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NON-APOPTOTIC LINKER CELL DEATH IN C. ELEGANS

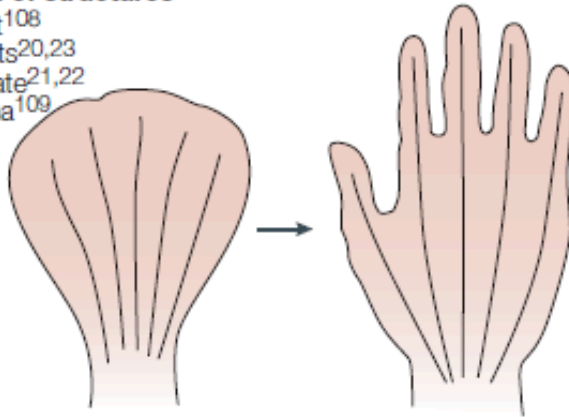
Why is the Study of Cell Death Important?

- Cell death is an important step in the development of an organism
- Understanding of cell death will help us with:
 - Neurodegenerative diseases
 - Cancerous cells, tumors

Cell Death is Important During Normal Development

a Formation of structures

Chick heart¹⁰⁸
Mouse digits^{20,23}
Mouse palate^{21,22}
Mouse retina¹⁰⁹



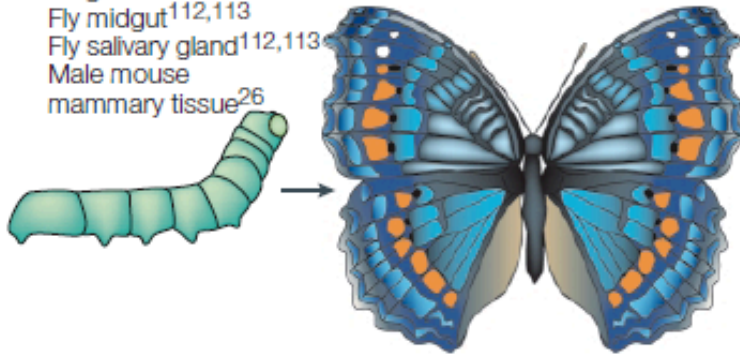
c Control of cell numbers

Chick motor neurons³⁰
Worm neurons¹¹⁴
Fly eye pigment cells¹¹⁵
Fly glia²⁸
Fly neurons⁶¹
Rat glia²⁷
Mouse muscles¹¹⁶



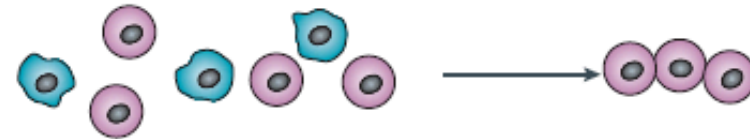
b Deletion of structures

Frog tail¹¹⁰
Frog intestine²⁴
Frog notochord¹¹¹
Fly midgut^{112,113}
Fly salivary gland^{112,113}
Male mouse mammary tissue²⁶



d Elimination of abnormal cells

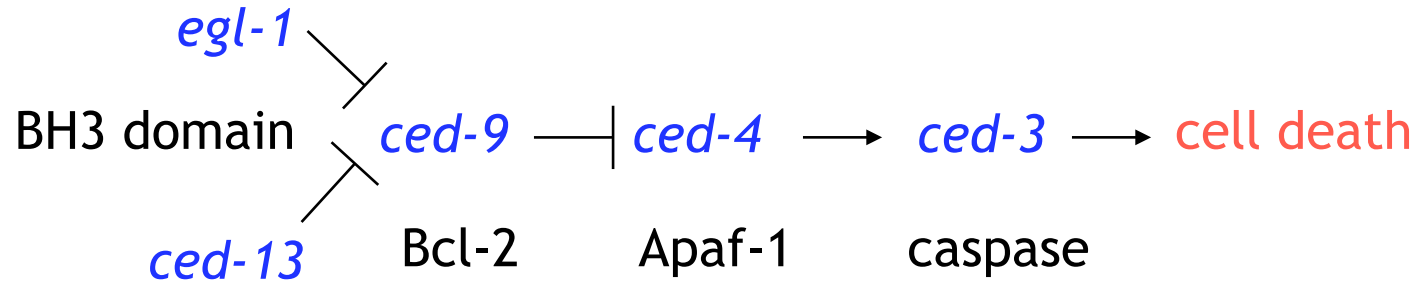
Fly cells harbouring DNA damage¹¹⁷
Mouse cells harbouring DNA damage¹¹⁸



