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RESEARCH ARTICLE SUMMARY

AGING

Taurine deficiency as a driver of aging

Parminder Singh^{†*}, Kishore Gollapalli[‡], Stefano Mangiola[‡], Daniela Schraner[‡], Mohd Aslam Yusuf[‡], Manish Chamoli[‡] *et al.*

INTRODUCTION: Aging is an inevitable multifactorial process. Aging-related changes manifest as the “hallmarks of aging,” cause organ functions to decline, and increase the risk of disease and death. Aging is associated with systemic changes in the concentrations of molecules such as metabolites. However, whether such changes are merely the consequence of aging or whether these molecules are drivers of aging remains largely unexplored. If these were blood-based drivers of aging, then restoring their concentration or functions to “youthful” levels could serve as an antiaging intervention.

RATIONALE: Taurine, a semiessential micro-nutrient, is one of the most abundant amino acids in humans and other eukaryotes. Earlier studies have shown that the concentration of taurine in blood correlates with health, but it is unknown whether blood taurine concentrations affect aging. To address this gap in knowledge, we measured the blood concentration of taurine during aging and investigated the effect of taurine supplementation on health span and life span in several species.

RESULTS: Blood concentration of taurine declines with age in mice, monkeys, and humans. To investigate whether this decline contributes to aging, we orally fed taurine or a control solution once daily to middle-aged wild-type female and male *C57Bl/6J* mice until the end of life. Taurine-fed mice of both sexes survived longer than the control mice. The median life span of taurine-treated mice increased by 10 to 12%, and life expectancy at 28 months increased by about 18 to 25%. A meaningful antiaging therapy should not only improve life span but also health span, the period of healthy living. We, therefore, investigated the health of taurine-fed middle-aged mice and found an improved functioning of bone, muscle, pancreas, brain, fat, gut, and immune system, indicating an overall increase in health span. We observed similar effects in monkeys. To check whether the observed effects of taurine transcended the species boundary, we investigated whether taurine supplementation increased life span in worms and yeast. Although taurine did not affect the replicative life span of unicellular yeast, it increased life span in multicellular worms. Investigations into the mechanism or mechanisms through

which taurine supplementation improved the health span and life span revealed that taurine positively affected several hallmarks of aging. Taurine reduced cellular senescence, protected against telomerase deficiency, suppressed mitochondrial dysfunction, decreased DNA damage, and attenuated inflammation. An association analysis of metabolite clinical risk factors in humans showed that lower taurine, hypotaurine, and *N*-acetyltaurine concentrations were associated with adverse health, such as increased abdominal obesity, hypertension, inflammation, and prevalence of type 2 diabetes. Moreover, we found that a bout of exercise increased the concentrations of taurine metabolites in blood, which might partially underlie the antiaging effects of exercise.

CONCLUSION: Taurine abundance decreases during aging. A reversal of this decline through taurine supplementation increases health span and life span in mice and worms and health span in monkeys. This identifies taurine deficiency as a driver of aging in these species. To test whether taurine deficiency is a driver of aging in humans as well, long-term, well-controlled taurine supplementation trials that measure health span and life span as outcomes are required. ■

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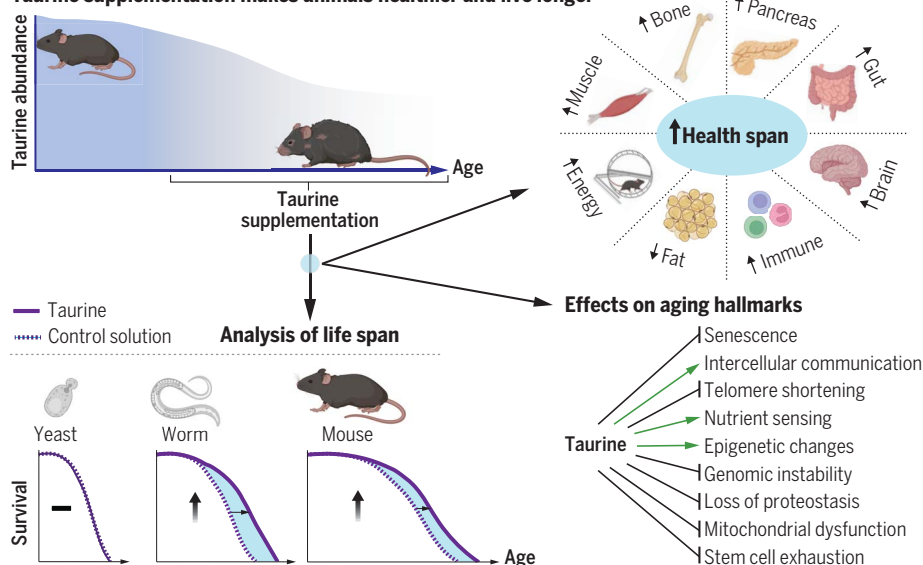
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Cite this article as P. Singh *et al.*, *Science* **380**, eabn9257 (2023). DOI: 10.1126/science.abn9257

