

Small-Molecule Mn Antioxidants in *Caenorhabditis elegans* and *Deinococcus radiodurans* Supplant MnSOD Enzymes during Aging and Irradiation

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Take-home message

Cells survive radiation because of **tiny manganese molecules**, not the enzyme everyone credited. As a cell ages it loses those molecules, and its radiation resistance goes with them.

34.74 Gy/h

chronic dose rate under which worms with no SOD enzymes outlived normal ones

1,000× worse

survival after 10 weeks of drying once MnSOD is deleted: the stress where the enzyme is essential

8,000 Gy

dose an enzyme survived in *C. elegans* extract, versus ~150 Gy without it

6 lines

the manganese EPR fingerprint, now tracked across a whole life span

1 Introduction

Why keep an enzyme the cell can live without?

Superoxide is blamed for ageing and radiation damage, and **MnSOD** is the enzyme built to destroy it. Yet deleting MnSOD costs *C. elegans* no lifespan and *D. radiodurans* no radiation resistance.

Both organisms instead stockpile small manganese complexes (**H-Mn**) that scavenge superoxide just as well. Breaking a cell open destroys that chemistry, so H-Mn has to be read in place. EPR spectroscopy can do this, and here it is applied across a whole life span for the first time.

Aim. Track radiation resistance and manganese chemistry across the life spans of both organisms, with and without MnSOD.

Hypothesis. H-Mn, not MnSOD, sets radiation survival.

2 Methods

Strains. *D. radiodurans* wild-type and Δ MnSOD (*sodA*⁻); *L. plantarum*, which has no SOD genes; *C. elegans* N2, a Δ MnSOD double mutant (*sod-2,3*) and a five-SOD knockout (*sod-1,2,3,4,5*).

Ageing. Cultures grown 10 days without fresh broth, sampled at days 1, 2, 6 and 10, then given 0, 10 or 15 kGy (⁶⁰Co) and scored by colony count.

EPR. 35-GHz spectra of frozen whole cells at 2 K; H-Mn and L-Mn fractions separated by fitting the lineshape in EasySpin.

Worms. 40 irradiated adults per strain (10 per plate, 4 plates), plus 40 unirradiated controls, under ¹³⁷Cs at 34.74 Gy/h for 8 days.

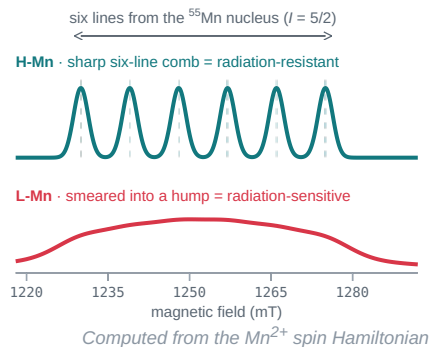
Drying. Cells desiccated over Drierite at room temperature; survivors counted weekly to 15 weeks.

Statistics. Kaplan-Meier with 95% CI. The worm curves crossed, so a Weibull parametric hazard model replaced the log-rank test.

3 Results

FIGURE 1 · THE TOOL

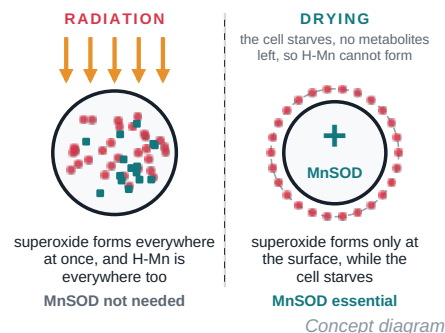
Seeing manganese in a living cell



The ⁵⁵Mn nucleus splits manganese's signal into **six lines**. In a small, symmetric pocket (H-Mn) they stay sharp; bound into a protein (L-Mn) they smear into a hump. Sharp comb = protected cell, smeared hump = vulnerable cell.

FIGURE 3 · THE EXPLANATION

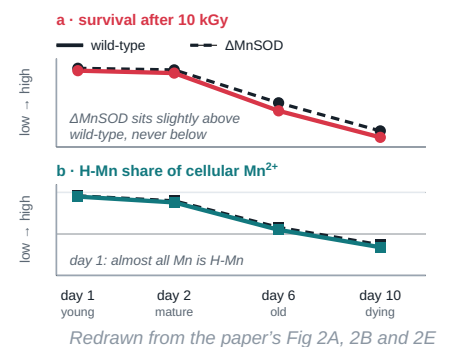
Two stresses, two defences



Radiation makes superoxide everywhere at once, and H-Mn is everywhere too, so the cell copes without the enzyme. Drying makes superoxide at the cell surface, while the cell starves, and a starving cell cannot build H-Mn. Only then is MnSOD essential.

FIGURE 2 · THE MAIN FINDING

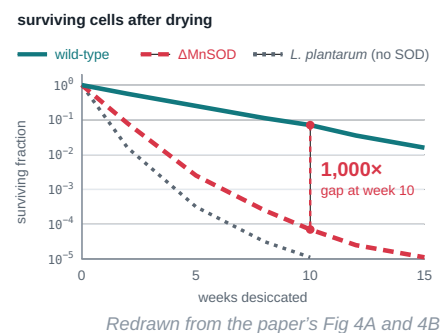
Resistance and H-Mn fall together



Across a 10-day life span, radiation survival (a) and H-Mn content (b) fall in step. Deleting MnSOD reduces **neither**: the Δ MnSOD curve sits slightly above wild-type throughout. Whatever protects these cells, it is not the enzyme.

FIGURE 4 · THE ANSWER

When does the enzyme matter?



Under radiation, losing MnSOD costs nothing: SOD-free worms survived **better** ($p = 0.001$). Under drying it is close to fatal, 1,000× below wild-type by week 10. The enzyme only matters when the cell is too starved to build its own shield.

Plain English

Superoxide ($O_2^{\cdot-}$) a damaging scrap left over when radiation hits water

MnSOD the enzyme assumed to mop that scrap up

H-Mn small manganese “sponges” built by the cell

EPR a magnetic scanner for manganese in place

Gray (Gy) a dose of radiation; 10 kGy would kill a human thousands of times over

Desiccation drying out completely

In vivo inside a living organism, not in a test tube

4 Discussion

Hypothesis supported. In a bacterium and an animal, radiation survival tracked H-Mn content and ignored MnSOD. The classic oxidative damage theory has to widen.

But MnSOD still earns its place. Losing it leaves *D. radiodurans* and *L. plantarum* sensitive to drying and paraquat: stresses where a starving cell cannot build H-Mn.

Limits. The evidence is correlative: without a genetic switch for H-Mn, another age-linked factor could drive the decline, and mitochondrial Mn was not mapped.

5 Conclusion

Small manganese molecules can stand in for a dedicated enzyme. The enzyme earns its keep only when the cell is too starved to make them.

Two defences, different jobs.

FUTURE DIRECTIONS

Run EPR on tumour biopsies. H-Mn level might predict how much radiation a tumour shrugs off, and so guide the dose.