (UV) light, and interstrand cross-linking agents (ICLs) [3]. For a vegetative cell, D. radiodurans R1 is particularly resistant to UV radiation, surviving doses as high as 750 Jm^{-2} with minimal loss of viability [4]. In comparison, the D_{37} dose (the dose that on average is necessary to inactivate a cell) for E. coli B/r is approximately 30 Jm^{-2} [5]. UV exposures as high as those that D. radiodurans tolerates introduce enormous amounts of DNA damage. Exposure to a fluence of 500 Jm^{-2} UV should generate 5000 thymine-containing pyrimidine dimers per genome in this species [6,7], an average of one lesion of this type for every 640 base pairs. Clearly, D. radiodurans expresses efficient mechanisms for dealing with UV-induced DNA damage, and it is not unreasonable to assume that UV resistance in this species might rely on processes not found in more UV sensitive microorganisms.

D. radiodurans R1 encodes all of the components of the UvrABC-dependent nucleotide excision repair (NER) system characterized in many species including E. coli [8]. In contrast to E. coli, inactivating NER does not reduce D. radiodurans resistance to UV light. NER-defective strains of D. radiodurans only become sensitive to UV when a second locus, designated uvs (DR1819) [8], is also inactivated [9,10]. The uvs gene encodes a UV DNA damage endonuclease similar to that reported in Schizosaccharomyces pombe [11,12] that is capable of completely compensating for the loss of NER. Likewise, if the uvs gene is inactivated in an otherwise wild type background, the resulting strain exhibits near wild-type levels of UV resistance, because of the overlapping action of NER. Thus, while the presence of two excision repair systems is a distinctive characteristic of D. radiodurans, the cell does not require this redundancy for UV resistance, making it difficult to argue that the presence of two repair systems contributes significantly to the species’ extraordinary tolerance of UV light. Mutational inactivation of the polA locus of R1 results in strains that are sensitive to all forms of DNA damage [13,14], indicating that DNA polymerase I of D. radiodurans (like its
Table 1. Strain List.

| Strain   | Description                        | Reference |
|----------|------------------------------------|-----------|
| LSU2000  | As R1 but uvrA1, uvs::TnpDrCat     | [9]       |
| TNK101   | As R1 but ΔddrC::pkat-aadA         | [16]      |
| TNK102   | As R1 but ΔddrC::pkat-cat          | [16]      |
| TNK103   | As R1 but ΔddrD::pkat-kan          | [16]      |
| TNK104   | As R1 but ΔddrD::pkat-hyg          | [16]      |
| TNK105   | As R1 but ΔpprA::pkat-aadA         | [16]      |
| TNK106   | As R1 but ΔrecA::pkat-cat          | [16]      |
| TNK112   | ΔddrB::pkat-cat, ΔddrC::pkat-aadA  | [16]      |
| TNK113   | ΔddrC::pkat-aadA, ΔddrD::pkat-kan  | [16]      |
| TNK114   | ΔddrA::pkat-hyg, ΔddrC::pkat-aadA  | [16]      |
| TNK115   | ΔddrC::pkat-aadA, ΔpprA::pkat-aadA | [16]      |
| TNK116   | ΔddrB::pkat-cat, ΔddrD::pkat-kan   | [16]      |
| TNK117   | ΔddrA::pkat-hyg, ΔddrB::pkat-cat   | [16]      |
| TNK118   | ΔddrB::pkat-cat, ΔpprA::pkat-aadA  | [16]      |
| TNK119   | ΔddrC::pkat-hyg, ΔddrD::pkat-kan   | [16]      |
| TNK120   | ΔddrD::pkat-kan, ΔpprA::pkat-aadA  | [16]      |
| TNK121   | ΔddrA::pkat-hyg, ΔddrB::pkat-cat   | [16]      |

All strains are derived from Deinococcus radiodurans R1 ATCC13939.

