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How radiation kills cells: Survival of *Deinococcus radiodurans* and *Shewanella oneidensis* under oxidative stress ☆

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Abstract

We have recently shown that *Deinococcus radiodurans* and other radiation resistant bacteria accumulate exceptionally high intracellular manganese and low iron levels. In comparison, the dissimilatory metal-reducing bacterium *Shewanella oneidensis* accumulates Fe but not Mn and is extremely sensitive to radiation. We have proposed that for Fe-rich, Mn-poor cells killed at radiation doses which cause very little DNA damage, cell death might be induced by the release of Fe(II) from proteins during irradiation, leading to additional cellular damage by Fe(II)-dependent oxidative stress. In contrast, Mn(II) ions concentrated in *D. radiodurans* might serve as antioxidants that reinforce enzymic systems which defend against oxidative stress during recovery. We extend our hypothesis here to include consideration of respiration, tricarboxylic acid cycle activity, peptide transport and metal reduction, which together with Mn(II) transport represent potential new targets to control recovery from radiation injury.

Keywords: Oxidative stress; UV; Desiccation; Ionizing radiation; Cytochromes; Flavins; Nucleoid; Manganese; Iron; *Shewanella*; *Deinococcus*; *Kineococcus*

Contents

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1. What makes *Shewanella oneidensis* so sensitive to ionizing radiation?

The central dogma of radiation biology is that the cytotoxic and mutagenic effects of radiation are principally the result of DNA damage caused during the course of irradiation. This might not always be the case since environmental organisms such as *Shewanella oneidensis* (MR-1) (ATCC 700550) [1], which encode relatively complex DNA repair systems [2,3], are killed at radiation doses that cause relatively little DNA damage. The ionizing radiation doses that yield 17% survival of *Escherichia coli* and *Deinococcus radiodurans* are higher by factors of 20 and 200, respectively, than those for *S. oneidensis* [2]. Whereas 90% of *S. oneidensis* cells do not survive 70 Gy, a dose that induces less than one DNA double strand break (DSB) per genome, 10% of *D. radiodurans* cells survive 12,000 Gy, a dose that induces 120 DSBs per genome [2], and 10% of *E. coli* survive 700 Gy, a dose that induces 7 DSBs per genome (Table 1) [2]. Drying cells is also known to cause genomic DSBs [4], and *S. oneidensis* is killed after exposure to desiccation for only one day whereas similarly treated *D. radiodurans* can survive for months (Table 1) [2]. When the generation of reactive oxygen species (ROS) (superoxide, hydrogen peroxide and hydroxyl radicals) produced by irradiation or metabolism exceeds the capacity of endogenous scavengers to neutralize them, cells become vulnerable to damage, a condition referred to as oxidative stress (Fig. 1) [5,6].

Until recently, there have been no clear physiologic predictors of a cell's ability to recover from radiation or desiccation. In general, most of the resistant bacteria reported have been Gram-positive and the most sensitive have been Gram-negative [7,8]. However, there are several reported exceptions to this paradigm, the Gram-negative cyanobacterium *Chroococcidiopsis* is extremely radiation- and desiccation-resistant [9], whereas the Gram-positive *Micrococcus luteus* (*Sarcinia lutea*) is sensitive [10–12]. We recently reported that the differences in resistance to γ-radiation and desiccation for different bacteria mirror their intracellular Mn/Fe concentration ratios, where very high, moderate and very low Mn/Fe ratios correlate with very high, moderate and very low resistances, respectively [2]. *D. radiodurans* (Mn/Fe ratio: 0.24) accumulates 150 times more Mn than *S. oneidensis* (Mn/Fe ratio: 0.0005) and is sensitized to ionizing radiation when Mn(II) is restricted, and *S. oneidensis* accumulates 3.3 times more Fe than *D. radiodurans* (Table 1) [2]. In the case of *S. oneidensis* exposed to doses $\geqslant$70 Gy, Fe(II)-dependent oxidative stress produced

Table 1
Relationship between *c*-type cytochrome number, Mn/Fe levels and resistance

Strain (genomic sequence)	Genome size (Mb)	Total no. of *c*-type cytochromes	[a] Intra-cellular Mn/Fe ratio	[b] D_{10}, IR survival (kGy)	[b] D_{10}, desiccation survival (days)
[c]*Deinococcus radiodurans*	3.28	7	0.24	10–12	>30
[d]*Deinococcus geothermalis*	3.23	7	0.46	10	>30
[e]*Escherichia coli*	4.64	6	0.007	0.7	7
[f]*Pseudomonas putida*	6.18	17	<0.001	0.25	2
[g]*Shewanella oneidensis*	5.13	39	<0.001	0.07	1

[a] Mn/Fe ratios were previously reported [2].
[b] 10% cell-survival values (D_{10}) for ionizing radiation (Gy) or desiccation (days) were previously reported [2].
[c] http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db = genomeprj & cmd = Retrieve & dopt = Overview & list_uids = 65.
[d] Draft annotation at Oak Ridge National Laboratory, Oak Ridge TN (http://genome.ornl.gov/microbial/dgeo/).
[e] http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db = genomeprj & cmd = Retrieve & dopt = Overview & list_uids = 225.
[f] http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db = genomeprj & cmd = Retrieve & dopt = Overview & list_uids = 267.
[g] http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db = genomeprj & cmd = Retrieve & dopt = Overview & list_uids = 335.