

RCCN Workshop: Measuring Biologic Age

How Useful are Phenotypic Extremes (Centenarians)?

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Albert Einstein College of Medicine

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Staying healthy as we get older!

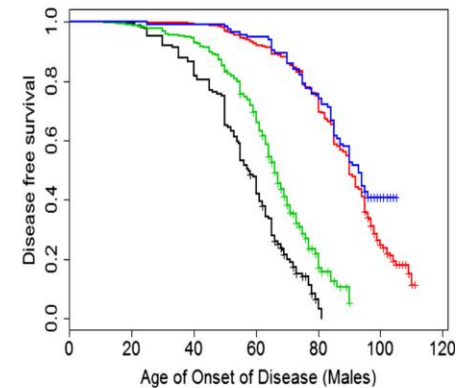
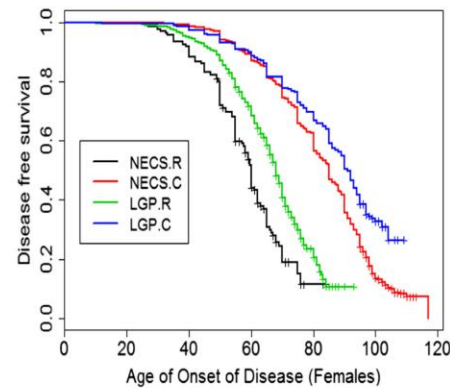
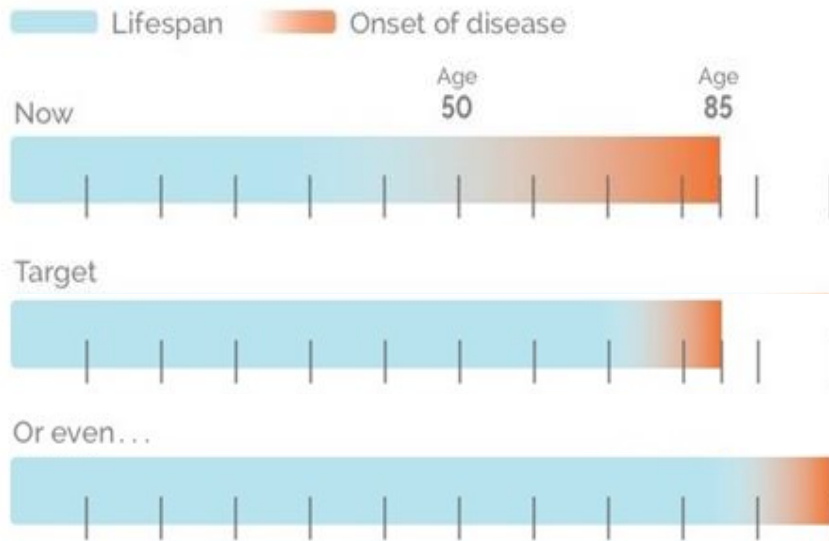


