Experiment Overview

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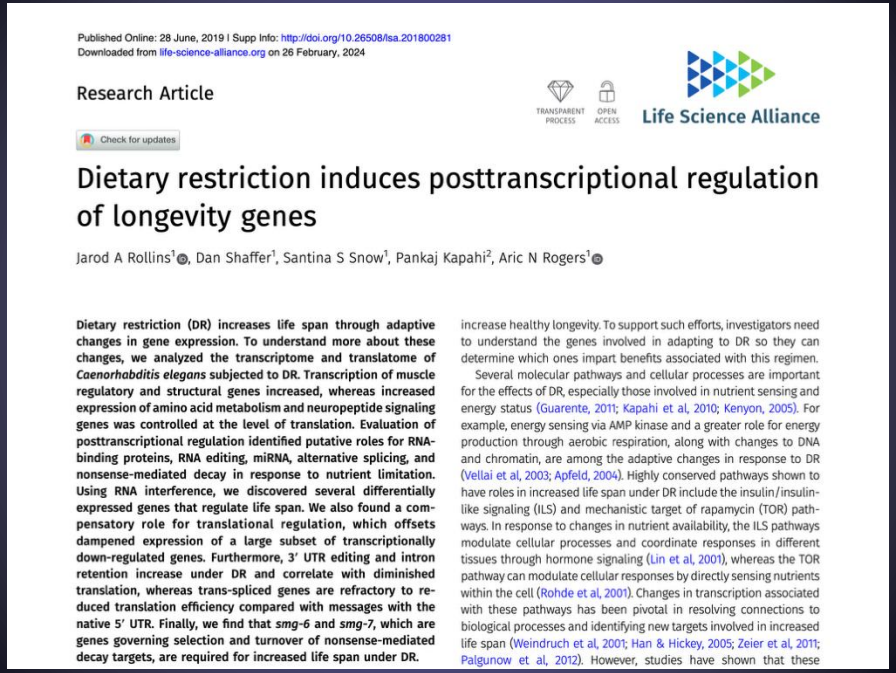

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Research Article

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Dietary restriction induces posttranscriptional regulation of longevity genes

Jarod A Rollins[1], Dan Shaffer[1], Santina S Snow[1], Pankaj Kapahi[2], Aric N Rogers[1]

Dietary restriction (DR) increases life span through adaptive changes in gene expression. To understand more about these changes, we analyzed the transcriptome and translatome of *Caenorhabditis elegans* subjected to DR. Transcription of muscle regulatory and structural genes increased, whereas increased expression of amino acid metabolism and neuropeptide signaling genes was controlled at the level of translation. Evaluation of posttranscriptional regulation identified putative roles for RNA-binding proteins, RNA editing, miRNA, alternative splicing, and nonsense-mediated decay in response to nutrient limitation. Using RNA interference, we discovered several differentially expressed genes that regulate life span. We also found a compensatory role for translational regulation, which offsets dampened expression of a large subset of transcriptionally down-regulated genes. Furthermore, 3′ UTR editing and intron retention increase under DR and correlate with diminished translation, whereas trans-spliced genes are refractory to reduced translation efficiency compared with messages with the native 5′ UTR. Finally, we find that *smg-6* and *smg-7*, which are genes governing selection and turnover of nonsense-mediated decay targets, are required for increased life span under DR.

increase healthy longevity. To support such efforts, investigators need to understand the genes involved in adapting to DR so they can determine which ones impart benefits associated with this regimen.

Several molecular pathways and cellular processes are important for the effects of DR, especially those involved in nutrient sensing and energy status (Guarente, 2011; Kapahi et al, 2010; Kenyon, 2005). For example, energy sensing via AMP kinase and a greater role for energy production through aerobic respiration, along with changes to DNA and chromatin, are among the adaptive changes in response to DR (Vellai et al, 2003; Apfeld, 2004). Highly conserved pathways shown to have roles in increased life span under DR include the insulin/insulin-like signaling (ILS) and mechanistic target of rapamycin (TOR) pathways. In response to changes in nutrient availability, the ILS pathways modulate cellular processes and coordinate responses in different tissues through hormone signaling (Lin et al, 2001), whereas the TOR pathway can modulate cellular responses by directly sensing nutrients within the cell (Rohde et al, 2001). Changes in transcription associated with these pathways has been pivotal in resolving connections to biological processes and identifying new targets involved in increased life span (Weindruch et al, 2001; Han & Hickey, 2005; Zeier et al, 2011; Palgunow et al, 2012). However, studies have shown that these

Samples

AL-total_rep1
AL-total_rep2
AL-total_rep3

DR-total_rep1
DR-total_rep2
DR-total_rep3

Samples

AL-total_rep1
AL-total_rep2
AL-total_rep3

DR-total_rep1
DR-total_rep2
DR-total_rep3

AL = ad libitum
DR = dietary restriction

total = Total RNA
ploy = polysome bound RNA