Materials and Methods

All strains used in this study are described in Table 1. The D. radiodurans strains are derived from the R1 type strain (ATCC13939), and were grown at 30°C in TGY broth (0.8% tryptone, 0.1% glucose, 0.4% yeast extract) or on TGY agar (1.5% agar) as described previously [17,18]. D. radiodurans survival following exposure to UV radiation and mitomycin C was assessed in cultures during exponential phase growth (at a density between 2 x 10^6 and 4.5 x 10^7 CFU/ml). Prior to exposure to UV light, cells were harvested by centrifugation and re-suspended in an equivalent volume of sterile saline (0.9% NaCl). One ml aliquots were placed in a sterile Petri dish and irradiated uncovered at 25°C using a germicidal lamp emitting at a calibrated dose rate of 25 J/m^2 s^-1 UV–C. Irradiated cultures were diluted in saline, prior to plating on TGY agar. Cultures to be exposed mitomycin C were grown to the appropriate density, harvested by centrifugation, and re-suspended in an equivalent volume of TGY broth containing 20 µg/ml mitomycin C. Cultures were incubated at 30°C and aliquots of the MC-treated culture were removed at ten minute intervals, washed twice in an equal volume of TGY broth, diluted, and plated on TGY agar. With the exception of TNK113 ΔddrC ΔddrD, survival was scored using colony counts three days after plating. TNK113 is very slow growing and colony formation was not evident until seven days after plating.

Results

Deletion of pprA (DRA0346) sensitizes D. radiodurans R1 to UV light

Strains TNK101 ΔddrC, TNK102 ΔddrB, TNK103 ΔddrD, and TNK104 ΔddrA, and TNK105 ΔpprA were evaluated for their ability to tolerate exposure to UV light (Figure 1) relative to their parent. Single deletions of ddrA, ddrB, ddrC, or ddrD have no effect on the UV resistance of D. radiodurans R1. Only deletion of pprA had a demonstrable effect on UV resistance. The reduction in the mean survival of TNK105 ΔpprA becomes statistically significant (unpaired t test, p=0.01, degrees of freedom df = 16) relative to R1 at 500 J/m^2, at 1000 J/m^2 TNK105 is approximately eight-fold more sensitive to UV light when compared to R1.

For comparison, the survival curves for the UV sensitive strains LSU2000 [9] and TNK106 [16] are also included in Figure 1. LSU2000 carries a deletion in the uvrA1 (DR1771) coding sequence and an insertion into the uvs (DR1819) gene [9], eliminating excision repair by the UvABC complex and the species’ UV damage endonuclease (UVDE). TNK106 is a ΔrecA strain incapable of RecA-dependent homologous recombination [16].

Deletion of ddrA (DRO423) in a ΔpprA background sensitizes D. radiodurans R1 to UV light

Deleting ddrA has no effect on the UV resistance of R1 (Figure 1), and strains TNK114 ΔddrA ΔddrC, TNK117 ΔddrA...
ΔddrB, and TNK119 ΔddrA ΔddrD are as resistant TNK104 ΔddrA ΔpprA demonstrates a rapid drop in UV resistance; there is a statistically significant (unpaired t test, \( p < 0.0001, \text{df} = 22 \)) two-fold reduction in the mean survival of TNK121 relative to TNK105 ΔpprA after exposure to a fluence of 250 J m\(^{-2}\). Values are the means ± standard deviations of three independent experiments (n = 9).

doi: 10.1371/journal.pone.0069007.g001

The combined deletion of ΔddrB (DR0070) and ΔddrC (DR0003) decreases the UV resistance of \( D. \) radioodurans R1

We find little evidence that DdrB or DdrC participate in UV resistance in \( D. \) radioodurans. TNK101 ΔddrC and TNK102 ΔddrB are as resistant to UV light as R1 (Figure 1). TNK113 ΔddrC ΔddrD and TNK116 ΔddrD ΔddrB do not significantly alter survival relative to TNK101, TNK102, or TNK103 ΔddrD (Figure 3). TNK115 ΔddrC ΔpprA is more sensitive to UV light relative to TNK101 ΔddrC, but its survival curve was identical to that of the UV sensitive strain TNK105 ΔpprA (Figure 1), indicating that loss of PprA alone was responsible for the sensitization observed.

The double mutant TNK112 ΔddrB ΔddrC is approximately ten-fold more sensitive than TNK101 or TNK102 (Figure 3) after exposure at 1000 J m\(^{-2}\). Although this increased sensitivity is reproducible (n=18, six independent trials, three replicates per trial), it is the only evidence that DdrB or DdrC affect UV resistance at the exposures examined.

