



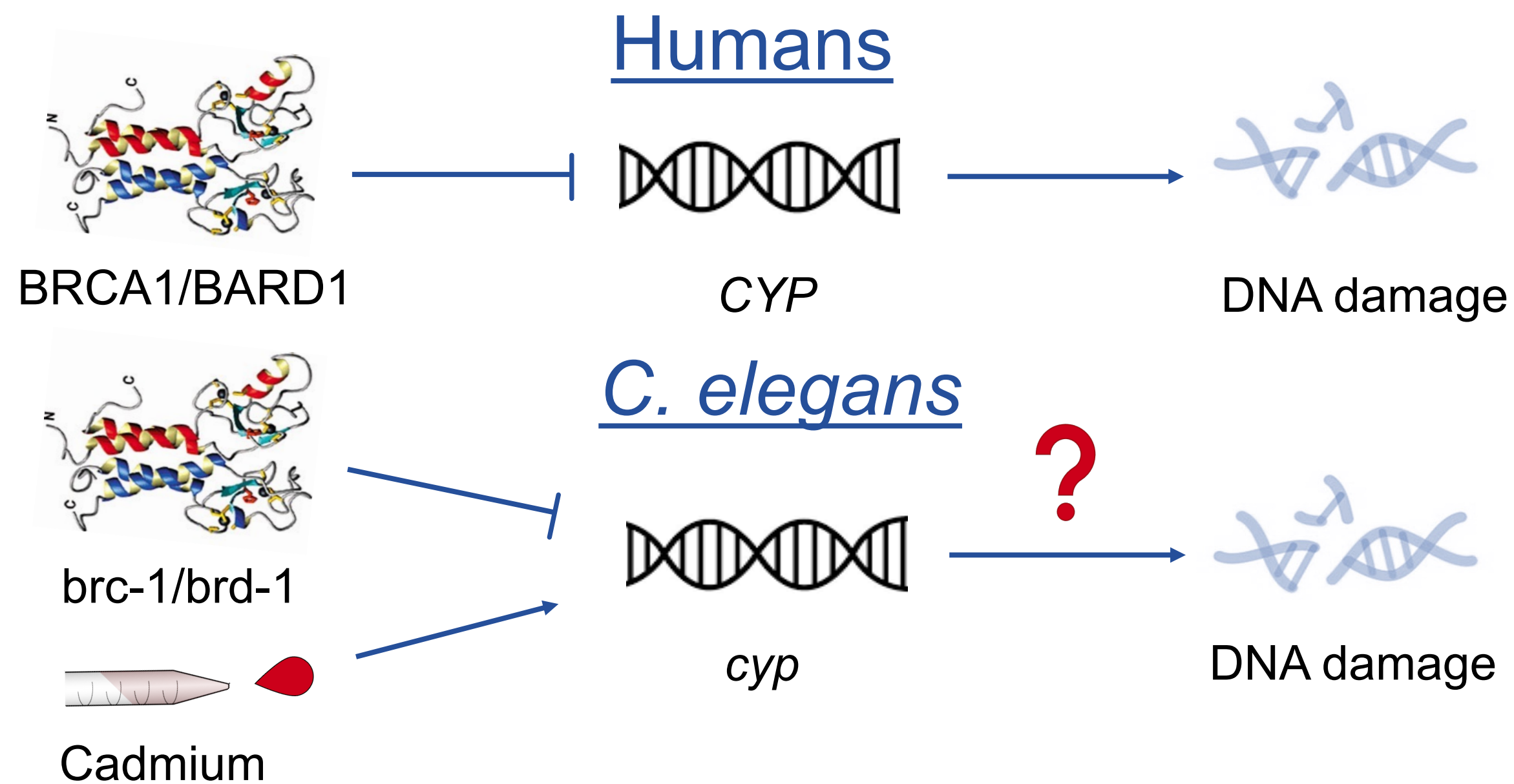
Determining the impact of a tumor suppressor gene in a model organism



