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Daily events are not simply individual concepts, but shared by the social environment we live in. The present study investigates the role of romantic partners in the co-regulation of cognitive functioning by the example of prospective memory (PM), the ability to remember and correctly execute future intentions. In this context, we examined the impact of social proximity (i.e., physical closeness and psychological intimacy) on interpersonal regulation. Over the course of 21 days, 64 younger couples (18-33 years) and 52 couples of older adults (57-87 years) completed an ambulatory assessment comprising a daily pseudo-randomized PM task. Results reveal that couples' PM performance was higher for younger than for older participants. Further, dyadic PM was correlated with psychological intimacy for both age groups, but the impact of time spent together on intimacy and PM performance, respectively, was stronger in older adults. Possible moderating factors and explanations for these findings will be discussed.

**Session 4510 (Symposium)**

BS GSA AND AAA JOINT SYMPOSIUM

**RIBOSOMAL PROTEIN 6 PHOSPHORYLATION REGULATES TRANSLATIONAL RESPONSES TO DIETARY RESTRICTION**

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Forms of dietary restriction like intermittent fasting (IF) and caloric restriction (CR) promote health and longevity through changes in gene expression. While the transcriptional changes that occur in response to DR have been well described across several species, the role of translational regulation has lagged. Using polysome profiling and mRNA-seq, we quantified changes in actively translated mRNAs that occur in C. elegans under CR compared to well-fed conditions. The analysis revealed hundreds of transcripts regulated on the translational level that would have been missed using conventional transcriptomics. Among the translationally down-regulated genes that where pro-longevity when knocked down were regulators of the cell-cycle: fbxb-24, sdz-33, kbp-1, and cdk-2. In search of the mechanisms regulating selective translation under CR we investigated a role for ribosomal protein 6 (RPS-6) as its phosphorylation status is thought to regulate cell cycle and selective translation of mRNA transcripts. Using RPS-6 phospho-null and phospho-mimetic mutants, we show that phosphorylation and de-phosphorylation of RPS-6 is necessary for the pro-longevity effects of CR and IF. Furthermore, we show that IF is more beneficial for retaining locomotion with age than CR and that endogenously tagged RPS-6::mCherry accumulates in body wall muscle under fasting. However, the benefit of IF on locomotion is lost in RPS-6 phospho-mimetic mutants.

Together, results suggest that protein translation is enhanced in the muscle under IF to prevent sarcopenia in a way dependent on RPS-6. Translatome analysis of the phosphomutant suggested a role for RPS-6 in selective translation of p38 mitogen-activated protein kinases.

**AGE-RELATED NEUROPROTECTION BY DIETARY RESTRICTION REQUIRES OXR1-MEDIATED RETROMER FUNCTION**

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Dietary restriction (DR) is the most robust method to delay aging and the onset of neurodegenerative disorders across multiple species, though the mechanisms behind this phenomenon remain unknown. To elucidate how DR mediates lifespan extension, we analyzed natural genetic variants that associate with increased longevity under DR conditions in the Drosophila Genetic Reference Panel. We found that neuronal expression of the fly homolog of human Oxidation Resistance 1 (OXR1) is necessary for DR-mediated lifespan extension. Neuronal knockdown of OXR1 also accelerated visual decline but not physical decline, arguing for a specific role of OXR1 in neuronal signaling. Further, we find that overexpression of the TLDc domain from human OXR1 is sufficient for lifespan extension in a diet-dependent manner. Studies from the Accelerating Medicines Partnership - Alzheimer’s Disease network show that patients with reduced OXR1 protein levels are more prone to Alzheimer’s disease diagnosis, and we find that overexpression of human OXR1 is protective in animal and cell Alzheimer’s models. In seeking the mechanism by which OXR1 protects against age-related neuronal decline, we discovered that it provides a necessary function in regulating the neuronal retromer complex, which is essential for the recycling of transmembrane receptors and for maintenance of autophagy. We further discovered that OXR1 deficiency can be rescued by genetic or pharmacological enhancement of retromer function, and that this enhancement extends lifespan and healthspan. Understanding how OXR1 operates could help uncover novel mechanisms to slow neurodegeneration including Alzheimer’s disease.

**AGING PREDISPOSES B CELLS TO MALIGNANCY BY ACTIVATING C-MYC AND PERTURBING THE GENOME AND EPIGENOME**

Jose Castro,1 Alessandro Barbieri,2 João Paulo,3 Olga Strelkova,3 John Sedivy,4 John Manis,3 Vadim Gladyshev,5 and Anastasia Shindyapina,6 1. I 3. S, Porto, Porto, Portugal, 2. Boston Children’s Hospital, Boston, Massachusetts, United States, 3. Harvard Medical School, Boston, Massachusetts, United States, 4. Brown University, Providence, Rhode Island, United States, 5. Brigham and Women’s Hospital, Boston, Massachusetts, United States, 6. Brigham and Women’s Hospital, Harvard

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