Transdifferentiation causing Programmed Cell Death in *C. elegans*

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Abstract

Cancer remains one of the leading causes of death worldwide. A way to understand how cells exhibiting initial cancerous characteristics are destroyed is by observing the programmed cell death (PCD) of a cell before it initiates tumorigenesis. The widely studied model organism Caenorhabditis elegans contains many homologous genes with humans and can therefore be studied and related to human cancers. Transdifferentiating specific cells in a particular worm strain (JR3642) by forcing the overexpression of the elt-7 transcription factor via heat shock puts stress on individual cells, possibly causing some to undergo PCD. To quantify the amount of transdifferentiate stress necessary to cause PCD, the JR3642 strain and quantified the post heat-shock corpses at different time points. When compared to a control, the difference in corpses found is not sufficient to provide conclusive results. The JR3642 strain was also crossed with strains containing fluorescent tags fused to the protein directly involved in corpse engulfment (coded by ced-1 gene), allowing for more accurate identification of cell corpses to provide more decisive results. We hypothesize that if the overexpression of the elt-7 transcription factor in *C. elegans* causes sufficient transdifferentiate stress within pharyngeal cells, then the cell will undergo programmed cell death.

Methods

Transdifferentiation: the reprogramming of adult cells, used to control the amount of stress the cells are undergoing.

Results

Analysis following heat shock and transdifferentiation proved to be difficult due to cell corpse identification being tedious and inaccurate because of minimal distinction between corpses and vacuoles. Fluorescent tags were crossed into the strain with reprogrammable pharyngeal cells to allow for more accurate corpse quantification.

Discussion

The preliminary data acquired when comparing the number of corpses found in the experimental (JR3642) and control strains gave inconclusive results due to the minimal difference between the two corpse counts. The transdifferentiation was successful in the experimental strain starting at hour 3 following heat-shock, eliminating transdifferentiation inconsistency as a source of error. The corpse formation starting an hour after transdifferentiation began hints that the transdifferentiation could be the driving factor of the programmed cell death. However, because the lac-2 control strain also had corpses, we cannot yet determine whether transdifferentiate stress causes programmed cell death in *C. elegans* or not. The results remain inconclusive because of the level of error involved in scoring corpses which are not fluorescently tagged. Looking into the future, successful crossing of the JR3642 (transdifferentiating) strain with the ced-1::gfp strain will allow for more accurate corpse quantification. The results from this experiment will likely provide a conclusive outcome by eliminating the main source of error. Additionally, a cross will be performed to knockout the ced-1 gene in the JR3642 strain to limit corpse engulfment, allowing for more time to quantify the corpses before they are engulfed. Although the results were inconclusive, they provided a key foundation into further experimentation which could lead to a better understanding tumorigenesis and how to stop it.

References:


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Further information:


Please reference https://db.umn.edu/dig/what-c-elegans for more information on *C. elegans* and why it is so widely used as a model organism.