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Title
An essential role of the iron-sulfur cluster assembly enzyme *isu-1* in the aging and stress responses of *Caenorhabditis elegans*

Hypothesis
Iron is essential for animal cellular homeostasis by acting in the biogenesis of two important redox-reactive prosthetic groups of enzymes: iron sulfur clusters (ISC) and heme. Previous studies have indicated that the misregulated iron metabolism is associated with multiple aging-related neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease. However, how iron metabolism modulates the aging process remains largely elusive. We hypothesis that the iron-sulfur cluster assembly enzyme isu-1 can modulate the aging and stress response via the transcription factors to regulate the downstream genes expressing.

Background/Aims
In the current study, we aim to reveal the roles and mechanisms of iron metabolism in the aging process of C. elegans, a well-established genetic model organism for aging research. We will characterize the mechanisms underlying the effects of iron-sulfur cluster in animal aging and stress response using various genetic and biochemistry approaches.

Methods
We will combine the molecular biology techniques, biochemical techniques, genetic technology and imaging techniques to address this question.

Results and Conclusions
Through our preliminary studies, we have found that the iron–sulfur cluster assembly gene isu-1 plays an important role in the lifespan modulation and stress resistance of C. elegans. Specifically, RNAi knocking-down of isu-1 causes a significantly upregulated mitochondrial unfolded protein response (mitoUPR). Furthermore, the isu-1 RNAi-treated worms are significantly more resistant to heat shock and oxidative stress. Lastly, isu-1 RNAi significantly extends lifespan (~25.7%). Currently, we are examining the transcription factors downstream of isu-1 in regulating aging and stress responses. Surprisingly, the isu-1 RNAi-triggered lifespan extension is independent of insulin and IGF pathway, an evolutionarily conserved master regulator of animal growth and aging.