Cell Death in *C. elegans* is Similar to Cell Death in Other Organisms

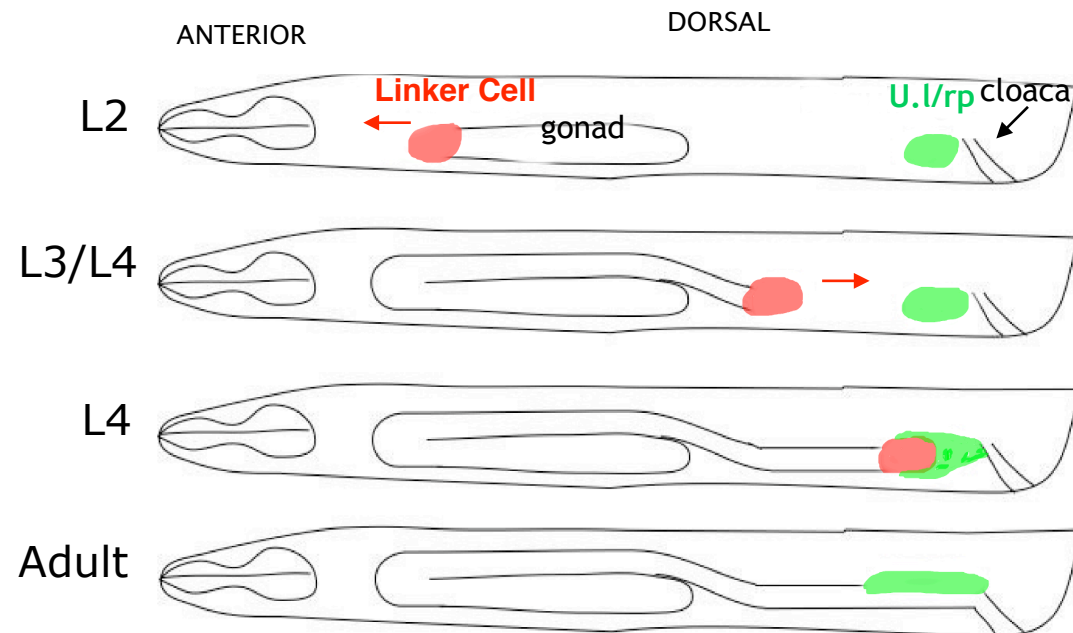
- Caspase based cell death (apoptosis) is present in other organisms.
- The genes that mediate and control programmed cell death (PCD) in *C. elegans*: *ced-3*, *ced-4*, and *ced-9* have similar roles in other organisms.

C. elegans Cell Death Pathway is Conserved



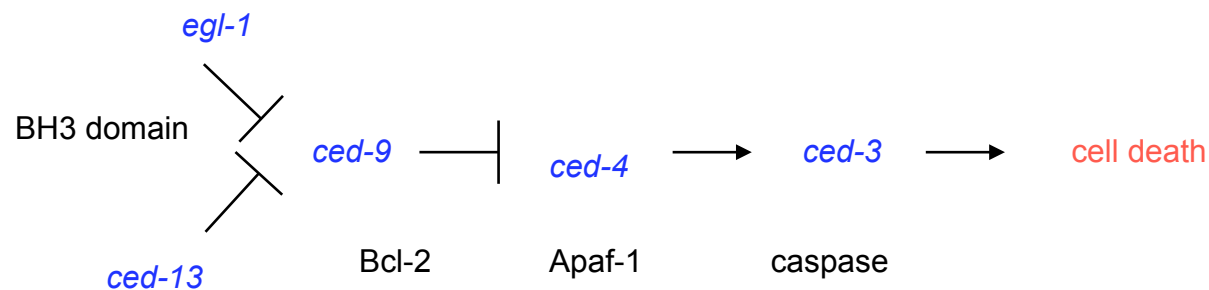
What is Linker Cell?

- Linker cell is the cell that leads and shapes the gonad in *C. elegans*. (gonad is the germ line and egg-laying apparatus of the worm.)