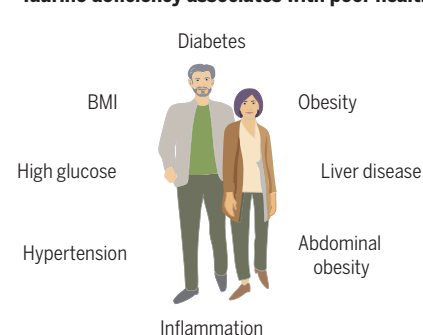
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Taurine supplementation makes animals healthier and live longer



Taurine deficiency as a driver of aging. Taurine concentration in blood declines with aging (top left). A reversal of this drop through taurine supplementation increased healthy life span in mice and worms but not in yeast (bottom left and top middle). Taurine supplementation affected several hallmarks of aging (middle). In humans, lower taurine concentrations were associated with multiple diseases (top right). A randomized controlled clinical trial in humans is warranted to assess the antiaging effects of taurine (bottom right). BMI, body mass index.

Taurine deficiency associates with poor health



Missing piece: Randomized clinical trial



RESEARCH ARTICLE

AGING

Taurine deficiency as a driver of aging

Parminder Singh^{1†‡}, Kishore Gollapalli^{2‡§}, Stefano Mangiola^{3,4,5,6¶}, Daniela Schraner^{7,8¶}, Mohd Aslam Yusur^{9¶}, Manish Chamoli^{10¶}, Sting L. Shi^{2#}, Bruno Lopes Bastos¹¹, Tripti Nair¹², Annett Riermeier⁷, Elena M. Vayndorf¹³, Judy Z. Wu¹³, Aishwarya Nilakhe¹, Christina Q. Nguyen¹³, Michael Muir¹³, Michael G. Kiflezghi¹³, Anna Foulger¹⁰, Alex Junker¹⁴, Jack Devine¹⁴, Kunal Sharan¹⁵, Shankar J. Chinta¹⁰, Swati Rajput¹⁶, Anand Rane¹⁰, Philipp Baumert⁷, Martin Schönfelder⁷, Francescopaolo Iavarone¹⁷, Giorgia di Lorenzo¹⁷, Swati Kumari¹, Alka Gupta¹, Rajesh Sarkar¹, Costerwell Khyriem^{18,19}, Amanpreet S. Chawla^{20,21}, Ankur Sharma^{18,19}, Nazan Sarper²², Naibedya Chattopadhyay¹⁶, Bichitra K. Biswal¹, Carmine Settembre^{17,23}, Perumal Nagarajan^{24,25}, Kimara L. Targoff²⁶, Martin Picard¹⁴, Sarika Gupta¹, Vidya Velagapudi²⁷, Anthony T. Papenfuss^{3,4}, Alaattin Kaya²⁸, Miguel Godinho Ferreira¹¹, Brian K. Kennedy^{29,30,31}, Julie K. Andersen¹⁰, Gordon J. Lithgow¹⁰, Abdullah Mahmood Ali³², Arnab Mukhopadhyay¹², Aarno Palotie^{27,33,34}, Gabi Kastenmüller⁸, Matt Kaeberlein¹³, Henning Wackerhage⁷, Bhupinder Pal^{3,4,5,6}, Vijay K. Yadav^{1,2,15,35*}

Aging is associated with changes in circulating levels of various molecules, some of which remain undefined. We find that concentrations of circulating taurine decline with aging in mice, monkeys, and humans. A reversal of this decline through taurine supplementation increased the health span (the period of healthy living) and life span in mice and health span in monkeys. Mechanistically, taurine reduced cellular senescence, protected against telomerase deficiency, suppressed mitochondrial dysfunction, decreased DNA damage, and attenuated inflammaging. In humans, lower taurine concentrations correlated with several age-related diseases and taurine concentrations increased after acute endurance exercise. Thus, taurine deficiency may be a driver of aging because its reversal increases health span in worms, rodents, and primates and life span in worms and rodents. Clinical trials in humans seem warranted to test whether taurine deficiency might drive aging in humans.

