CV : BIOSKETCH

MICHAEL JOHN DALY, Ph.D.

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Department:	Pathology
Academic Rank:	Full Professor
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Laboratory Website:	http://www.usuhs.edu/pat/deinococcus
Security Clearance:	Secret. Top-Secret

EDUCATION

Ph.D.	Genetics	University of London, U.K.	1988
B.Sc. (Hons.)	Molecular Biology	University of London, U.K.	1984
A-levels	Bio./Chem./Phys.	King's School, Canterbury, U.K.	1981

EMPLOYMENT RECORD

Full Professor of Pathology, and Molecular & Cell Biology, USU	2007-Present
Committee on the Outer Planets, National Academy of Sciences	2010-2012
Chairman, USU Radiation Safety Committee	2005-Present
Associate Professor of Pathology, and Molecular & Cell Biology, USU	2002-2007
Committee on the Origins of Life, National Academy of Sciences	2003-2006
Assistant Professor of Pathology, and Molecular & Cell Biology, USU	1997-2002
Planetary Task Group Member, National Academy of Sciences	1999-2001
Adjunct Associate Professor, Birla Institute of Science, Pilani, India	1999-2005
Principal Investigator, Dept. of Pathology, USU	1996-Present
Research Associate, Dept. of Pathology, USU	1992-1997
NIH Postdoctoral Fellow - Laboratory of Biochemistry, NCI, NIH	1988-1992
Ph.D. Student (Genetics), University of London, U.K.	1984-1988

AWARDS:	Henry Wu Award for Excellence in Research, USU	2003
	United Kingdom Research Scholarship	1984-1987
	University of London Drapers Foundation Scholarship	1985-1987

ACTIVE GRANTS

Daly (PI). **$757,486**. **04/10/10-04/09/13**. **Air Force Office of Scientific Research**, **DoD**. Title: "Novel Protection Paradigms Based on *Deinococcus radiodurans.*"

Daly (PI). **$600,000**. **04/08/12-07/15**. **Defense Threat Reduction Agency**, **US Department of Defense, DoD**. Title: "A Revolutionary Approach to Irradiated Vaccine Production Based on *Deinococcus* Mn^{2+} Complexes."

ACADEMIC SUMMARY FOR M. J. DALY

The chronology and history of the most relevant and innovative publications are summarized below, where the numbered citations correspond to 17 peer-reviewed *Deinococcus* publications (1995-2013).

Since joining USU in 1992, my goal has been the development of the extremely radiation resistant bacterium *Deinococcus radiodurans* as a system to study DNA repair, as a model for functional genomics, and for cleanup of radioactive waste sites. Today, *D. radiodurans* is one of the dominant organisms investigated by the US Department of Energy (DOE). Based on a rubric for DNA recombination in yeast, used as a postdoc at NIH, I developed a variety of novel techniques to study ionizing radiation (IR)-induced *recA*-dependent gene conversions and crossovers *in vivo*. Between 1992 and 1997, I published eight papers which were the first to show that it was possible to observe the progression of DNA repair in bacteria exposed to extremely high doses of IR. The results of those studies were broadly consistent with the canonical version of the double-strand break (DSB) repair model (**17**), but also revealed an unusually efficient *recA*-independent DNA annealing pathway. A turning point for my laboratory was in 1996 when *D. radiodurans* was chosen by DOE as one of the first free-living organisms to be subjected to whole-genome sequencing. Together with my collaborators at The Institute for Genomic Research, Rockville, MD, our consortium published two genome papers in *Science* in 1999, one reporting its sequence, the other reporting its mapping (**16**). Between 1999 and 2006, using the whole-genome sequence as a guide, we engineered *D. radiodurans* for bioremediation of radioactive mixed waste sites (**12-15**). In 2001, we published a very highly-cited comparative genomics review which included predictions on *D. radiodurans* operon organization, and some of the earliest evidence for horizontal gene transfer (**11**). In 2002, with DOE collaborators, we published breakthrough research in *PNAS* which validated our functional predictions by a whole-proteome, mass-spectrometry-based approach using Fourier Transform Ion Cyclotron Resonance (FTICR); and, in 2003 we published a second, related *D. radiodurans* paper in *PNAS* that reported the construction and utilization of one of the world's first whole-genome microarrays (**10**). Since then, we and others have shown that few of the uncharacterized genes, at least individually, make a substantial contribution to recovery of irradiated *D. radiodurans*, and our focus shifted to cell-cleaning functions. In 2004, we reported in *Science* the identification of a widespread manganese(II)-dependent, nonenzymic mechanism required for extreme radiation resistance (**9**). Next, in a 2006 theoretical paper (**8**), I formulated a hypothesis on the nature of targets protected by Mn(II) ions. And, in an article published in *PLoS Biology* (**7**), we showed that intracellular Mn(II) accumulated in resistant bacteria protects proteins, and proposed a solution to the paradox of how a relatively small set of structurally unremarkable DNA repair proteins in *Deinococcus* species work with such great efficiency. Since then, we have identified key radioprotective Mn-peptide complexes in *D. radiodurans* (**6**). In January 2012, I published a review on the new paradigm for radiation toxicity and its applications (**5**); and in April 2012, we published a breakthrough paper on how to apply Mn antioxidants of *D. radiodurans* to the production of irradiated vaccines – a novel approach which could expedite vaccine production for emerging and established pathogens for which no protective vaccines exist (**4**). Related papers followed (**2,3**), with a paper on the structure of *Deinococcus* Mn complexes now under formal review at *PNAS* (**1**).