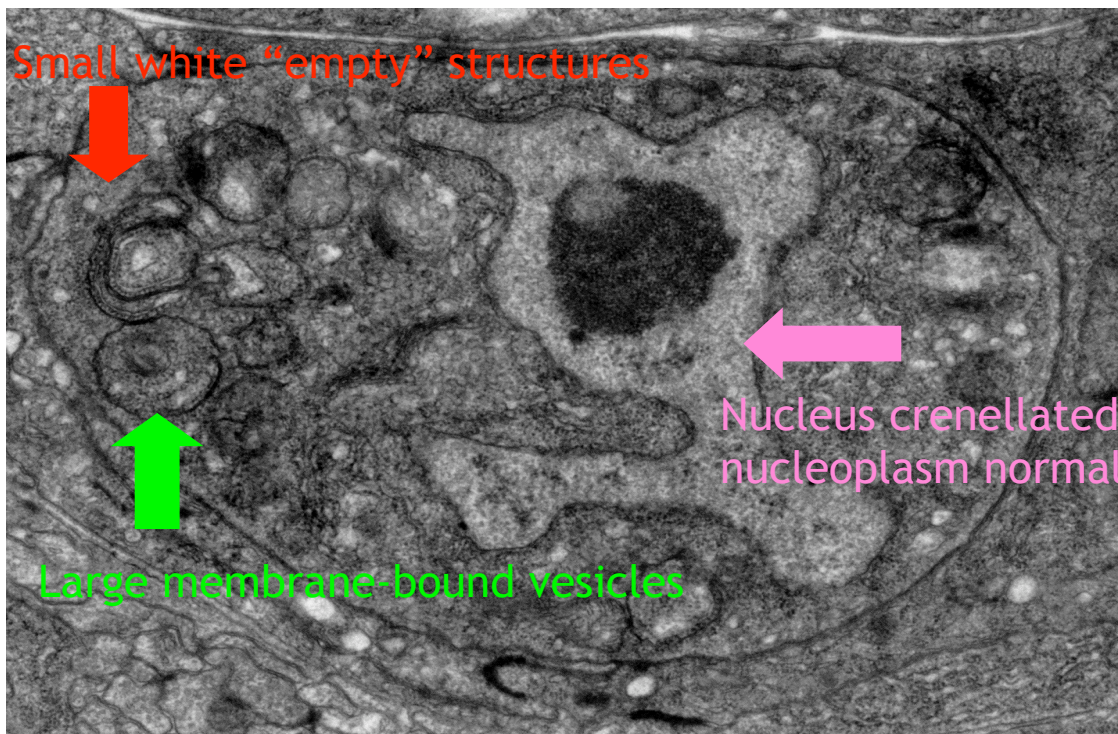
Linker Cell Death is Independent of all Known Cell Death Genes

Genotype	% Linker Cell Survival (n>30)
Wild type	0
<i>ced-3(n717)</i>	0
<i>ced-4(n1162)</i>	0
<i>ced-9(n1950)</i>	0
<i>egl-1(n1084n3082)</i>	3
<i>ced-13(sv32)</i>	0



