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Title: Evaluation of proteostasis across mammalian lifespan

Abstract: Proteostasis is a highly regulated process involving the proteostasis network responsible for maintaining the cellular proteome. When proteostasis is altered, proteome and proteostasis network disruptions occur, leading to accumulation of protein aggregates, characteristic of several age-related diseases. Previous work performed in *Caenorhabditis elegans* and zebrafish unveiled asymptomatic protein aggregation (ARPA), characterized by generalized increased accumulation of insoluble proteins through aging in healthy animals. Whether ARPA is a causative process in aging and contributes to age-related diseases is not clear and to date the consequences of protein homeostasis imbalances in the context of normal aging in mammals remains largely unexplored.

We hypothesize that accumulation of insoluble proteins occurs through aging in mammals and that it contributes to activate the stress response and disrupt protein synthesis rate and protein quality control mechanisms. To elucidate if ARPA occurs along the lifespan of mice, C57BL/6 mice with different ages (1, 6, 13, 18, 24 and 29 months) were used and the detergent-insoluble fractions were isolated from total protein extracts of different tissues. The total and detergent-insoluble protein profiles were characterized by automated capillary electrophoresis separation using the LabChip GX equipment (PerkinElmer). Our preliminary results show that there is an increase in insoluble proteins until at least 18 months old in particular tissues in mice. Identification of the proteins more prone to aggregate during aging will be performed by mass spectrometry and characterized to establish the functions and biological processes affected by ARPA. This will allow identifying novel aging biomarkers that may be relevant for disease onset and progression.

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