Deletion of ΔddrD (DR0326) decreases the UV resistance of the ΔpprA strain TNK105

Deletions of ΔddrD alone (Figure 1) or in combination with deletions of ΔddrA (Figure 2), ΔddrB (Figure 3), or ΔddrC (Figure 3) do not demonstrate sensitivity to UV light. However, the combination of ΔddrD and ΔpprA in TNK120 dramatically increases UV sensitivity relative to TNK105 ΔpprA (Figure 4). At 250 Jm\(^{-2}\), there is a significant (unpaired t test, \( p < 0.0001, \text{df} = 25 \)) ten-fold difference in viability and at 1000 J/m\(^{-2}\) TNK120 is three orders of magnitude more sensitive than TNK105.

Deletion of ΔddrA (DR0423) sensitizes \( D. \) radioodurans R1 to mitomycin C

To further assess whether DdrA, DdrD, and PprA participate in excision repair or homologous recombination, strains carrying deletions of loci encoding these proteins were evaluated for resistance to the cross-linking agent mitomycin C (MC). Mitomycin C is highly toxic to prokaryotic cells [19]. After enzymatic reduction within the cell, MC generates reactive species that form DNA interstrand cross-links (ICLs) and a variety of guanine monoadducts in the minor groove [20,21]. There is an obligatory requirement for homologous
recombination and NER during the repair of MC-induced DNA damage by *D. radiodurans* [22,23]. At their D$_{37}$ dose, *uvrA* and *recA* defective strains are 60 and 300 times more sensitive to MC than R1, respectively.

TNK103 ΔddrD and TNK105 ΔpprA are as resistant to MC as R1 (Figure 5). In contrast, TNK104 ΔddrA cultures are very sensitive to mitomycin C (MC) relative to R1 (Figure 5) [24]; at each time interval sampled, R1 is between 150- and 400-fold more resistant to this reagent. Combining ΔddrA with ΔpprA does not change MC resistance; the sensitivity of TNK121 ΔddrA ΔpprA is indistinguishable from that of TNK104, indicating that loss of the DdrA is solely responsible for the phenotype. TNK120 ΔddrD ΔpprA is as resistant to MC as TNK103 ΔddrD, TNK105 ΔpprA, and R1 (Figure 5), suggesting that the sensitivity observed when *ddrD* and *pprA* are simultaneously deleted (Figure 4) is specific to UV-induced damage.

**Deletion of ddrC (DR0003) or ddrD (DR0326) in a ddrB (DR0070) background significantly reduces the mitomycin resistance of *D. radiodurans* R1**

As illustrated in Figure 8, TNK102 ΔddrB is approximately ten-fold more sensitive to mitomycin C relative to R1 at exposures of 20 minutes or longer. Including the ΔddrC or ΔddrD alleles in a ΔddrB background further reduces cell viability on exposure to this DNA damaging agent. TNK112 ΔddrB ΔddrC and TNK116 ΔddrB ΔddrD are between 100- and 150-fold more sensitive to MC than R1 at all exposure times.

**Discussion**

*Deinococcus radiodurans* R1 is the type species for a family of bacteria characterized by its exceptional capacity to tolerate DNA damage [2,25,26]. Notably, exponential phase cultures of this species can withstand exposure to 5000Gy ionizing radiation and 500Jm$^{-2}$ UV light; doses that will all but eradicate many bacterial cultures. Wild-type *D. radiodurans* cultures are also more resistant to ICLs than are most vegetative bacteria [27,28,29]. This species survives incubation in the presence of 20µg ml$^{-1}$ MC for 10 min at 30°C with minimal loss of viability. Kitayama [28] reported that under these conditions greater than 90% of isolated genomic DNA exists as non-denaturable...
double stranded DNA with an average molecular weight of $2 \times 10^7$ Daltons, and estimated that this level of exposure corresponds to approximately 100 MC-induced ICLs per D. radiodurans genome [28,29]. Approximately 20 ICLs are sufficient to inactivate repair proficient strains of Escherichia coli [30].

In this study, we have demonstrated that the proteins DdrA, DdrD, and PprA play critical but previously unidentified roles in the UV resistance of D. radiodurans R1. The deletion of pprA in a wild type background sensitizes the resulting strain to UV light (Figure 1) and that sensitivity dramatically increases when ddrA or ddrD is also deleted from this background (Figures 2 and 4). The level of sensitivity we report for TNK120 ΔddrD ΔpprA is comparable to that observed in an uvrA uvs background that cannot carry out NER- and UVDE-mediated excision repair (Figures 1 and 4). TNK121 ΔddrD ΔpprA is approximately ten-fold more UV resistant than TNK120, but the strain remains significantly more sensitive than D. radiodurans R1 (Figure 2). The enhanced UV sensitivity of TNK120 and TNK121 suggest that the activities of PprA overlap with those of DdrA and DdrD; either they catalyze similar functions or they are required for separate processes that have an equivalent effect on UV resistance. The central role of homologous recombination and excision repair in reversing UV and mitomycin C-induced DNA damage in other species has been recognized for many years [31,32] forcing us to consider the possibility that DdrA, DdrD, and PprA contribute to these processes in D. radiodurans.