A complete list of Daly's 54 *Deinococcus* publications (PDF format) and the history of his group's accomplishments can be accessed on the World Wide Web: **http://www.usuhs.edu/pat/deinococcus/labpublications.html**

17 REPRESENTATIVE PUBLICATIONS (of 54): 2013 → 1995

1. A. Sharma, E.K. Gaidamakova, V.Y. Matrosova, B. Bennett, **MICHAEL J. DALY** and B.M. Hoffman (2013) Differential responses of Mn^{2+} speciation in *Deinococcus radiodurans* and *Escherichia coli* to ionizing radiation: advanced paramagnetic resonance studies. Submitted *Proc. Natl. Acad. Sci. U S A* (Jan, 2013).

2. L.A. Klobutcher, E.K. Gaidamakova, B. Setlow, **MICHAEL J DALY** and P. Setlow (2013) Effects of Mn^{2+} levels on the resistance properties of spores of *Bacillus cereus. J. Bacteriol. Res.* (In press) [Epub ahead of print].

3. V.C. Culotta and **MICHAEL J. DALY** (2012) Manganese complexes: diverse metabolic routes to oxidative stress resistance in prokaryotes and yeast. Antioxid. Redox. Signal. Published Dec 18. [Epub ahead of print].

4. E. K. Gaidamakova, I. A. Myles, D. P. McDaniel, C. J. Fowler, P. A. Valdez, M. Gayen, P. Gupta, A. Sharma, P. J. Glass, R. K. Maheshwari, S. K. Datta and **MICHAEL J. DALY** (2012) A reconstituted Mn^{2+}-peptide complex of *Deinococcus radiodurans* preserves immunogenicity of lethally irradiated vaccines against viruses and *Staphylococcus aureus*. *Cell Host Microbe* **12**,117-124.

In collaboration with NIH, we demonstrated that a *D. radiodurans* Mn^{2+} complex preserved antigenic structures in aqueous preparations of viruses and bacteria during supralethal irradiation (25-40 kGy). A Mn^{2+}-peptide-based irradiated vaccine protected mice against *Staphylococcus aureus*. This approach could expedite vaccine production for emerging and established pathogens for which no protective vaccines exist. Next targets: VEEV and HIV.

5. **MICHAEL J. DALY** (2012) Death by protein damage in irradiated cells. *DNA Repair* (Amst), **11**, 12-21.

Mounting experimental evidence does not fit into the classical model that DNA in irradiated cells is the principal target responsible for toxicity. Instead, in most cell-types radiation resistance appears to be governed by protein damage. Reviewed are recent studies from several independent labs which implicate protein damage as the major probable cause of death in irradiated cells.

6. **MICHAEL J. DALY,** E.K. Gaidamakova, V. Y. Matrosova, J.G. Kiang, R. Fukumoto, D.Y. Lee, N.B. Wehr, G.A. Viteri, B.S. Berlett and R.L. Levine (2010) Small-molecule antioxidant proteome-shields in *Deinococcus radiodurans. PLoS ONE*, 5(9), e12570.

Deinococcus Mn-complexes were shown to be immensely protective of irradiated enzymes, preserving their structure and function at vast doses of gamma rays. This has presented the scientific community with a novel and highly defensive chemical strategy to combat oxidative stress in diverse settings, including bioremediation of radioactive waste, preparation of irradiated vaccines, and aging.

7. **MICHAEL J. DALY**, E. K. Gaidamakova, V. Y. Matrosova, A. Vasilenko, M. Zhai, B. Ravel, B. Lai, R. D. Leapman, S.-M. W. Li, K. M. Kemner and J. K. Fredrickson (2007) Protein oxidation implicated as the primary determinant of bacterial radioresistance. *PLoS Biology*, **5**(4) e92.

The dramatic differences observed in the susceptibility to IR of proteins in resistant and sensitive bacteria far exceeded our expectations. How could 50 years of radiobiology research have missed this? The reason: commercial protein damage assays are now available. DNA no longer is the only complex biologically active material that can be easily tested with respect to its IR response.