According to the World Population Prospects of the United Nations, the number of people aged 65 and older will increase from 1 in 11 in 2019 to 1 in 6 in 2050 (1). Although this is a success of modern medicine and of government policies, it is vital to ensure that the elderly also remain healthy, because this will increase the quality of life and reduce the costs associated with societal aging (2–5). Over the past two decades, efforts to identify antiaging interventions that reduce morbidity and increase life span have intensified (2–11). This has led to the identification of compounds that may increase healthy life span (the period of life span spent in good health) such as rapamycin, metformin, nicotinamide

adenine dinucleotide (NAD) precursors, and senolytics (2–6, 12).

Aging is a complex process that affects all organs (13, 14). The age-induced decline in organ functions involves several cell-autonomous events termed “hallmarks of aging.” The central hallmarks include genomic instability, deregulated nutrient sensing, mitochondrial dysfunction, stem cell exhaustion, and accumulation of senescent cells (13). Aging-associated decline in organ functions also results from changes in the concentrations of endogenous metabolites, hormones, and micronutrients in blood (15–17). However, it is unclear whether these changes are passengers or drivers of aging. If a molecule in blood is a driver of aging, then

a correction to its youthful levels would delay aging and increase healthy life span.

Taurine (2-aminoethanesulfonic acid), a semiessential micronutrient, is one of the most abundant amino acids found in organisms across eukaryotic phyla (18–22). In mammalian cells, taurine is produced from cysteine through the action of cysteine sulfinic acid decarboxylase (CSAD) (20). Taurine can also be obtained from the diet and is taken up by cells through taurine transporters (20). Taurine deficiency during early life causes functional impairments in skeletal muscle, eye, and the central nervous system (23–26) that are related to aging-associated disorders. Moreover, concentrations of taurine and its metabolites decline in some tissues with age, and acute taurine supplementation in young animals enhances the functions of several organs (27–35). Given the decline in taurine abundance during aging and its known health effects, we aimed to find out whether taurine deficiency is a driver of aging and affects healthy life span.

Results

Decline of serum concentrations of taurine with age in mice, monkeys, and humans

To comprehensively study whether taurine abundance influences healthy life span, we measured blood taurine concentrations at different ages in mice, monkeys, and humans. In *C57Bl/6J* wild-type (WT) mice, serum taurine concentrations declined from 132.3 ± 14.2 ng/ml at 4 weeks to 40.2 ± 7.1 ng/ml at 56 weeks, which correlates negatively with age (slope = -25.7 ; $p < 2 \times 10^{-16}$) (Fig. 1A). In 15-year-old monkeys, serum taurine concentrations were 85% lower than in 5-year-old monkeys (Fig. 1B). Likewise, taurine concentrations in elderly humans were decreased by more than 80% compared with the concentration in serum of younger individuals (Fig. 1C).

Taurine supplementation increases the life span of mice

To determine whether the observed drop in taurine concentration contributes to aging, we