Figure 5. Survival curves for ΔpprA derivatives D. radiodurans R1 exposed to mitomycin C. TNK120 ΔddrD ΔpprA and TNK121 ΔddrD ΔpprA are compared with D. radiodurans R1, TNK103 ΔddrD, and TNK105 ΔpprA. Values are the means ± standard deviations of three independent experiments (n = 9).

doi: 10.1371/journal.pone.0069007.g005

Figure 6. Survival curves for ΔddrC and ΔddrD derivatives of TNK104 ΔddrA exposed to mitomycin C. TNK114 ΔddrA ΔddrC, TNK117 ΔddrA ΔddrB, and TNK119 ΔddrA ΔddrD are compared with D. radiodurans R1 and TNK104 ΔddrA. Values are the means ± standard deviations of three independent experiments (n = 9).

doi: 10.1371/journal.pone.0069007.g006

TNK103 ΔddrD, TNK104 ΔddrA, TNK105 ΔpprA, TNK119 ΔddrA ΔddrD, TNK120 ΔddrD ΔpprA and TNK121 ΔddrA ΔpprA are considered recombination-proficient [16]. These strains undergo natural transformation, a process that requires RecA-dependent recombination, with efficiencies identical to that of R1. In addition, the double mutants TNK119 ΔddrA ΔddrD, TNK120 ΔddrD ΔpprA and TNK121 ΔddrA ΔpprA display varied responses to DNA damaging agents. TNK119 is modestly sensitive to IR [16], but as resistant as R1 to UV (Figure 2) and mitomycin C (Figure 6). TNK120 is sensitive to UV (Figure 4), but resistant to IR [16] and mitomycin (Figure 5). TNK121 is sensitive to IR [16], mitomycin (Figure 5), and UV (Figure 2). Since homologous recombination is required to survive exposure to IR, UV, and ICLs in D. radiodurans [22], the different patterns of resistance among these strains suggests that if DdrA, DdrD, or PprA contribute to DNA repair involving homologous recombination, their role is constrained in a manner specific to the DNA damaging agent or the lesions generated by that agent.

For similar reasons, it also seems unlikely that DdrA, DdrD or PprA are affecting excision repair. TNK120 is sensitive to UV and resistant to mitomycin. If one postulates that the inactivation of DdrD and PprA resulted in an excision repair defective strain, these opposing phenotypes cannot be reconciled. In addition, the UV sensitive double mutants TNK120 and TNK121 are wild type with respect to the uvrA, uvrB, uvrC, uvs, and polA genes that encode for excision repair
systems capable of dealing with all major forms of UV-induced DNA damage [9]. It is difficult to comprehend how eliminating PprA and DdrA or PprA and DdrD could stop the contributions of NER and UVDE to UV resistance unless combined loss of these proteins influence UV resistance by affecting the function of both excision repair pathways simultaneously – in effect, recreating the situation that arises when the NER and UVDE systems are both inactivated. This scenario could occur if loss of DdrA and PprA or DdrD and PprA affected the stability of an intermediate or the activity of a component shared by the two pathways. At present, there is no evidence to support this idea.

The function of PprA is obscure; the protein has not been extensively characterized. Although homologues of PprA are encoded by all sequenced *Deinococcus* species [33,34,35], this protein shares no similarity to any other protein, amino acid sequence motif, or conserved domain described in the protein databases. Purified PprA is reported to stabilize the free ends formed at DNA double strand breaks and to recruit DNA ligase to the site of these breaks, improving the efficiency of ligation *in vitro* [36]. This report led to speculation that PprA performs the same function *in vivo*, and a suggestion that PprA participates in a form of non-homologous end joining (NHEJ) [37,38]. However, attempts to demonstrate NHEJ activity following exposure to UV have failed to provide convincing evidence that this process is taking place [39,40]. While the results presented here do not directly support or refute the notion that *D. radiodurans* expresses the proteins needed for NHEJ, it is difficult to reconcile PprA’s central role in UV resistance with its possible involvement in NHEJ. Precedent suggests that NHEJ can play a minor role in repair of UV-induced DNA damage in bacteria [41]. The combined deletion of *ykoU* and *ykoV* of *Bacillus subtilis*, proteins that mediate NHEJ in this species, increases the strain’s sensitivity to UV light, but the effect is small, between one and a half and two-fold relative to the wild type at doses to 500 Jm⁻². In contrast, the combined loss of PprA and DdrD results in a strain that is as much as 1000-fold more UV sensitive relative to the wild type (Figure 4). Whatever its activity, PprA makes a substantive contribution to UV resistance, and it seems doubtful that any contribution PprA may make to NHEJ fully defines its function following exposure to UV.

