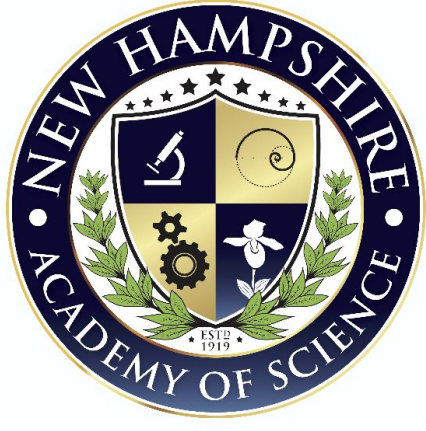


Glucose Impairs the Hypertonic Stress Response of *Daf-2*-deficient *C. elegans*

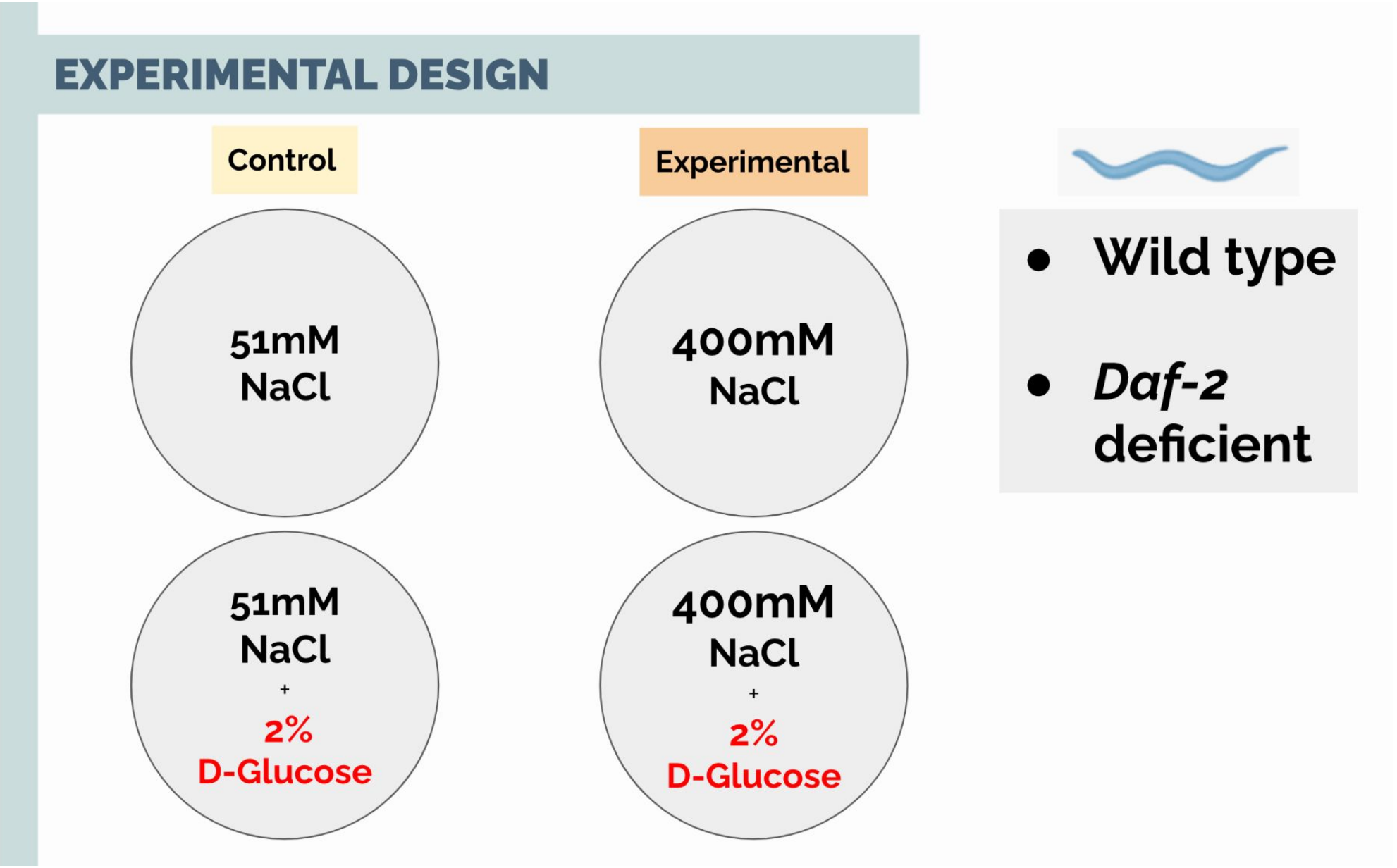


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BACKGROUND: Cellular viability relies on the maintenance of normal salt concentrations in the cytoplasm. The loss of water and an increase in intracellular tonicity lead to cellular death. Under hypertonic stress, cellular mechanisms are activated that prevent and repair damage.