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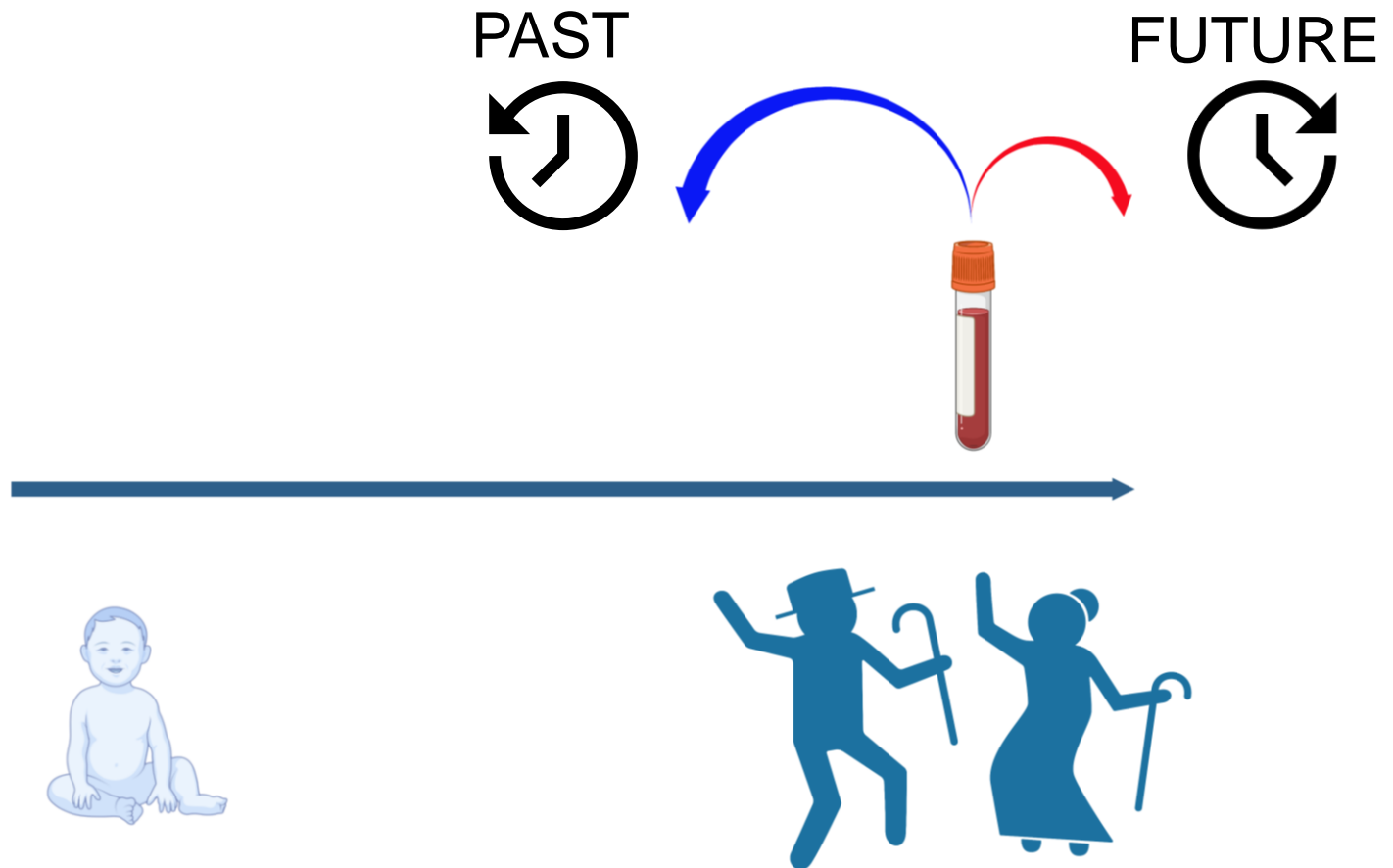
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Centenarians are a model of successful aging



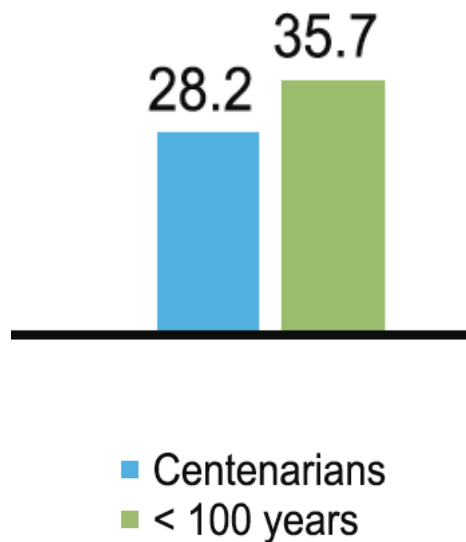
Biological Mechanism of Healthy Longevity