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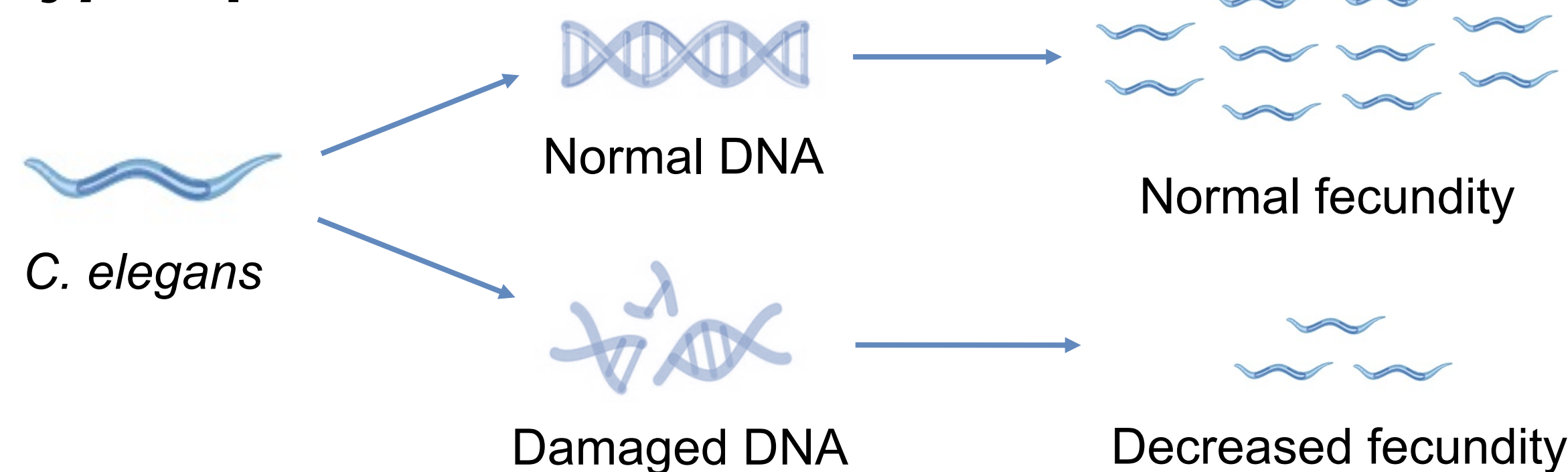
Introduction

Function of cytochrome p450 gene in *Caenorhabditis elegans*



Above: The BRCA/BARD1 protein complex represses the gene cytochrome p450 (*CYP*). *CYP* expression results in DNA damage in humans and can lead to breast cancer. The *Caenorhabditis elegans* contains *BRCA1/BARD1* and *CYP* homolog genes respectively known as *brc-1/brd-1* and *cyp*. The role of the *cyp* homolog and its repression has not yet been determined, but *cyp* is known to be upregulated by cadmium.

