Background

Biomarkers of ageing have long been sought after to help assess the biological age and general health status of individuals. Considerable efforts have been invested to identify such biomarkers, including physiologic readouts, metabolic parameters, glycomic profiles and others. Nevertheless, markers with strong predictive power have remained elusive.

Work in model organisms has identified several conserved signaling pathways that extend life span, such as reduced insulin/IGF signaling and dietary restriction mediated longevity. It is not clear though whether these pathways converge on common mechanisms. Identifying convergent processes and mechanisms is important, because it can elucidate core aspects underlying healthy ageing, and help identify molecular and cellular signatures of health that could be used as biomarkers of ageing applied in many clinical settings.

Technology

Researchers of the Max Planck have discovered that many longevity pathways converge on the nucleolus, a nuclear subcompartment that is the cellular site of ribosomal RNA synthesis, ribosome biogenesis, and assembly of various ribonucleoprotein particles.

Specifically, they found that these pathways strikingly reduce nucleolar size, as well as expression of nucleolar protein fibrillarin, ribosomal RNA and ribosomal proteins across different species (C. elegans, fruit flies and mice).

Furthermore, they found a striking inverse correlation between nucleolar size and longevity in C. elegans. In humans, they could show that muscle biopsies from individuals who underwent modest dietary restriction coupled with exercise also displayed small nucleoli.

This work suggests that small nucleoli are a visible hallmark of longevity and metabolic health, and that molecules associated with nucleolar function might serve as predictive, causal biomarkers of life expectancy.

Fig. 1: Schematic illustrating the experiment, which shows that longer-lived worms exhibit small nucleoli and vice versa.
Fig. 2: Muscle biopsies from humans undergoing DR and exercise exhibit small nucleoli. Scale bars represent 20 mm. *P < 0.05 paired t-test.

Work is underway to determine the effects of various interventions (genetic, pharmacologic and environmental) on the identified parameters of metabolic health. Also, assays that facilitate screening from more accessible tissues are being developed (saliva, blood).

We are now looking for a collaboration or a licensing partner to further develop these exciting findings.

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