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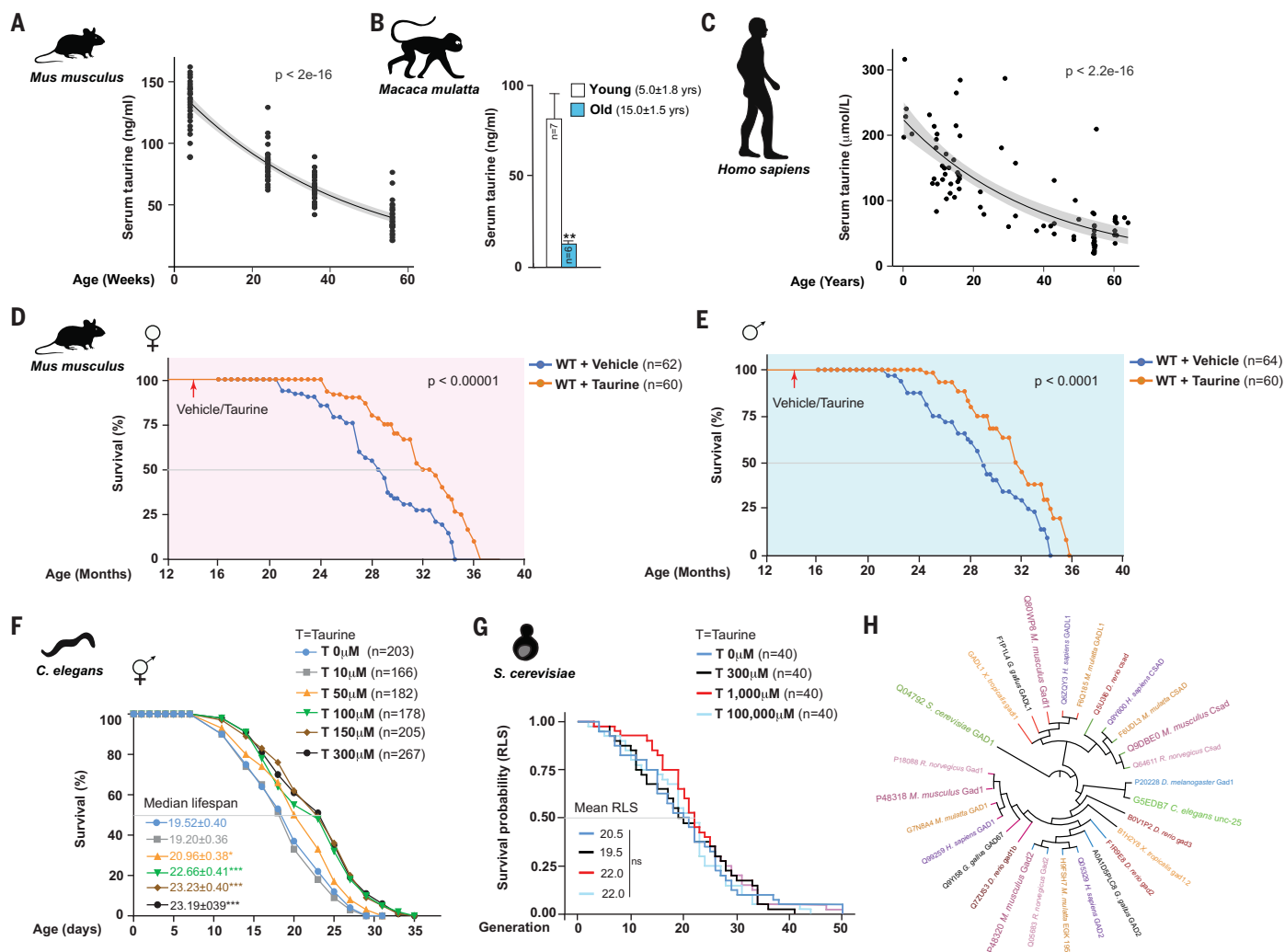


Fig. 1. Taurine deficiency is a driver of aging in evolutionarily divergent species. (A to C) Serum taurine levels in female mice at different ages (A), in young (5-year-old) and old (15-year-old) female monkeys (B), and in humans at different ages (C). In (A) and (C), shaded regions indicate standard error. (D and E) Life-span assay of middle-aged (14-month-old) WT female (D) and male (E) *C57Bl/6J* mice orally fed taurine (1000 mg per kg body weight per day) at 10:00 am until the end of life. (F) Life-span assay of WT nematodes that were fed diet supplemented with different concentrations of taurine (0, 10, 50, 100, 150, and 300 μM). (G) RLS assay in

yeast cultured on YPD plates with different concentrations of taurine (0, 300, 1000, and 100,000 μM). (H) Phylogenetic analysis of taurine biosynthesis enzymes in eukaryotes. Statistical analysis details are as follows: The OASIS software (<https://sbi.postech.ac.kr/oasis>) was used to calculate p values using a log rank test (the Mantel-Cox method) in mice and worm experiments, and a Wilcoxon rank-sum test was used to calculate p values in yeast RLS assays. N values are shown within the panels. All values are means \pm SEM. ns indicates not significant. $***p \leq 0.001$, $**p \leq 0.01$, and $*p \leq 0.05$ are versus WT or control.