C. elegans fecundity can be measured to demonstrate DNA damage levels caused by *cyp* expression.

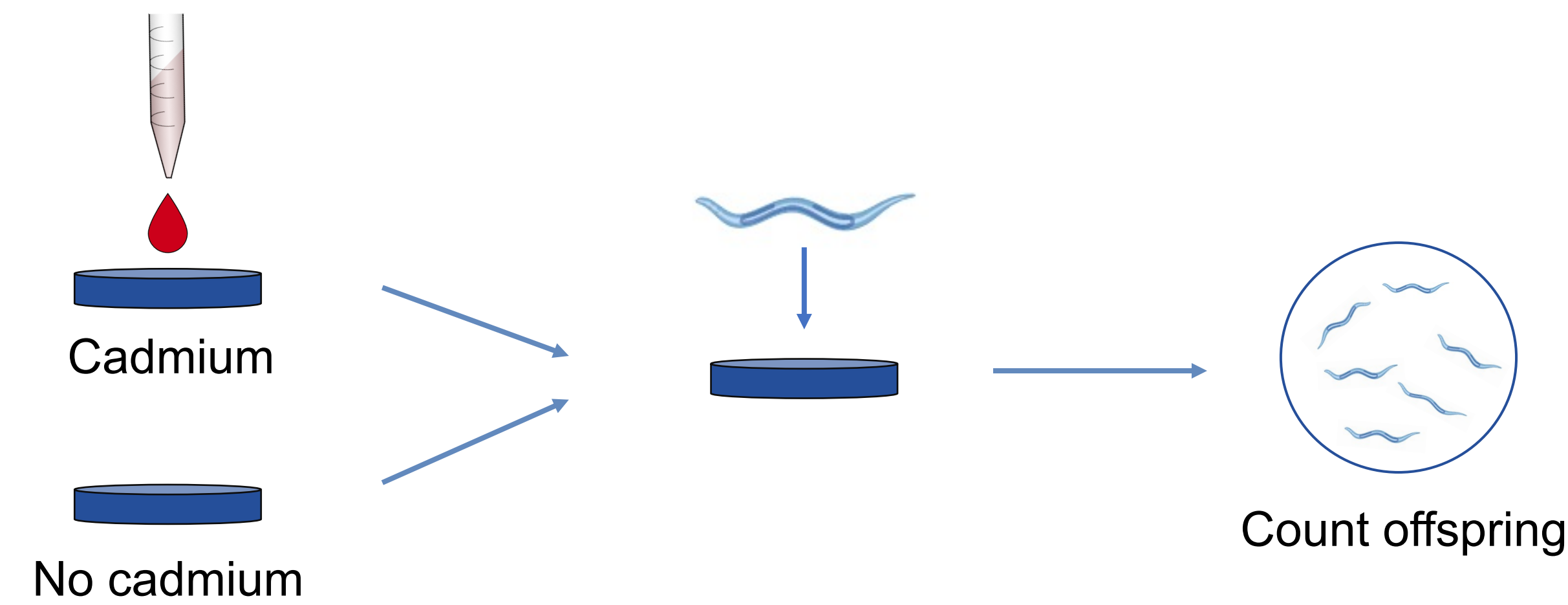


Above: DNA damage results in decreased *C. elegans* fecundity compared to undamaged DNA.

Objectives

- Measure *C. elegans* fecundity under cadmium exposure
- Determine whether the BRCA1/BARD1 method of *CYP* repression is the same in humans and worms