Phenotypic approach: Centenarians vs. General Population Control

Cross-sectional analysis

Prevalence of Abdominal Obesity

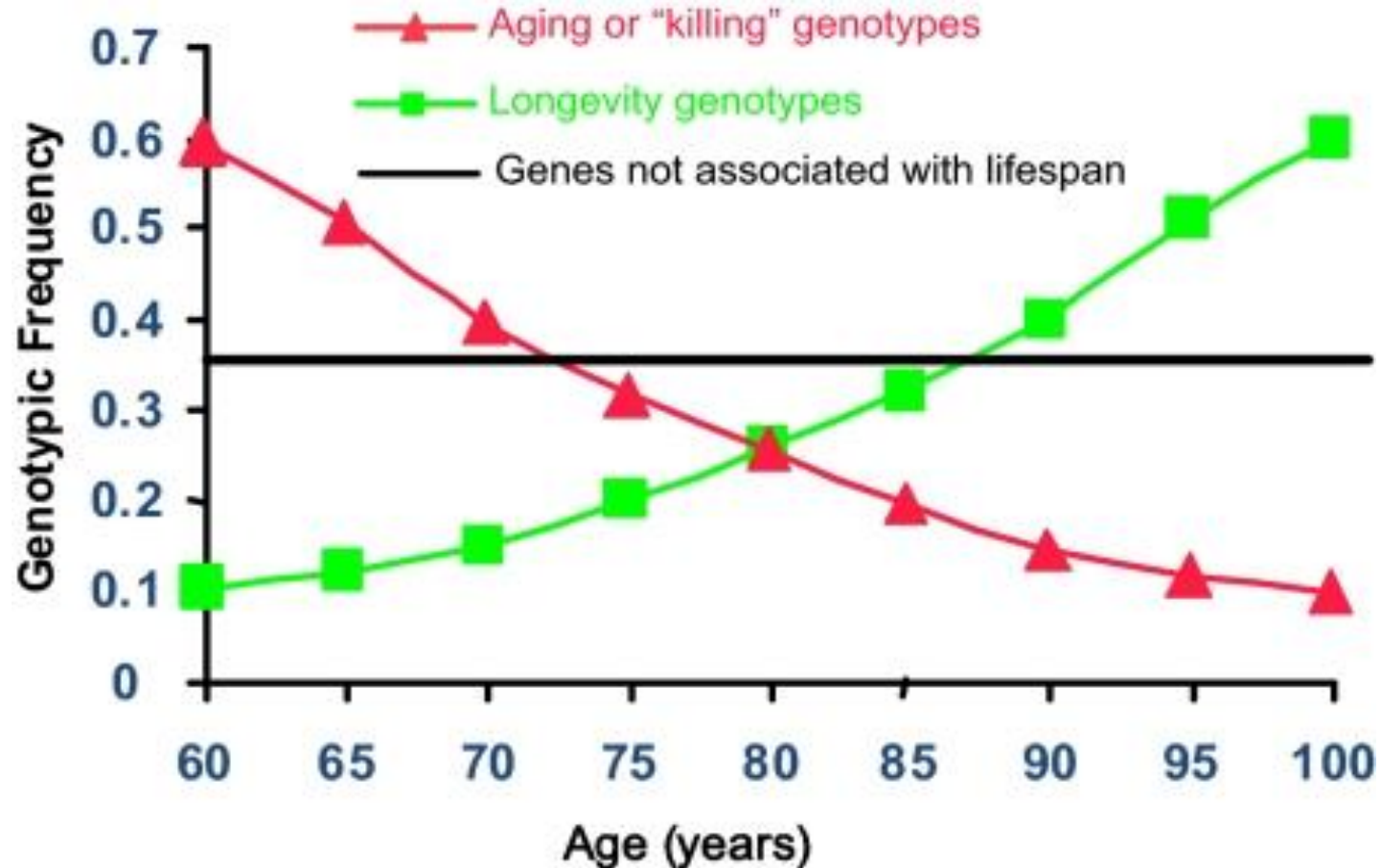


Retrospective analysis

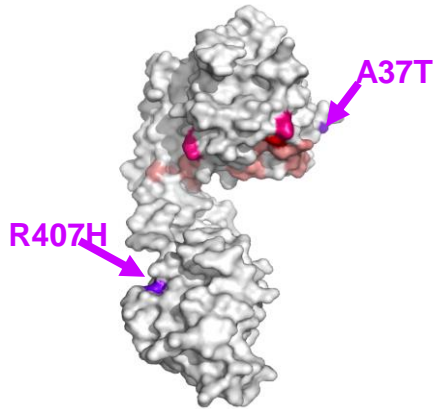
Maximum BMI and Prevalence of Overweight/Obesity
During the Lifetime in Females

BMI (kg/m ²)	Centenarians (n=249)	NHANES I (n=7,924)	P-value
Maximum, mean \pm SD	25.0 \pm 3.5	24.9 \pm 5.4	0.90
<25.0	56.2	58.8	0.33
>25.0	43.8	41.2	0.71