orally administered control solution or taurine at 1000 mg per kg body weight (T1000), once daily at 10:00 am, to 14-month-old (middle-aged) *C57Bl/6J* WT female and male mice until the end of life. The dose and frequency of taurine administration was selected based on a pilot study, which showed that when given once daily to middle-aged WT mice, this regimen increased the peak blood taurine concentrations to baseline concentrations in young (4-week-old) mice (see materials and methods and fig. S1, A to D, for a description of these studies). Regardless of their sex, taurine-fed mice survived longer than control mice (Fig. 1, D and E). The median life-span increase was

10 to 12%, and life expectancy at 28 months increased by 18 to 25% (Fig. 1, D and E). Median life-span estimates for control female and male mice were consistent in two independent cohorts (females: 871 to 885 days; males: 785 to 815 days). In these experiments, both control and taurine-fed mice had ad libitum access to the same chow (Teklad Irradiated 18% protein and 6% fat diet-2918). Thus, the improved survival of taurine-fed mice was not a consequence of low survival of control animals or differences in diet. Collectively, these results indicate that taurine deficiency is a driver of aging in mice because its reversal increases life span.

Taurine supplementation increases the life span of worms but not yeast

The taurine biosynthetic pathway is evolutionarily conserved among multicellular eukaryotes (21, 36). To find out whether taurine also affects aging in species other than mice, we conducted taurine supplementation experiments in lower species. First, we tested the effect of taurine in worms, which also exhibit an age-associated decline in taurine (37). Taurine supplementation significantly extended both the median and maximum life spans of *Caenorhabditis elegans* in a dose-dependent manner (Fig. 1F). Longevity, calculated using the median life span of untreated and taurine-treated worms,

was extended by 10 to 23% in worms treated with higher taurine concentrations in four independent worm cohorts and in two independent laboratories (University of Washington, Seattle, WA, USA, and the National Institute of Immunology, New Delhi, India) (Fig. 1F and fig. S1, E to G). We also investigated the effect of taurine on replicative life span (RLS) in budding yeast, *Saccharomyces cerevisiae*, which is a unicellular eukaryote. In contrast to mice and worms, taurine supplementation did not affect the RLS (38) of yeast cultured on nutrient-rich yeast extract-peptone-dextrose (YPD) plates or on a synthetic medium (Fig. 1G and fig. S1, H to J). These results may be explained by organismal differences in taurine metabolism. For example, the taurine metabolism enzymes yeast glutamate decarboxylase (GAD) and mammalian CSAD diverged early during evolution (Fig. 1H) (39). Thus, although taurine may not affect the RLS in unicellular eukaryotes, its effect on life span is conserved in invertebrates and mammals.

Taurine supplementation increases health span in aged WT female mice

A meaningful antiaging therapy should improve health span, or the period of healthy living (2–5, 40). To assess the effects of taurine supplementation on health span, we orally administered taurine at 500 (T500) and 1000 (T1000) mg per kg body weight per day to female mice once daily for 10 to 12 months, starting at the age of 14 months, and analyzed the health of bone, muscle, brain, pancreas, fat, gut, and the immune system through functional assays or tissue analysis of deceased animals (fig. S2A).

Reduced age-associated body-weight gain and improved bone mass in female mice treated with taurine

Taurine treatment suppressed age-associated body-weight gain by ~10% in the T1000 group compared with controls (Fig. 2A). Fat-pad weight divided by body weight percentage was dose-dependently reduced in taurine-treated mice (Fig. 2B). Taurine-administered

mice did not differ in body length and food consumption (in weight-stable mice) or suffer obvious toxic effects (as evidenced by a blinded histopathological scoring of tissue sections by a trained histopathologist) in multiple tissues compared with controls (fig. S2, B to D). Bone structure analysis through histology and microcomputed tomography (μ CT) showed that taurine treatment increased bone mass (bone volume divided by total volume percentage) in both the spine and femur compared with that in controls (Fig. 2C). A three-point bending test showed that femur maximal load and stiffness—two surrogates of bone quality—improved in taurine-treated mice compared with controls (Fig. 2D). Taurine also cured osteoporosis and suppressed ovariectomy-induced body-weight gain in a rodent model of menopause (fig. S2, E to G). This latter evidence indicates that the effect of taurine on health parameters in females might be linked to its effect on body weight in other conditions of aging, such as menopause.