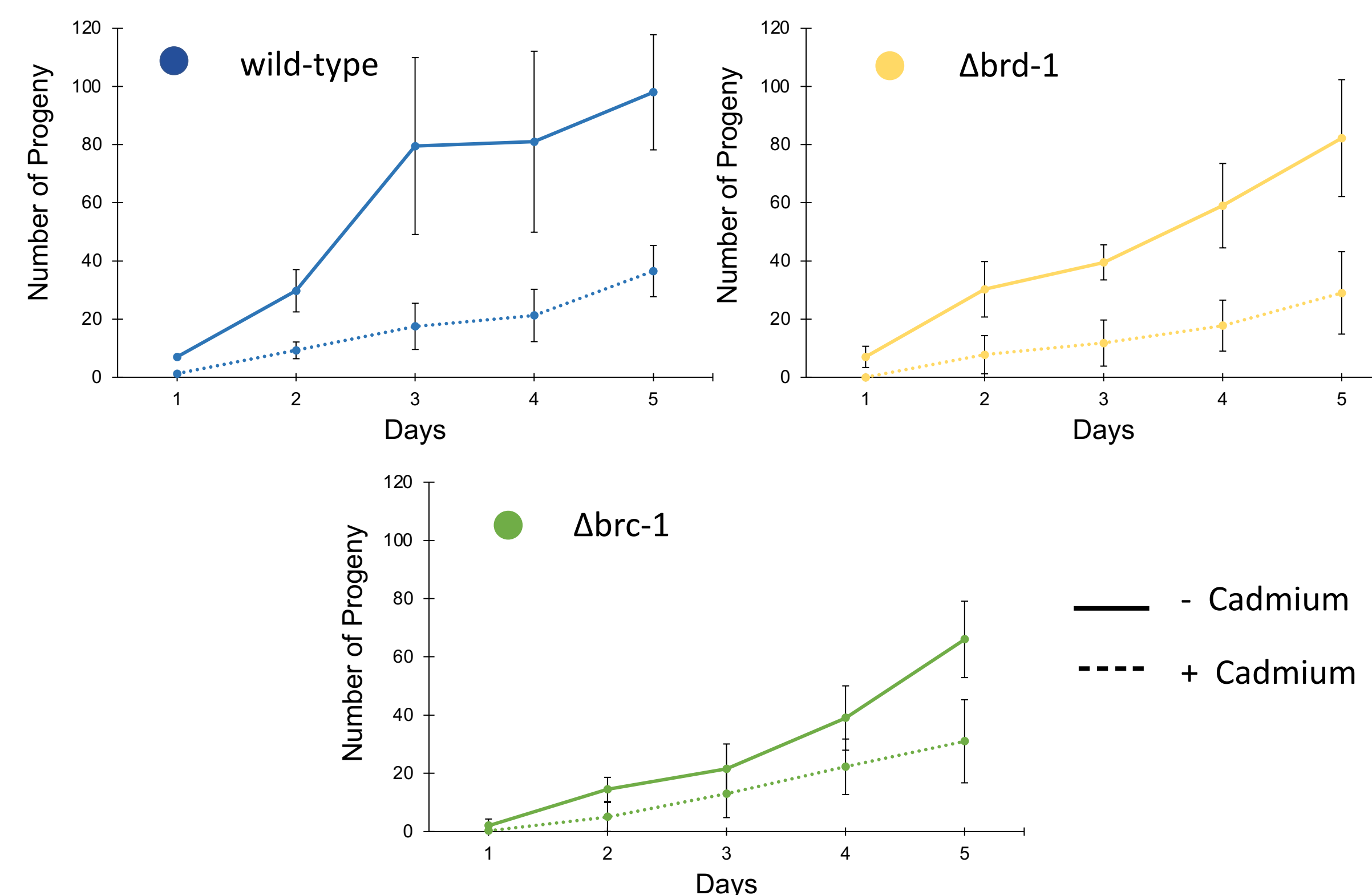
Fecundity Measurement of Cadmium-Exposed *C. elegans*



Above: *C. elegans* of each strain (wild type, $\Delta brd-1$, and $\Delta brc-1$) plated with 0 μ M or 100 μ M of cadmium and left in 20°C for 5 days. Number of offspring in each plate counted each day. Four trials were performed.