Genetic Approach to Exceptional Longevity

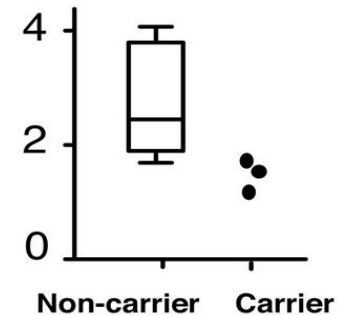


Genetic Approach to Exceptional Longevity: IGF/Insulin Signaling Pathway

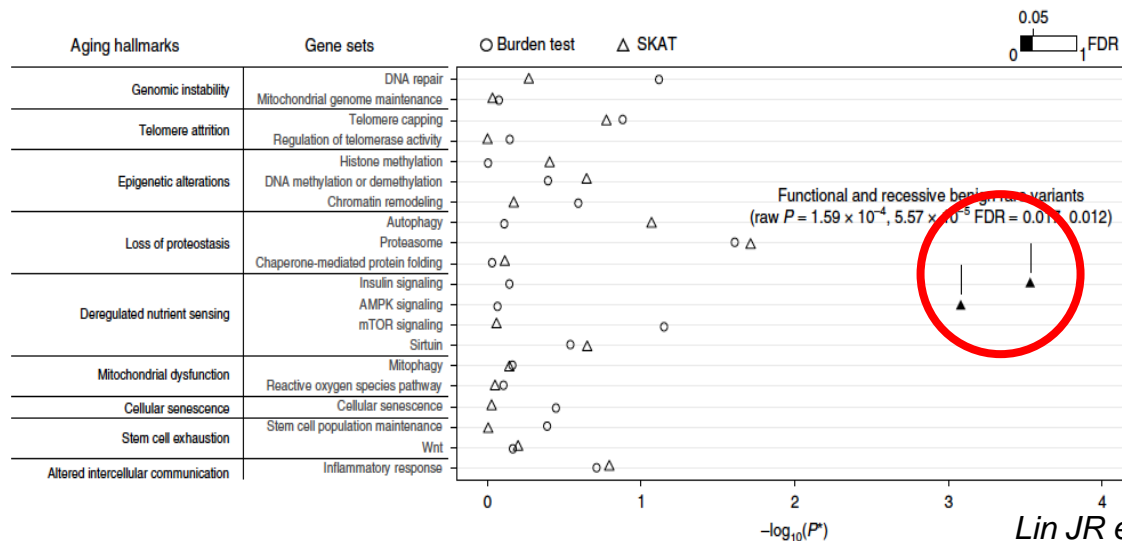


Genetic variation	Centenarians (n=384)	Controls (n=312)
Ala 37 Thr	2	0
Arg 407 His	7	1
$p=0.02$		