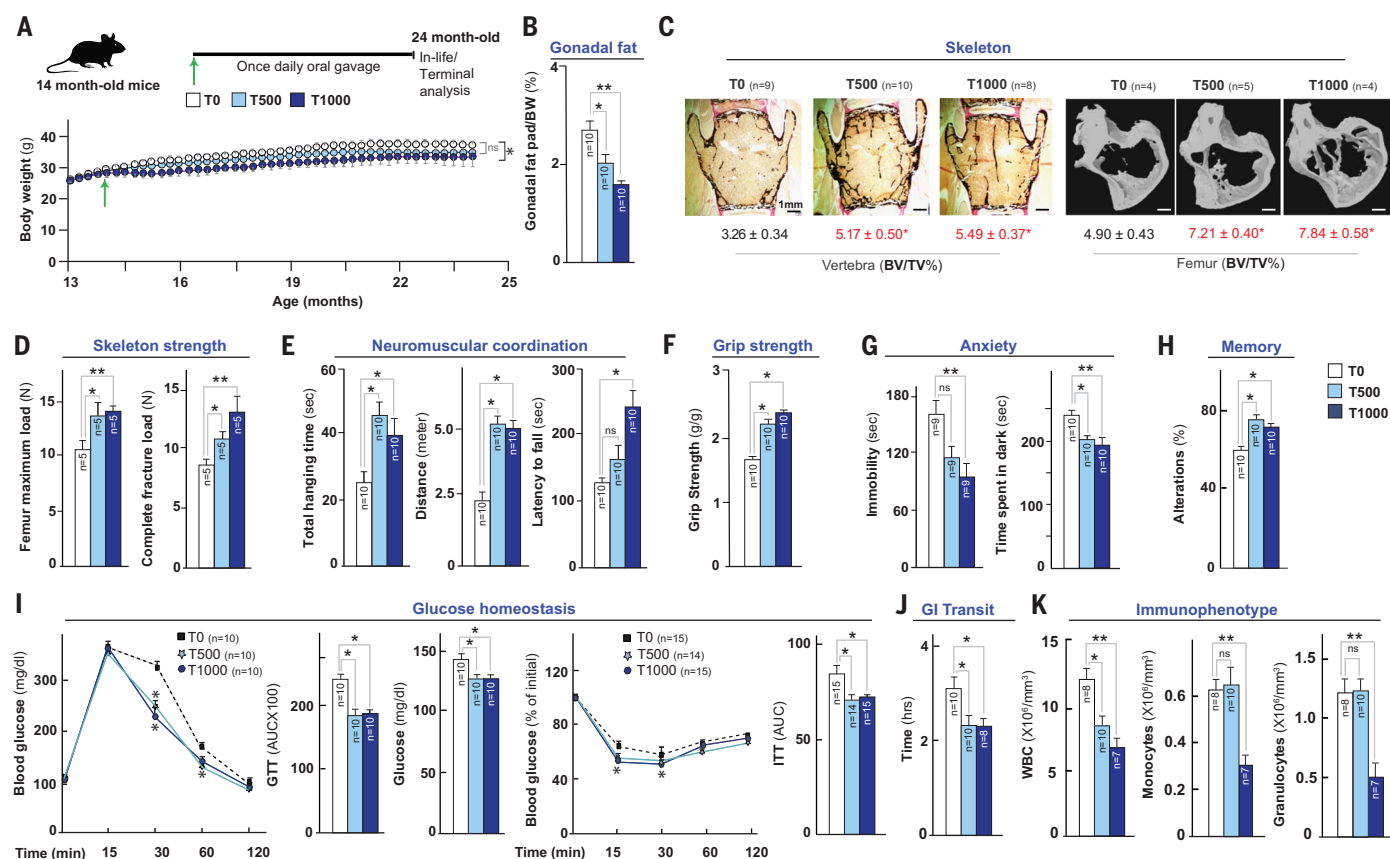


Fig. 2. Taurine supplementation increases health span in aged mice. (A to K) Changes in body weight (A), fat percentage (B), bone structure, strength parameters in spine and femur [(C) and (D)], neuromuscular and muscle strength [(E) and (F)] (rotarod, wire hang, and grip-strength tests), anxiety (G) (tail suspension and dark-light tests), memory (H) (Y maze test), pancreas function (I) (glucose and insulin tolerance tests), GI transit (J) (oral carmine dye test), and immunophenotyping (K) (immune cell parameters in blood) in 24-month-old WT C57Bl/6J female mice orally fed once daily with taurine (0, 500, or 1000 mg per kg