The ability of PprA to bind to the free ends created by DNA double strand breaks may explain why TNK121 ΔddrA ΔpprA is more sensitive to UV than TNK105 ΔpprA (Figure 2). DdrA is part of the Rad52 family of proteins [42]. In eukaryotes Rad52 promotes recombination and DNA double strand break repair through interaction with the Rad51 recombinase [43]. While DdrA contributes to the ionizing radiation resistance of *D. radiodurans* [16,24], there is no evidence that it behaves like the eukaryotic Rad52; the protein does not display DNA strand annealing activity [24]. In *D. radiodurans*, DdrA appears to

Figure 7. Survival curves for ΔddrC and ΔddrD, and ΔpprA derivatives *D. radiodurans* R1 exposed to mitomycin C. TNK101 ΔddrC, TNK103 ΔddrD, and TNK113 ΔddrC ΔddrD are compared with *D. radiodurans* R1. Values are the means ± standard deviations of eight independent experiments (n = 24). doi: 10.1371/journal.pone.0069007.g007

Figure 8. Survival curves for ΔddrC and ΔddrD derivatives of TNK104 ΔddrB exposed to mitomycin C. TNK102 ΔddrB, TNK112 ΔddrB ΔddrC, and TNK116 ΔddrB ΔddrD are compared with *D. radiodurans* R1. Values are the means ± standard deviations of eight independent experiments (n = 24). doi: 10.1371/journal.pone.0069007.g008
function in vitro and in vivo by binding to the 3' ends of single-stranded DNA and preventing DNA digestion by endogenous exonucleases following the cell's exposure to high dose ionizing radiation [24]. It has been proposed that DdrA is part of a DNA end-protection system that helps to preserve genome integrity following DNA damage. In this capacity, it is not difficult to envision a situation where DdrA and PprA protect an intermediate created during repair of UV damage, and evidence of this protection is only obvious when both proteins are inactive.

The apparent overlap in DdrD and PprA activity is not as easily explained. Each protein appears to be a component of an independent process that facilitates UV resistance. DdrD function is unknown and this protein, which is found only in the Deinococci, shares no amino acid sequence similarity with any other characterized protein or sequence motif [33,34,35]. Inactivation of both proteins reveals their roles in UV resistance, but it is difficult to argue the DdrD acts to protect DNA as described for PprA and DdrA. PprA function is necessary if cells are to survive IR-induced damage, but DdrD seems to have only a minor role in IR resistance [16].

Figure 6 may provide a clue to DdrD function. TNK104 ΔddrA is two orders of magnitude more sensitive to mitomycin C than D. radiodurans R1. If deletions of ddrC or ddrD are inserted in this background, mitomycin resistance is restored to wild type levels. This result suggests that DdrC and DdrD are at least partially responsible for the increased sensitivity to mitomycin C observed in a ddrA strain. In other words, it appears that DdrA prevents a lethal event caused, directly or indirectly, by the wild type DdrC and DdrD proteins, and when either protein is inactivated that event is avoided. Like DdrD, DdrC shares no similarity with other proteins and is only known to be encoded by members of the genus Deinococcus.

Since inactivating DdrC and DdrD has the same effect in a ΔddrA background (Figure 6) or ΔddrB background (Figure 8), it is reasonable to ask if these proteins are part of the same repair complex. This possibility seems unlikely given the differences in UV sensitivity associated with TNK115 ΔddrC ΔpprA (Figure 3) and TNK120 ΔddrD ΔpprA (Figure 4); TNK120 is 1000 fold more UV sensitive when compared with TNK115. In addition, the simultaneous inactivation of ddrC and ddrD results in a strain with slightly decreased mitomycin C resistance (Figure 7). If DdrC and DdrD were different parts of a protein complex that carried out a single function, survival of the double mutant should not be different than TNK101 ΔddrC or TNK103 ΔddrD. Pending further investigation, we argue that the DdrC and DdrD proteins are components of different complementary processes involved in DNA damage tolerance.