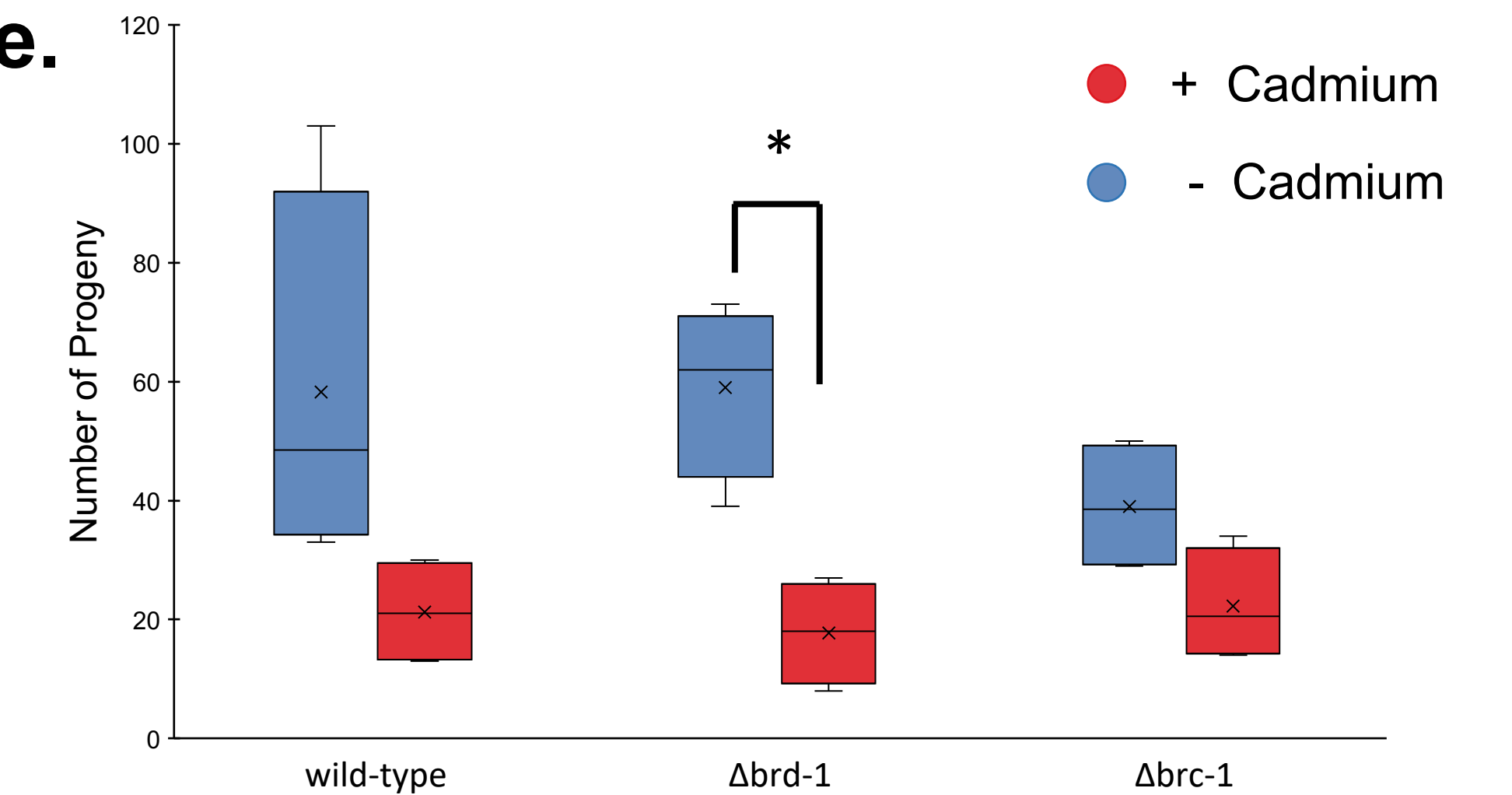
brc-1/brd-1 Does Not Affect *cyp* Response to Cadmium-Induced Stress

Cadmium exposure results in decreased *C. elegans* fecundity.



Above: Number of offspring of different *C. elegans* strains when exposed to 100 μ M cadmium and 0 μ M cadmium. All strains show that cadmium exposure has a negative effect on fecundity.

Strains lacking *brc-1* or *brd-1* show similar fecundities under cadmium exposure to wild-type.



Above: Fecundity of regular and cadmium-exposed *C. elegans* of different strains after four days. No significant difference in fecundity between strains under comparative conditions was noted.

Conclusion and Future Directions

Cadmium exposure induces DNA damage in *C. elegans*. The *brc-1/brd-1* protein does not affect the *cyp* response to cadmium. This could be due to one of two reasons:

- *brc-1/brd-1* does not function to repress *cyp* here.
- The *cyp* response to cadmium only increases to a limited extent independent of repression.

Further studies will be conducted to determine the role of *cyp* repression in *C. elegans*.

- *cyp* is also known to induce a reoxygenation response in *C. elegans*. *brc-1/brd-1* may repress *cyp* in this situation, limiting the response.
- We will measure *C. elegans* locomotion to determine the extent of the reoxygenation response and by extension *cyp* repression.

References and Acknowledgements

1. Cui, Y., McBride, S.J., Boyd, W.A. et al. *Genome Biol* 8, R122 (2007).
2. Stewart, Mikaela D. et al. *PNAS of the United States of America* vol. 115,6 (2018): 1316-1321.
3. Keller, Julia et al. *The Biochemical journal* vol. 464,1 (2014): 61-71.

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