8. **MICHAEL J. DALY** (2006) Modulating radiation resistance: Insights based on defenses against reactive oxygen species (ROS) in the radioresistant bacterium *Deinococcus radiodurans*. *Clin. Lab. Med*. **26**, 491-504.

This theoretical evaluation of how Mn(II) protects cells from IR was written long before we had experimental data showing the great differences in susceptibility to IR-induced protein oxidation in extremely resistant and sensitive bacteria. I pondered the impact of protein being the principal radiosensitive target, and the practical and clinical implications if this were the case.

9. **MICHAEL J. DALY**, E. K. Gaidamakova, V. Y. Matrosova, A. Vasilenko, M. Zhai, A. Venkateswaran, M. Hess, M. V. Omelchenko, H. M. Kostandarithes, K. S. Makarova, L. P. Wackett, J. K. Fredrickson and D. Ghosal (2004) Accumulation of Mn(II) in *Deinococcus radiodurans* facilitates gamma-radiation resistance. *Science* **306**, 1025-1028.

This report represents a major shift in our experimental strategy, away from DNA repair and chromosome morphology studies towards a potent form of intracellular Mn(II)-dependent cell-cleaning. However, the targets protected by Mn(II) were undefined. We showed that Mn(II) did not prevent IR-induced DSBs *in vivo*, and the editor redacted our speculation that proteins were the primary targets.

10. Y. Liu, J. Zhou, A. Beliaev, J. Stair, L. Wu, D. K. Thompson, D. Xu, A. Venkateswaran, M. Omelchenko, M. Zhai, E. K. Gaidamakova, K. S. Makarova, E. Koonin and **MICHAEL J. DALY** (2003) Transcriptome dynamics of *Deinococcus radiodurans* recovering from ionizing radiation. *Proc. Natl. Acad. Sci. U S A*, **100**, 4191-4196.

Beyond what is described in the Academic Summary, this work revealed that metabolic and respiratory control likely is important to recovery. Irradiated *D. radiodurans* strongly down-regulated the superoxide ($O_2^{\bullet-}$)-generating steps of the Krebs Cycle. In this context, $O_2^{\bullet-}$ is known to damage Fe-S domains present in many enzymes including DNA repair proteins.

11. K.S. Makarova, L. Aravind, Y.I. Wolf, R. L.Tatusov, K. Minton, E.V. Koonin and **MICHAEL J. DALY** (2001) The genome of the extremely radiation resistant bacterium *D*. *radiodurans* viewed from the perspective of comparative genomics. *Microbiol Mol Biol Rev* **65**, 44-79.

Currently, one of the most cited publications in the field of *Deinococcus*. In light of earlier reports that *D. radiodurans* was as susceptible to UV-induced DNA base damage as *E. coli in vivo*, we first defined a *D. radiodurans* paradox: Whereas numerous *D. radiodurans* gene families are expanded, its excision repair systems, surprisingly, did not proliferate.

12. C. Lange, L. P. Wackett, K. W. Minton and **MICHAEL J. DALY** (1998) Engineering a recombinant *Deinococcus radiodurans* for organopollutant degradation in radioactive mixed waste environments. *Nature Biotechnology* **16**, 929-933.

13. H. Brim, S. McFarlan, L. Wackett, K. W. Minton, M. Zhai, J. Fredrickson and **MICHAEL J. DALY** (2000) Engineering *Deinococcus radiodurans* for metal remediation in radioactive mixed waste environments. *Nature Biotechnology* **18**, 85-90.

14. **MICHAEL J. DALY** (2000) Engineering radiation-resistant bacteria for environmental biotechnology. *Current Opinion in Biotechnology* **11**, 280-285.

15. H. Brim, J.P. Osborne, H.M. Konstandarithes, J.K. Fredrickson, L.P. Wackett and **MICHAEL J. DALY** (2006) *Deinococcus radiodurans* engineered for complete toluene degradation facilitates Cr(VI) reduction. *Microbiology,* 152(8), 2469-2477.

In this research (12-15), metal-reduction and toxic organic degradation (including oxygenases) genes from *E. coli* and *P. putida* were functionally expressed in *D. radiodurans* growing under high-dose chronic gamma-radiation. The proteins cloned in *D. radiodurans* worked extremely efficiently during irradiation, as demonstrated using many different expression vectors designed for *D. radiodurans*.

16. J. Lin, R. Qi, C. Aston, J. Jing, T. Anantharaman, B. Mishra, O. White, **MICHAEL J. DALY**, K. W. Minton, J. C. Venter and D. C. Schwarzt (1999) Whole genome shotgun optical mapping of *Deinococcus radiodurans* using genomic DNA molecules. *Science* **285**, 1558-1561.

17. **MICHAEL J. DALY** and K. W. Minton (1995) Interchromosomal recombination in the extremely radioresistant bacterium *Deinococcus radiodurans. J. Bacteriol*. **177**, 5495-5505.