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Bayesian association scan reveals loci associated with human lifespan and linked biomarkers

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The enormous variation in human lifespan is in part due to a myriad of sequence variants, only a few of which have been revealed to date. Since many life-shortening events are related to diseases, we developed a Mendelian randomization-based method combining 58 disease-related GWA studies to derive longevity priors for all HapMap SNPs. A Bayesian association scan, informed by these priors, for parental age of death in the UK Biobank study ($n=116,279$) revealed 16 independent SNPs with significant Bayes factor at a 5% false discovery rate (FDR). Eleven of them replicate (5% FDR) in five independent longevity studies combined; all but three are depleted of the life-shortening alleles in older Biobank participants. Further analysis revealed that brain expression levels of nearby genes (*RBM6*, *SULT1A1* and *CHRNA5*) might be causally implicated in longevity. Gene expression and caloric restriction experiments in model organisms confirm the conserved role for *RBM6* and *SULT1A1* in modulating lifespan.

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