body weight per day) beginning at middle age (14 months). In (C), histology (left) and μ CT (right) images are shown. A statistical analysis was performed using Graph Pad Prism 7. Data were considered statistically significant at $p \leq 0.05$ calculated by using Student's t test, one-way analysis of variance (ANOVA), or two-way ANOVA. n values are shown within the panels. All values are means \pm SEM. ns indicates not significant. $**p \leq 0.01$, and $*p \leq 0.05$ are versus WT or control. BV, bone volume; BW, body weight; GTT, glucose tolerance test; ITT, insulin tolerance test; TV, total volume.

Increased muscle endurance, coordination, and strength in taurine-treated female mice

An analysis of the effect of taurine treatment on neuromuscular functions showed that total hanging time and distance run in the rotarod test was increased in the T500 and T1000 groups, whereas latency to fall in the wire hang test was increased in the T1000 group (Fig. 2E). Grip strength tests revealed that both doses of taurine increased muscle strength compared with controls (Fig. 2F).

Reduced depression-like behavior and anxiety and enhanced exploratory behavior and memory in taurine-treated female mice

Increased anxiety and decreased exploration are common age-induced behavioral changes (41). In the tail suspension test (42), taurine-treated mice showed less depression-like behavior compared with controls (Fig. 2G). The light-dark box test (43) revealed that taurine-treated mice spent less time in the dark area, which is indicative of lesser anxiety (Fig. 2G). The Y maze test (44) showed that taurine-treated mice had a higher natural curiosity for exploration compared with control mice (Fig. 2H).

Improved glucose homeostasis and gastrointestinal transit time in taurine-treated female mice

Analysis of glucose homeostasis using an intraperitoneal glucose tolerance test showed that taurine-treated mice metabolized oral glucose more efficiently than control mice and had lower glucose concentrations when fed ad libitum (Fig. 2I). Likewise, taurine-treated mice had improved insulin sensitivity in the insulin tolerance test (Fig. 2I). These improvements in glucose homeostasis might be a consequence of the reduced adiposity in taurine-treated mice. Gastrointestinal (GI) transit time increases with age (45). An analysis of intestinal transit time using non-absorbable red carmine dye administered by oral gavage (46) showed a faster transit in taurine-treated mice, which could contribute to the observed weight loss in these mice (Fig. 2J).

Ameliorated myeloid-leukocyte prominence in taurine-treated aged female mice

Aging alters immune cell numbers in the blood, resulting in increased susceptibility to infection (47). A complete blood count showed that taurine treatment decreased the number of white blood cells (WBCs), monocytes, and granulocytes but not the number of red blood cells (Fig. 2K and fig. S2H). Although there was no difference in the efficacy of T500 and T1000 doses on the WBC numbers, the numbers of monocytes and granulocytes were only decreased at the T1000 dose (Fig. 2K). These results show that the myeloid-leukocyte prominence associated with aging-related inflammatory states is ameliorated by high-dose taurine treatment.

Improved health-span metrics in middle-aged male WT mice after taurine administration

To assess whether taurine affects the health span of male mice, as it does in female mice, we treated 14-month-old WT male mice with or without T1000 for 8 to 16 weeks and measured fat, bone, muscle, pancreas, and brain health (fig. S3A). Taurine did not affect body-weight gain in males up to 16 weeks but significantly reduced fat-pad weight divided by body weight percentage compared to controls (fig. S3, B and C). To identify the cause of the reduced adiposity of taurine-treated mice, we analyzed energy expenditure. Taurine-treated mice consumed more oxygen, generated more carbon dioxide, and had higher respiratory exchange ratios and energy expenditures even though their total activity was decreased compared with that of controls (fig. S3, D to H). Taurine-treated male mice also showed greater muscle strength, neuromuscular coordination, bone density, glucose tolerance, and memory as well as reduced anxiety compared with controls (fig. S3, I to N). Thus, taurine supplementation improved the function of every organ investigated in middle-aged female and male mice and likely increased overall health span.