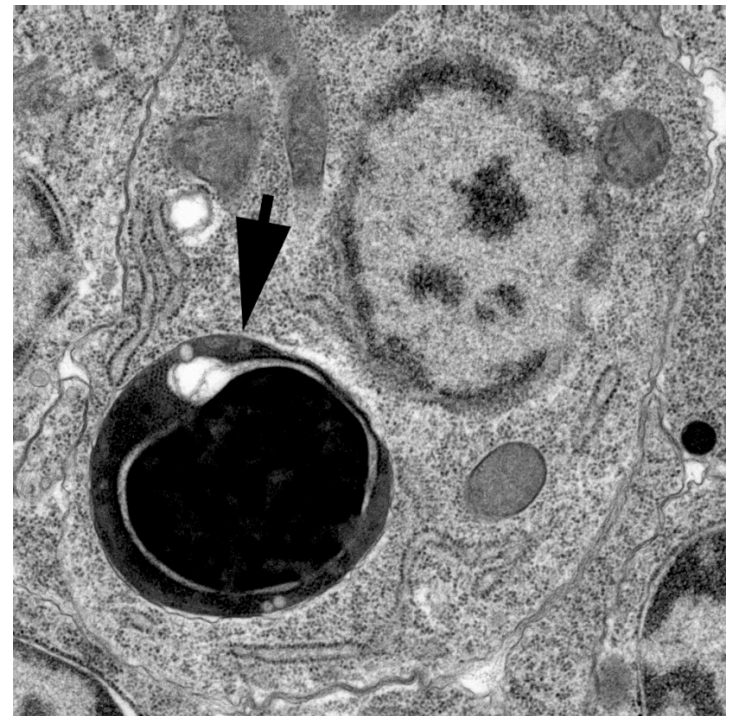
A Dying Linker Cell is Non-apoptotic

Linker cell death morphology



Abraham *et al.*, *Dev Cell* (2007)

Apoptotic morphology

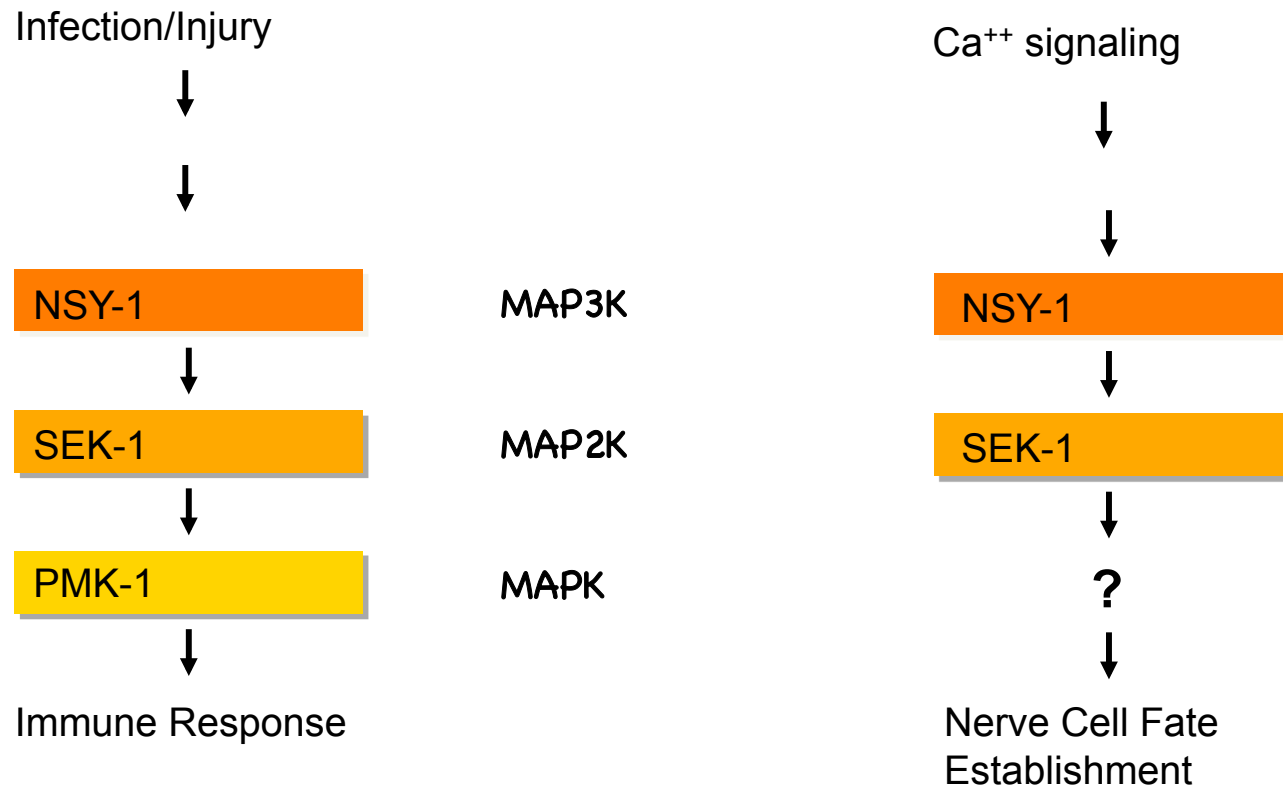


Images from *Nature Reviews Mol. Cell Biol.* (2001) & *Cell* (1997)

