Title: Understanding the role of non-coding circular RNAs in aging.

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Abstract: Among other physiological changes, aging is characterized by global changes in gene expression profiles. Circular RNAs (circRNAs) are a novel class of abundant non-coding RNAs, identified in eukaryotic organisms, with important roles in the regulation of gene transcription. However, the contribution of circRNAs to aging remains poorly understood. Here, we used a combination of next-generation sequencing and biochemical approaches to elucidate the role of circRNAs in aging. Using RNA-seq, we quantified the global changes in circRNA expression patterns in tissues from young and old mice, to identify and characterize properties of specific circRNA isoforms accumulating with aging. We also analyzed circRNAs in a panel of skin fibroblasts derived from different rodent species, and utilized comparative genomics approaches to uncover the contribution of circRNAs to regulating species lifespan. To confirm that accumulation of circRNAs globally or of specific isoforms occurs in cells during aging, we also performed a time-scale experiment to quantify circRNA expression in rodent fibroblasts undergoing senescence. Our data demonstrate that circRNAs accumulate with aging and might be involved in regulation of gene expression during aging. Implication of these findings for understanding the role of circRNAs in cellular senescence and regulation of gene transcription will be discussed.