## SUPPLEMENTARY TABLES

**Supplementary Table 1. Age-adjusted characteristics of subjects at baseline for *FOXO rs2802292 TT* genotype and *G*-allele carriers.**

| Variable | *TT* | *GT/GG* | p |
|---|---|---|---|
| n | 1901 | 1683 | |
| Age (years) | 77.0 ± 4.5 | 78.0 ± 4.7 | 0.0008 |
| BMI (kg/m²) | 23.5 ± 3.2 | 23.5 ± 3.1 | 0.81 |
| Fasting plasma glucose (mg/dl) | 112.3 ± 28.0 | 113.9 ± 31.0 | 0.090 |
| Smoking (pack-years) | 25.4 ± 33.5 | 27.0 ± 35.3 | 0.20 |
| Alcohol intake (oz/mo) | 18.7 ± 39.8 | 19.0 ± 41.4 | 0.83 |
| Physical activity index | 30.9 ± 4.7 | 30.9 ± 4.5 | 0.94 |
| Depressive symptoms (%) | 10.0 | 11.2 | 0.29 |
| Stroke (%) | 4.5 | 4.4 | 0.85 |
| Cancer (%) | 14.3 | 12.8 | 0.22 |
| CHD (%) | 22.3 | 18.7 | 0.009 |
| Diabetes (%) | 27.0 | 30.4 | 0.027 |
| Hypertension (%) | 53.1 | 54.1 | 0.55 |
| CHD or diabetes or hypertension (%) | 70.0 | 70.2 | 0.92 |

Values shown are age-adjusted mean ± SD for indirect measures and proportion for direct measurements.

**Supplementary Table 2. Effects of minor alleles on transcription factor (TF) binding.**

| SNP | Result | TF | Biological Pathways | Tissue* |
|---|---|---|---|---|
| *rs768023* | abolish | FOXA2 | stem cell maintenance, vascular epithelia, diabetes, energy response | Liver, Lung, Pancreas, Stomach |
| | abolish | HDAC | stem cell maintenance | Lymphoblasts, Colon, Esophagus, Ovary, Small Intesting, Spleen, Thyroid |
| *rs1536057* | abolish | NRF1 | stem cell maintenance | Brain |
| | abolish | E2F | DNA damage response | Lymphoblasts |
| | create | POU5F1 | stem cell maintenance | - |
| *rs2253310* | create | TFCP2L1 | stem cell maintenance | Kidney, Salivary Gland, Skin, Thyroid |
| *rs2802288* | create | MYF | stem cell maintenance, muscle atrophy | Muscle |
| *rs2764264* | abolish | NKX3 | stem cell maintenance | Salivary Gland, Prostate |
| *rs2802292* | create | HSF1 | stress response | most tissues, not Brain |
| *rs12202234* | abolish | FOXA | stem cell maintenance, vascular epithelia, diabetes, energy response | Bladder, Breast, Prostate |
| *rs17069665* | abolish | MITF | stem cell maintenance | Cervix, Uterus |
| *rs12213895* | create | MEF2 | stem cell maintenance | Artery, Lung, Skin |
| *rs12212067* | create | MZF1 | stem cell maintenance | Brain, Lung, Ovary, Pituitary, Prostate, Thyroid, Uterus |
| *rs9398171* | create | NR2F1 | stem cell maintenance | Bladder, Brain, Cervix, Fallopian Tube, Lung, Nerve, Ovary, Prostate, Uterus |
| | create | HNF4 | diabetes, energy response, | Colon, Liver, Small Intestine |
| | abolish | ONECUT1 | stem cell maintenance, diabetes, energy response | Liver, Pancreas |
| *rs73763159* | abolish | PRDM1 | stem cell maintenance | Esophagus, Vagina |
| *rs3800230* | abolish | FOXP1 | stem cell maintenance | - |
| *rs1935952* | abolish | MZF1 | stem cell maintenance | Brain, Lung, Ovary, Pituitary, Prostate, Thyroid, Uterus |

The 14 SNPs modify 19 TF binding sites shown below, along with their functions. SNP ID# is variant name from the database dbSNP, create/abolish refers to whether the minor allele creates or abolishes a TF binding site.
Significant variants were identified previously [Donlon, T.A., et al. FOXO3 longevity interactome on chromosome 6. Aging Cell. 2017; 16:1016-1025] using HaploReg (https://pubs.broadinstitute.org/mammals/haploreg/haploreg.php), which is a tool for exploring annotations of the noncoding genome at variants on haplotype blocks, such as candidate regulatory SNPs at disease-associated loci [Ward, L.D. & Kellis, M. HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. Nucleic Acids Res. 2012; 40 (Database issue):D930-934]. Expression data are from GTEX; * >100 TPM.