Objective

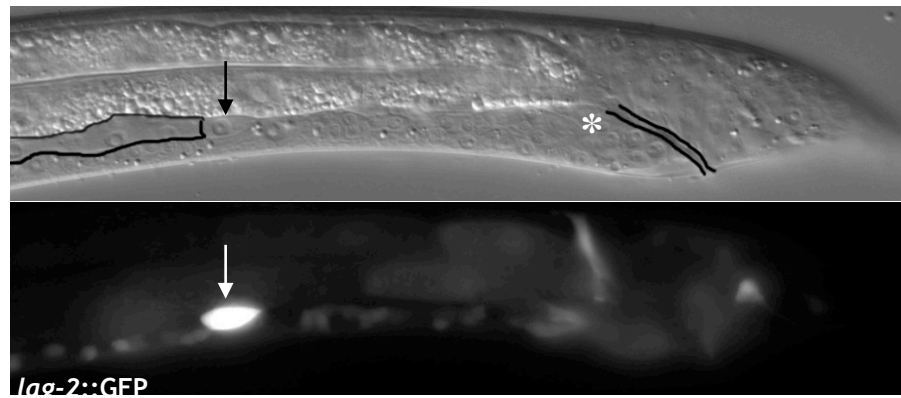
- To find new genes that control linker cell death
- To test genes to see if they activate *sek-1* or are activated by *sek-1*

SEK-1 Functions in the MAP Kinase Pathway in *C. elegans*



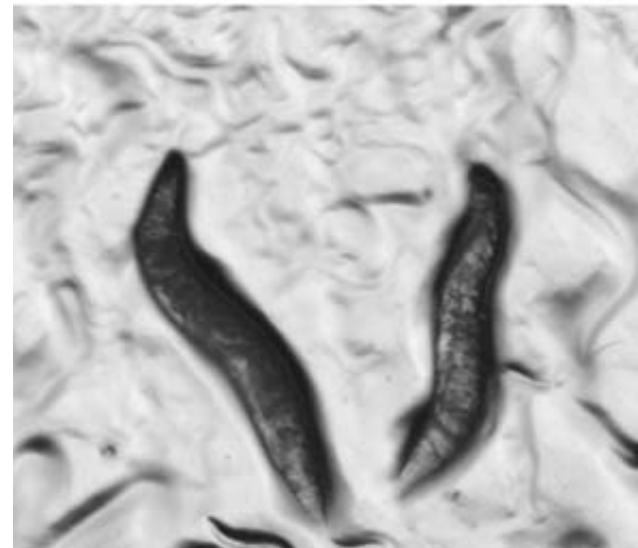
Methodology

- Develop a cross strategy to test different genes.
- Score new strains to see if there's a linker cell death defect.
- Visualize linker cell by using GFP



dpy-5 is Used to Track *mtk-1*

- They're both in chromosome 1 so it's easy to track *mtk-1*.



Cross Strategy for *mtk-1*

- Cross *qls56 him-5* males with *dpy-5* hermaphrodites
- Pick 6 GFP+ non-dumpy males
- Cross the GFP positive non-dumpy males with *mtk-1* hermaphrodites
- Pick 18 GFP+ non dumpy hermaphrodites and let them self

Cross Strategy for mtk-1

- Score the plates for the absence of dumpies
- On plates with dumpies, pick 32 non-dumpy GFP+ hermaphrodites to individual plates, let them self
- Look at the plates, we want 100% GFP+ and 100% non-dumpy.

Results

- We are at the last step of the cross strategy right now.
- The cross is successful so far with mtk-1
- We're going to make a new cross with pek-1
- Once the cross is completed, we will score for linker cell survival.

Future Work

- We are going to finish the cross with *mtk-1*, and look at the results.
- Finish the new cross with *pek-1* and *qls56 him-5* to test *pek-1* gene
- Test more MAP kinases

References

- Jacobson et al. Programmed cell death in animal development. *Cell* (1997) vol. 88 (3) pp. 347-54
- Baehrecke. How death shapes life during development. *Nat Rev Mol Cell Biol* (2002) vol. 3 (10) pp. 779-87
- Meier et al. Apoptosis in development. *Nature* (2000) vol. 407 (6805) pp. 796-801

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Questions?





THANK YOU