IGF-1-induced Phos/total AKT ratio

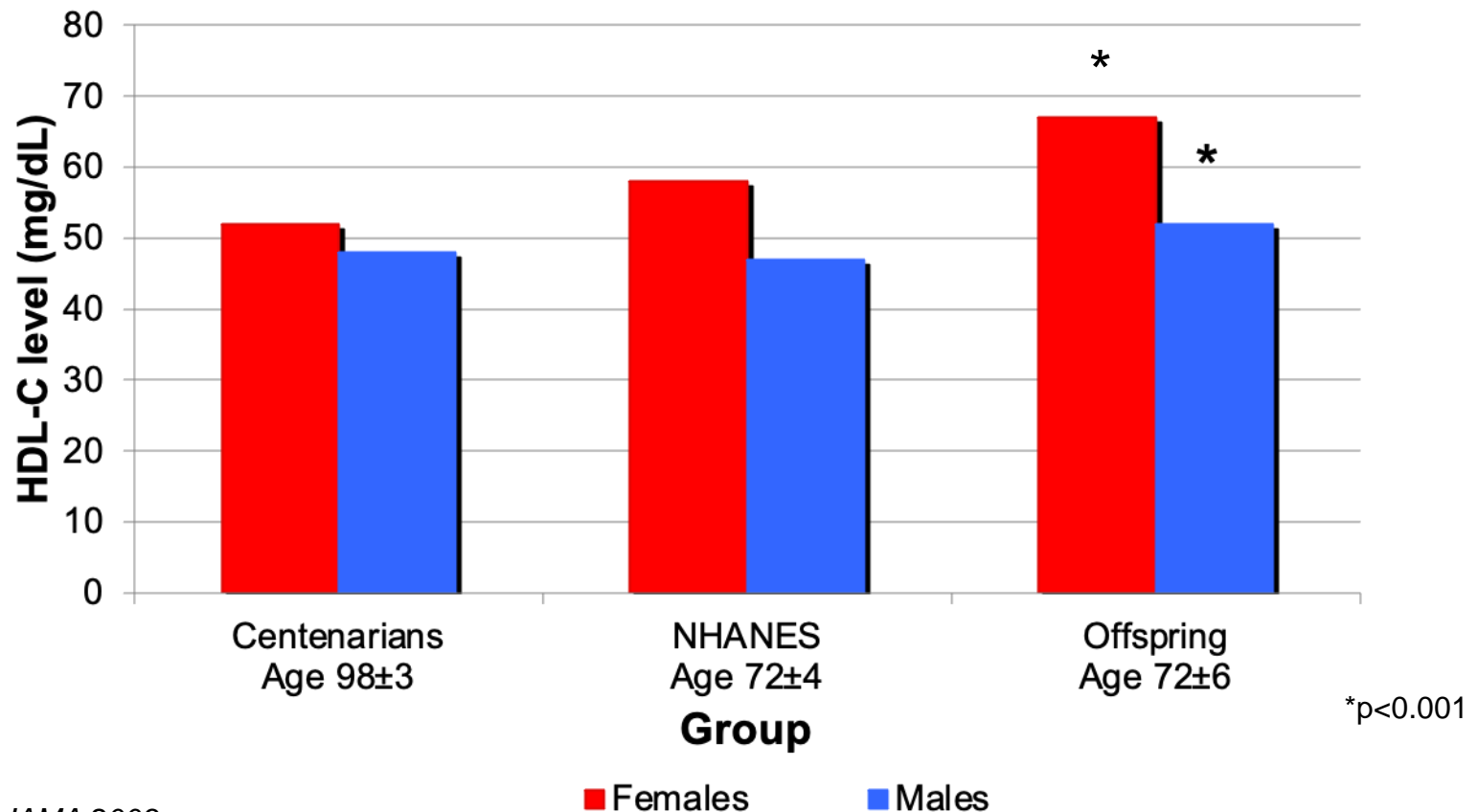


Suh Y et al. PNAS 2008



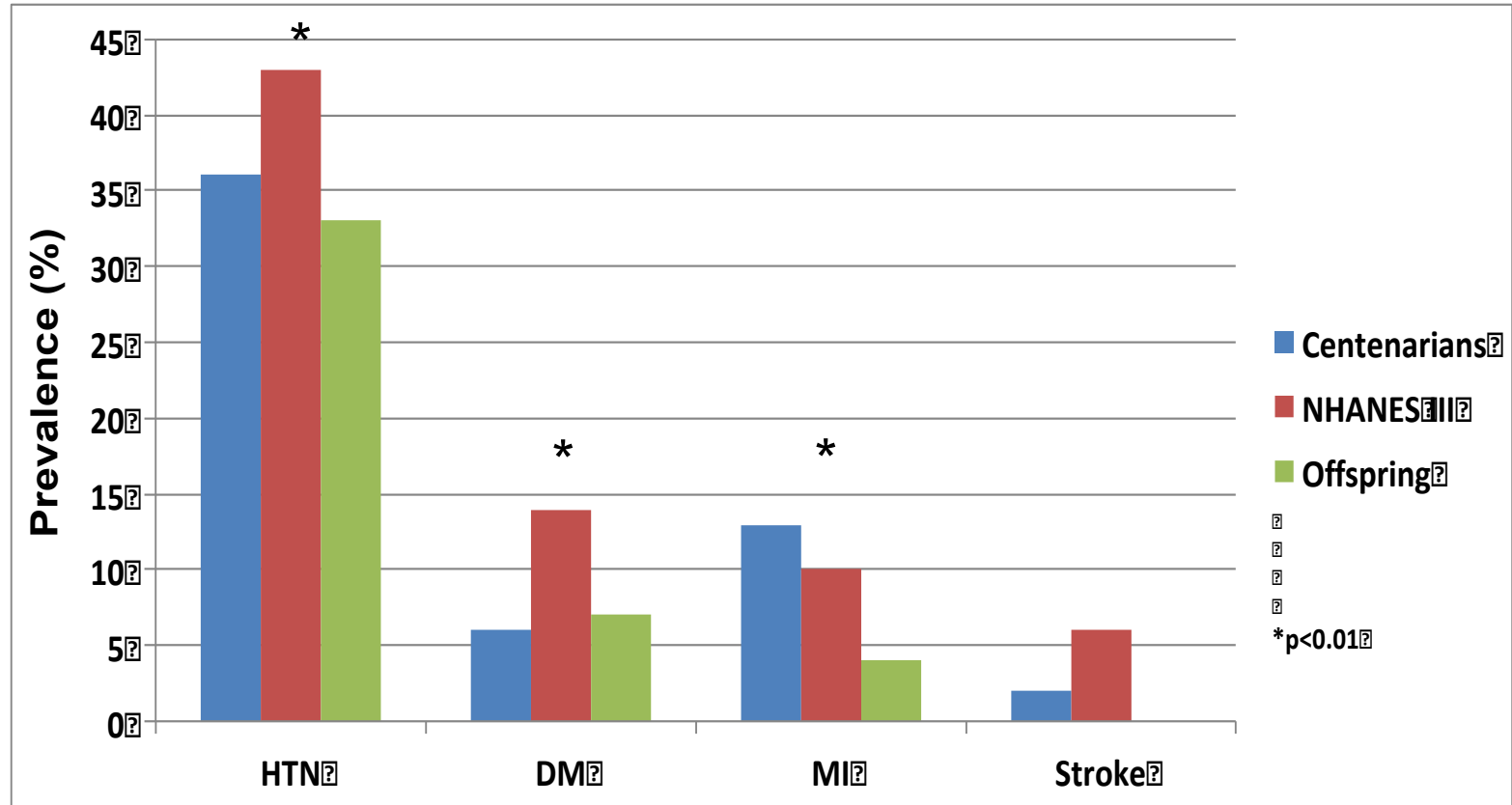
Lin JR et al. Nat Aging 2021; in press