In *Caenorhabditis elegans*, DAF-16 controls the expression of proteins that protect against hypertonic stress and other environmental challenges. DAF-16 expression is downregulated via the DAF-2 insulin signaling pathway. Loss-of-function *daf-2(-)* mutants possess both a heightened ability to withstand hypertonic stress and unique longevity, for which an intact copy of the *daf-16* gene is required. In prior research, this life span was dramatically reduced by adding glucose to the worms’ diet, theorized to inhibit DAF-16 activity by activating the weakened DAF-2 insulin signaling pathway. As both the increased ability to withstand hypertonic stress and prolonged lifespan of *daf-2(-)* mutants appear to be DAF-16 dependent, we studied the effects of dietary glucose on the worms in hypertonic conditions.

METHODS: We compared the survival of wild type and *daf-2(-)* *C. elegans* on standard growth medium (51 mM NaCl) and hypertonic growth medium (400 mM NaCl) with and without added dietary glucose.



The ability to live longer and to survive in high salt environments in *daf-2 (-)* *C. elegans* may be controlled by the same cellular signaling pathway.

Glucose Impairs HTSR in *Daf-2(-)*

Daf-2(-) Worms Survive Hypertonic Stress better than Wild type, but not when Glucose is added.

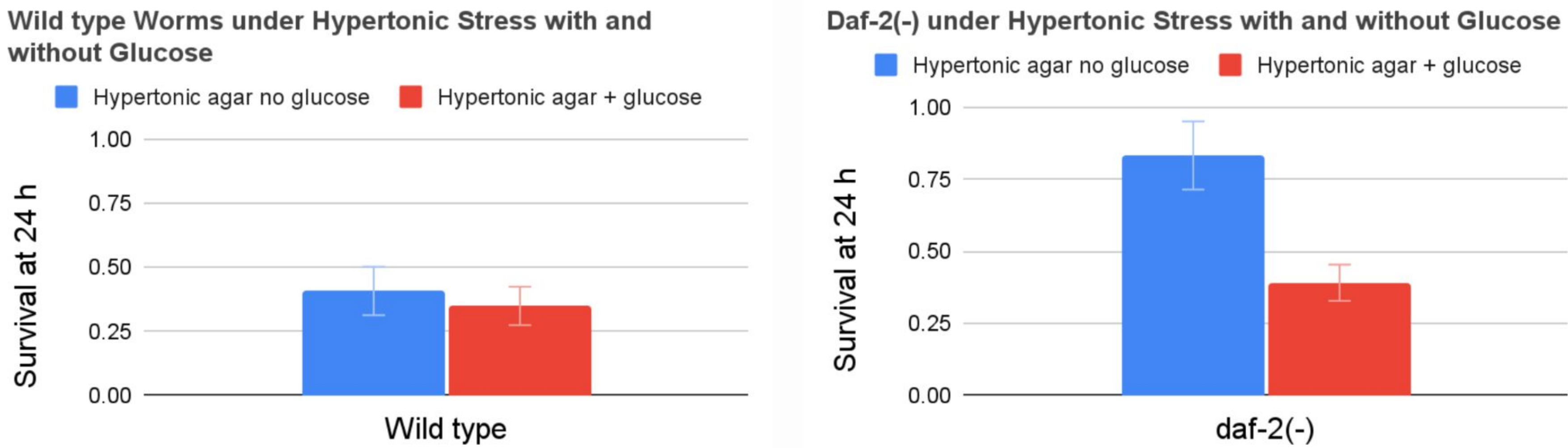
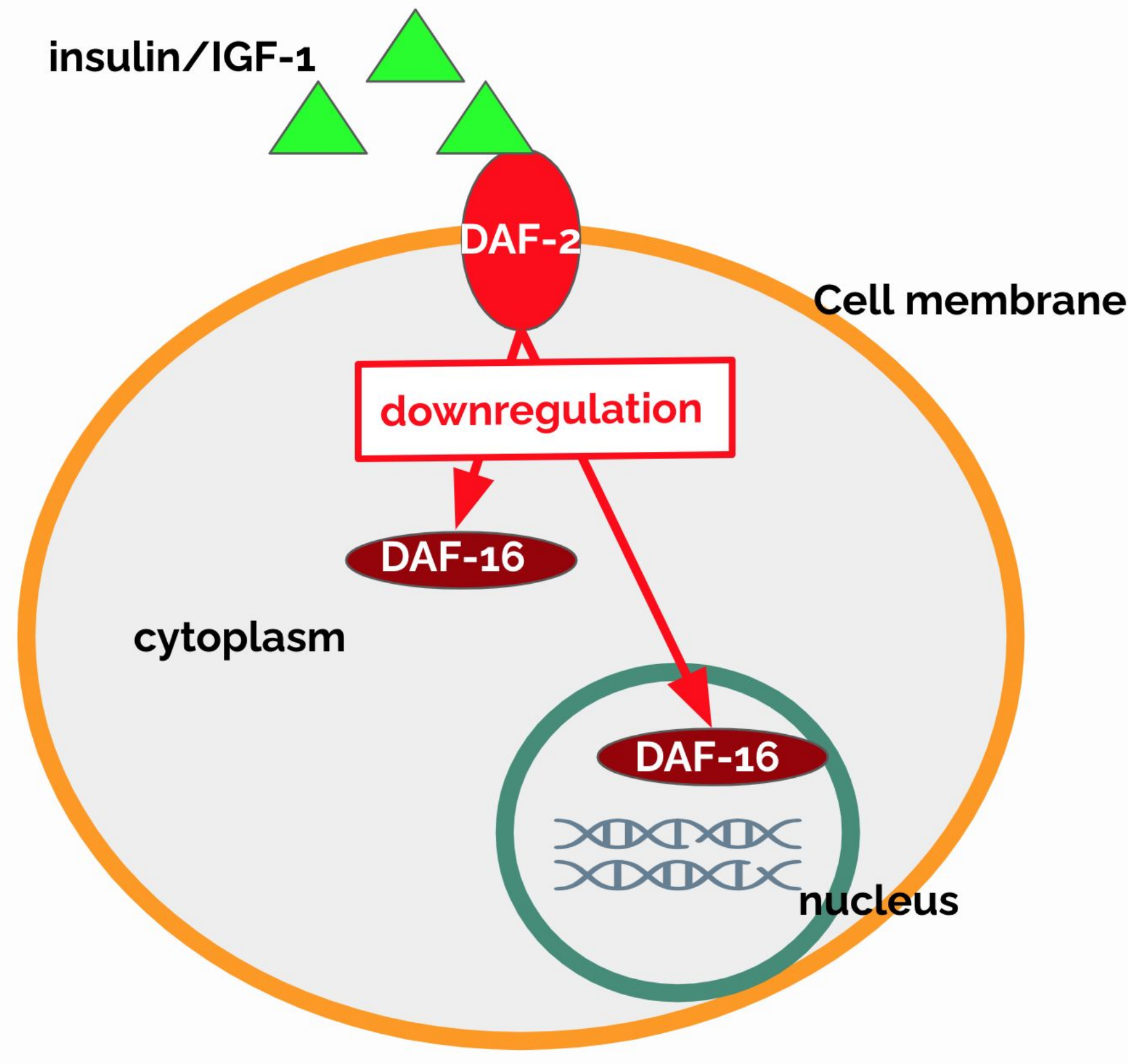


Figure 1. Wild-type and *daf-2(-)* survival after 24 hours in hypertonic media with and without glucose. A: Wild-type worms on hypertonic agar (400mM NaCl) showed survival of 36% after 24 hours. On hypertonic agar with the addition of D-glucose, wild-type survival was 31% (p=0.22222). B: *Daf-2(-)* worms on hypertonic agar (400mM NaCl) showed 84% survival. The addition of D-glucose lowered survival to 47% (p=0.04978).