At present, the phenotypes reported here are perhaps best explained by assuming that DdrA, DdrD, and PprA affect the efficiency of UV- and MC-induced lesion repair without directly catalyzing the removal of those lesions. We posit that these proteins suppress potentially lethal events that arise as repair proceeds following massive genetic insult, thereby facilitating survival. If this occurs, it may provide a context in which to better understand the extreme resistance of D. radiodurans to DNA damaging agents. We contend that these proteins assist the cell by allowing the cell enough time to achieve necessary repairs. Repair of damage after insult should be more effective if the time available for repair – the time between the appearance of damage and the lethal consequences of that damage – is extended. Assuming that a bacterial cell has the necessary repair proteins and sufficient time to carry out repairs, extreme tolerance to multiple DNA damaging agents could be conveniently explained.

Acknowledgements

The authors wish to thank L. Alice Simmons, Danielle R. Fontenot, and Blythe E. Johnson for their technical assistance in determining the UV survival curves.

Author Contributions

Conceived and designed the experiments: JRB. Performed the experiments: KS JRD MT. Analyzed the data: JRB KS JRD MT. Contributed reagents/materials/analysis tools: JRB. Wrote the manuscript: JRB KS.

References

1. Battista JR, Rainey FA (2001) Phylum BIV. "Deinococcus-Thermus" Family 1. Deinococaceae Brooks and Murray 1981, 356.xp emend. Rainey, Nobre, Schumann, Stackebrandt and da Costa 1997, 513. In: DR BooneRW Castenholz. Bergey's Manual of Systematic Bacteriology. 2nd ed. New York: Springer Verlag. pp. 395-414.
2. Cox MM, Battista JR (2005) Deinococcus radiodurans - the consummate survivor. Nat Rev Microbiol 3: 882-892. doi:10.1038/nrmicro1264. PubMed: 16261171.
3. Moseley BEB (1983) Photobiology and radiobiology of Micrococcus (Deinococcus) radiodurans. Photochem Photobiol Rev 7: 223-275.
4. Moseley BE, Mattingly A (1971) Repair of irradiation transforming deoxyribonucleic acid in wild type and a radiation-sensitive mutant of Micrococcus radiodurans. J Bacteriol 105: 976-983. PubMed: 4922986.
5. Sweet DM, Moseley BE (1974) Accurate repair of ultraviolet-induced damage in Micrococcus radiodurans. Mutat Res 23: 311-318. doi: 10.1016/0027-5107(74)90104-3. PubMed: 4407662.
6. Boling ME, Setlow JK (1966) The resistance of Micrococcus radiodurans to ultraviolet radiation. 3. A repair mechanism. J Bacteriol 105: 976-983. PubMed: 4929286.
7. Varghese AJ, Day RS 3rd (1970) Excision of cytosine-thymine adduct from the DNA of ultraviolet-irradiated Micrococcus radiodurans. Photochem Photobiol 11: 511-517. doi:10.1111/j.1751-1097.1970.tb06022.x. PubMed: 5456276.
8. White O, Eisen JA, Heidelberg JF, Hickey EK, Peterson JD et al. (1999) Genome sequence of the radioreistant bacterium Deinococcus radiodurans R1. Science 286: 1571-1577. doi:10.1126/science.286.5444.1571. PubMed: 10567266.
9. Earl AM, Rankin SK, Kim KP, Lamedrella ON, Battista JR (2002) Genetic evidence that the uvsE gene product of Deinococcus radiodurans R1 is a UV damage endonuclease. J Bacteriol 184: 1003-1009. doi:10.1128/jb.184.4.1003-1009.2002. PubMed: 11807860.
10. Moseley BE, Evans DM (1983) Isolation and properties of strains of Micrococcus (Deinococcus) radiodurans unable to excise ultraviolet light-induced pyrimidine dimers from DNA: evidence for two excision pathways. J Gen Microbiol 129(8): 2437-2445. PubMed: 6415229.
11. Bowman KK, Sidik K, Smith CA, Taylor JS, Doetsch PW et al. (1994) A new ATP-independent DNA endonuclease from Schizosaccharomyces pombe that recognizes cyclobutane pyrimidine dimers and 6-4 photoproducts. Nucleic Acids Res 22: 3062-3072. doi:10.1093/nar/22.15.3062. PubMed: 8065916.
12. Takao M, Yonemasa R, Yamamoto K, Yasui A (1996) Characterization of a UV endonuclease gene from the fission yeast Schizosaccharomyces pombe and its bacterial homolog. Nucleic Acids Res 24: 1267-1271. doi:10.1093/nar/24.7.1267. PubMed: 8614629.
Analysis of ionizing radiation and desiccation reveals novel proteins that contribute to the extreme radioresistance of Deinococcus radiodurans. J Bacteriol 175: 3581-3590. PubMed: 8501062.