Phenotypic approach: Centenarians' Offspring vs. General Pop Control

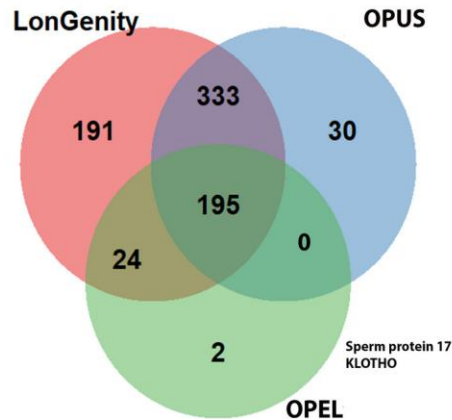
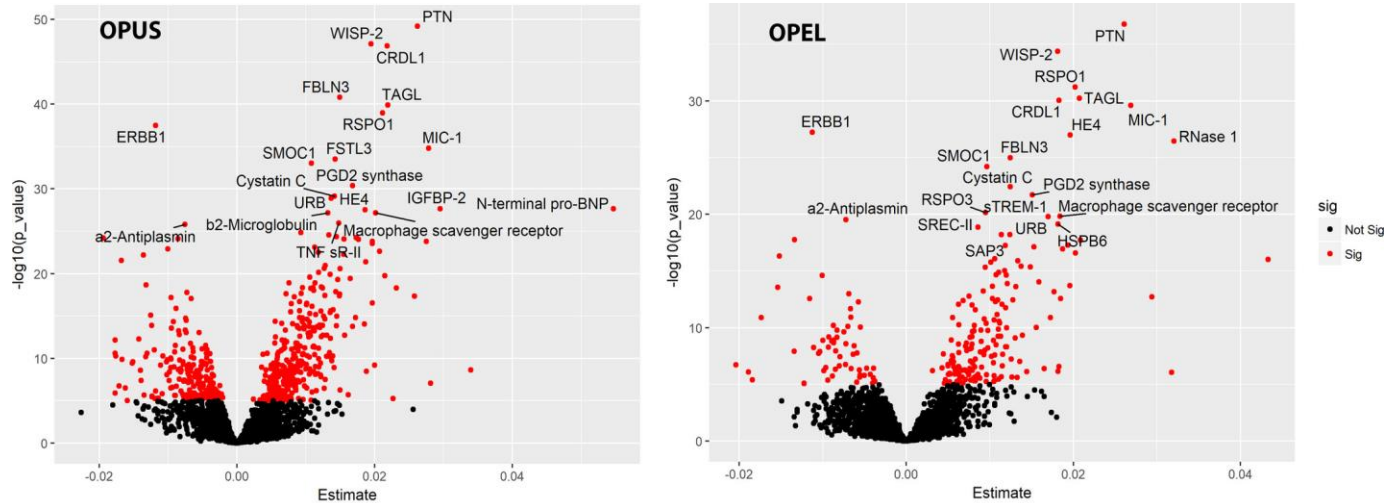