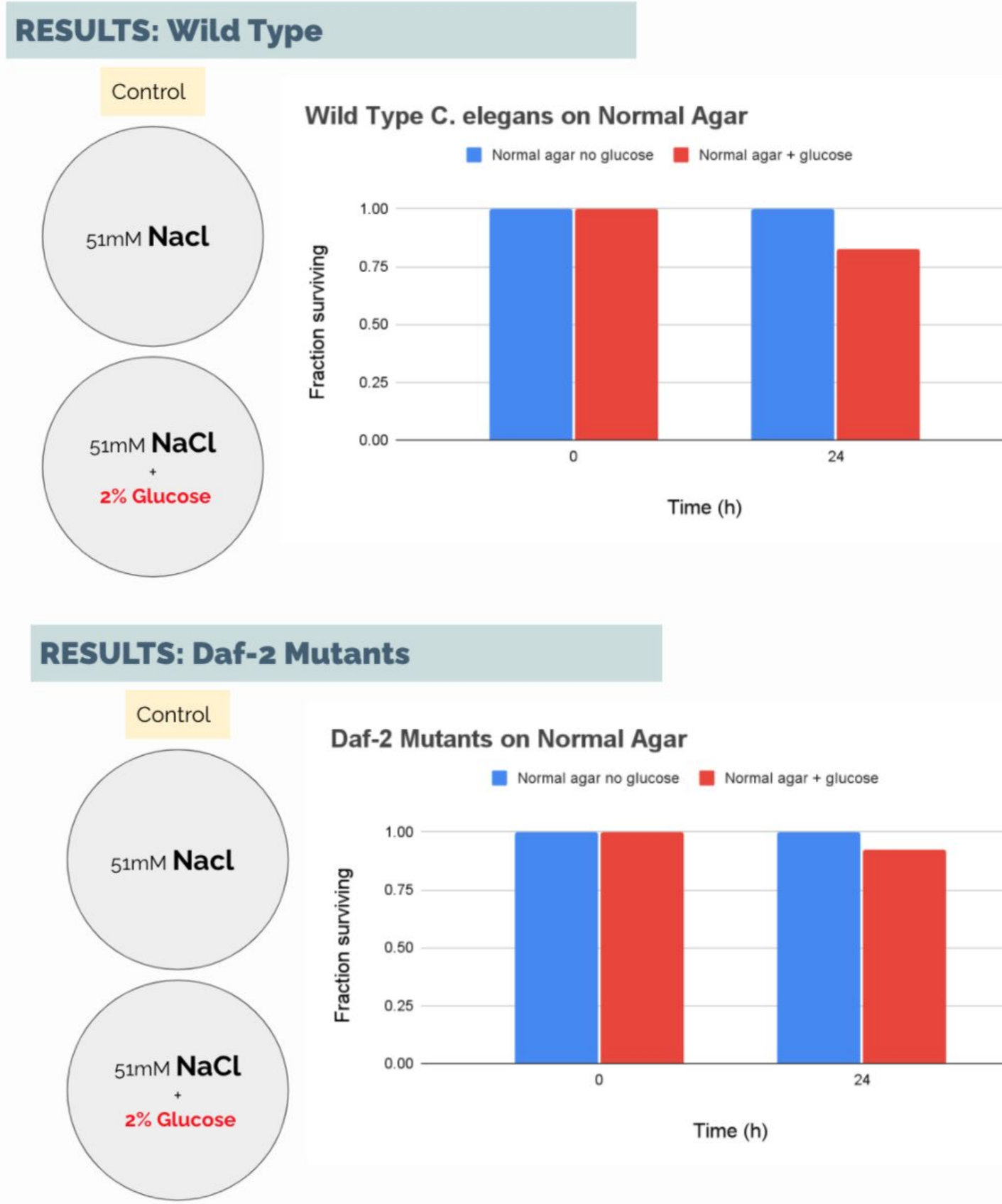
The Insulin Signaling Pathway



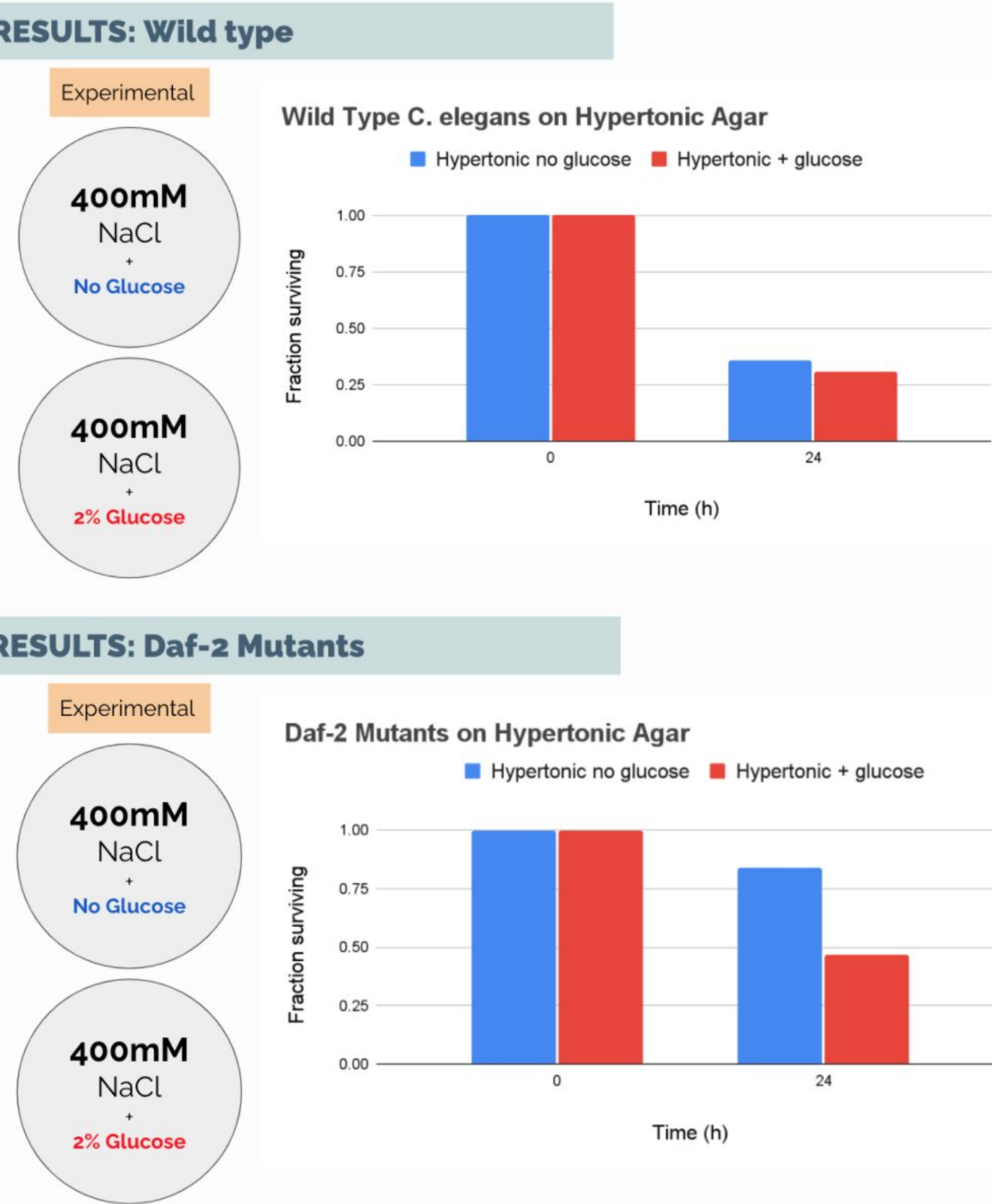
Drawing by Viazmenski, adapted from Davy et al. (2018), FOXO3 and Exceptional Longevity: Insights From Hydra to Humans. <https://doi.org/10.1016/bs.ctdb.2017.10.001>

RESULTS: Survival of *daf-2(-)* worms on hypertonic media at 24 hours was reduced when glucose was added.

Controls: Wild Type v. *Daf-2(-)*



Results: Wild Type v. *Daf-2(-)*



DISCUSSION: *Daf-2(-)* worms normally survive better under hypertonic stress than their wild type counterparts. Our data support the hypothesis that *daf-2(-)* *C. elegans* exhibit a decreased ability to mount a hypertonic stress response (HTSR) when fed D-glucose. We hypothesize that this is due to the inhibition of the DAF-16-dependent stress response pathway and that this is the same mechanism responsible for life span shortening that was previously observed by Lee. et al. (2009).