Micrococcus radiodurans mutants are required for the extreme radioresistance of Deinococcus radiodurans. J Bacteriol 177: 5232-5237. PubMed: 7665511.

Amplification of Deinococcus radiodurans' transcriptional response to ionizing radiation and desiccation reveals novel proteins that contribute to extreme radioresistance. Genetics 168: 21-33. doi:10.1534/genetics.104.029248. PubMed: 15454524.

Hansen MT (1982) Rescue of mitomycin C- or psoralen-inactivated Escherichia coli. J Bacteriol 143: 10729-10734. PubMed: 7104365.

Makarova KS, Avrind L, Wolf YI, Tatusov RL, Minton KW et al. (2001) Genome of the extremely radiation-resistant bacterium Deinococcus radiodurans viewed from the perspective of comparative genomics. Microbiol Mol Biol Rev 65: 44-79. doi: 10.1128/MMBR.65.1.44-79.2001. PubMed: 11239895.

Tanaka M, Earl AM, Howell HA, Park MJ, Eisen JA et al. (2004) Preservation of genome integrity: the DdrA protein of Deinococcus radiodurans. Nat Genet 33: 308-310. PubMed: 15109476.

Misra HS, Khairnar NP, Kota S, Shrivastava S, Joshi VP et al. (2006) An exonuclease I-sensitive DNA repair pathway in Deinococcus radiodurans. Mol Microbiol 54: 278-285. doi: 10.1007/j.1365-2958.2004.04272.x. PubMed: 1458422.

Kota S, Misra HS (2006) PprA: A protein implicated in radioreistance of Deinococcus radiodurans stimulates catalase activity in Escherichia coli. Appl Microbiol Biotechnol 72: 790-796. doi: 10.1007/s00253-006-0330-7. PubMed: 16586106.

Misra HS, Khaimeh NP, Kota S, Shrivastava S, Joshi VP et al. (2006) An exonuclease I-sensitive DNA repair pathway in Deinococcus radiodurans: a major determinant of radiation resistance. Mol Microbiol 59 (3): 1308-1316. doi: 10.1111/j.1365-2958.2005.05006.x. PubMed: 16430702.

Zahradka K, Slade D, Bailone A, Sommer S, Averbeck D et al. (2006) Reassembly of shattered chromosomes in Deinococcus radiodurans. Nature 443: 569-573. PubMed: 17006450.

Daly MJ, Ling O, Minton KW (1994) Interplasmidic recombination following irradiation of the radioreistant bacterium Deinococcus radiodurans. J Bacteriol 176: 7506-7515. PubMed: 8002574.

Zahradka K, Slade D, Bailone A, Sommer S, Averbeck D et al. (2006) Reassembly of shattered chromosomes in Deinococcus radiodurans. Nature 443: 569-573. PubMed: 17006450.

Moeiiler R, Stackebrandt E, Reitz G, Berger T, Redtenbarg P et al. (2007) Role of DNA repair by nonhomologous-end joining in Bacillus subtilis sporereistance to extreme dryness, mono- and poly-chromatic UV, and ionizing radiation. J Bacteriol 189: 3306-3311. doi: 10.1128/JB.00018-07. PubMed: 17293412.

Iyer LM, Koonin EV, Aravind L (2002) Classification and evolutionary history of the single-strand annealing proteins, RecT, Redβ, ERF and RAD52. BMC Genomics 3: 8. doi: 10.1186/1471-2164-3-8. PubMed: 11914131.

Mortensen UH, Bendixen C, Sunjevaric I, Rothstein R (1996) DNA strand annealing is promoted by the yeast Rad52 protein. Proc Natl Acad Sci U S A 93: 10729-10734. doi: 10.1073/pnas.93.20.10729. PubMed: 8855248.