Barzilai et al. JAMA 2003
Milman et al. Curr Vasc Pharm 2014

Centenarians and their offspring have lower prevalence of age-related diseases

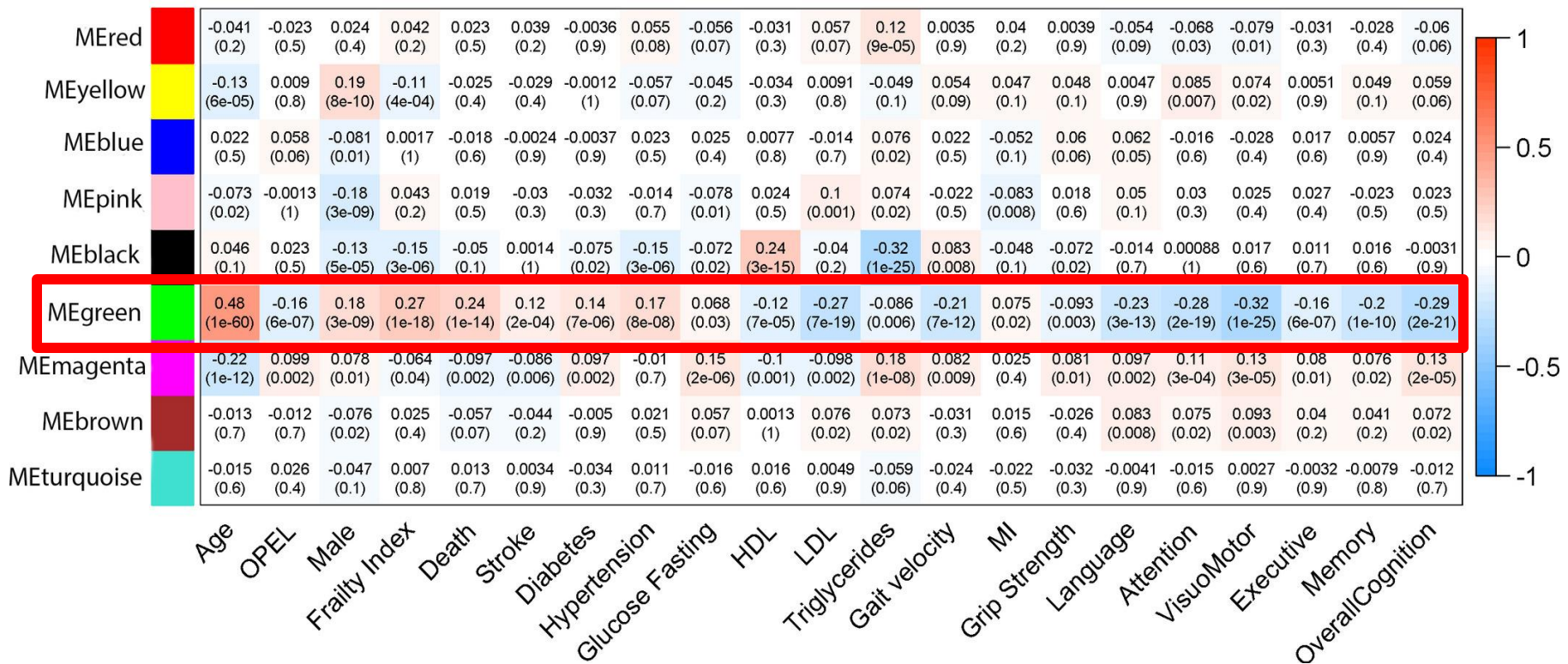


Plasma proteomic profile of age in Offspring (OPEL) vs. Control (OPUS)



Plasma proteomic profile of age in Offspring (OPEL) vs. Control (OPUS)

Module-trait relationships



Conclusions

- Centenarians are a model of delayed biological aging
- At end of life, centenarians' biochemical phenotype may not always reflect longevity, but be a marker of aging
- Centenarians' offspring should be used for identifying healthy aging and resilience biomarkers
- Centenarians and their offspring are valuable for identifying genetic determinants of delayed aging

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* Former team members