Effects of taurine on cellular mechanisms in increasing healthy life span

What are the mechanisms through which taurine affects cellular functions to increase healthy life span? To address this question, we performed an RNA-sequencing (RNA-seq) analysis in taurine-deficient and control osteoblasts from mice. These bone-forming cells were chosen because they abundantly express a taurine transporter (encoded by *Slc6a6*), whose deletion impairs differentiation and function of mutant cells in culture and in mice (fig. S4, A to E). Conversely, numbers and function of WT osteoblasts were increased by taurine treatment in vitro and in vivo. (fig. S4, A to E). RNA-seq analysis (48) of taurine-deficient osteoblasts showed that the top biological functions identified in the gene-set enrichment analysis (GSEA) are related to aging mechanisms (13) such as telomere function, oxidative stress, immune system function, protein translation, and stem cell maintenance (Fig. 3A and figs. S4, F to M). A search for the term “aging” in the GSEA pathways output showed significant alterations in six gene signatures (see table S1 for details). All six signatures showed the expected direction of change (up- or down-regulation) for a pro-aging effect (fig. S4N). Together, these results imply that taurine deficiency generates an aging-related transcriptional signature in cells.

Suppression of senescence by taurine

A network analysis of taurine-regulated genes showed that senescence-associated secretory phenotype (SASP) genes, such as *p16* and *p21*,

which encode inhibitors of cyclin-dependent kinases and promote cell cycle arrest, formed the highest number of genetic interactions (fig. S4O). Consistent with the idea that taurine suppresses senescence, irradiation-induced increase in senescence-associated β -galactosidase (SA β -gal) staining in osteoblasts cultured with taurine was about one-fourth of that in cells cultured without taurine (fig. S4P). In neuronal culture experiments, taurine supplementation increased neuronal survival after treatment with paraquat, a DNA damaging agent that induces senescence (49) (fig. S4Q). Moreover, taurine supplementation decreased an age-associated increase in senescence in mice (Fig. 3, B and C, and fig. S5A). To test whether taurine deficiency causes accumulation of senescent cells, we used mice lacking the taurine transporter *Slc6a6* (23). Lack of *Slc6a6* compromises taurine entry into embryonic cells, rendering embryos deficient in taurine. The phenotypes observed postnatally in 0.5- to 3-month-old *Slc6a6* mutant mice (23) could be due to taurine deficiency affecting these phenotypes during development or postnatally (hereafter, we refer to these mice as congenitally taurine-deficient mice). Adult *Slc6a6*^{-/-} mice showed accelerated aging-related phenotypes, including decreased bone density, poor neuromuscular coordination, compromised muscle strength, increased anxiety, and decreased memory (fig. S5, C to L). Analysis of bone, muscle, brain, fat, and liver showed increased senescence in taurine-deficient mice compared with controls (fig. S5, A and B). To investigate whether accumulation of senescent cells in these organs contributes to the compromised health span of taurine-deficient mice, we treated 8-month-old *Slc6a6*^{-/-} mice with or without a combination of senolytics—dasatinib (D) (50) and quercetin (Q) (D+Q treatment)—bimonthly for 4 months. Relative to controls, D+Q-treated *Slc6a6*^{-/-} mice had a lower abundance of SASP markers (fig. S5M). D+Q treatment also improved bone-, muscle-, anxiety-, and memory-related parameters in *Slc6a6*^{-/-} mice (fig. S5, N to Q). Taurine-deficient mice had shorter lives than WT mice, and the median life span of mutant mice that received senolytic treatment until the end of life increased by ~21% (Fig. 3D). The finding that senolytic treatment did not rescue the shorter life span of taurine-deficient mice suggests that taurine also affects other factors besides senescence. We therefore assessed molecular and cellular features of other aging hallmarks in taurine-supplemented middle-aged mice and in taurine-deficient mice.

Taurine suppresses adverse consequences of telomerase deficiency

Replication-based telomere shortening triggers cellular senescence and affects aging (51). Taurine supplementation in mice or zebrafish or its deficiency in mice did not affect telomerase

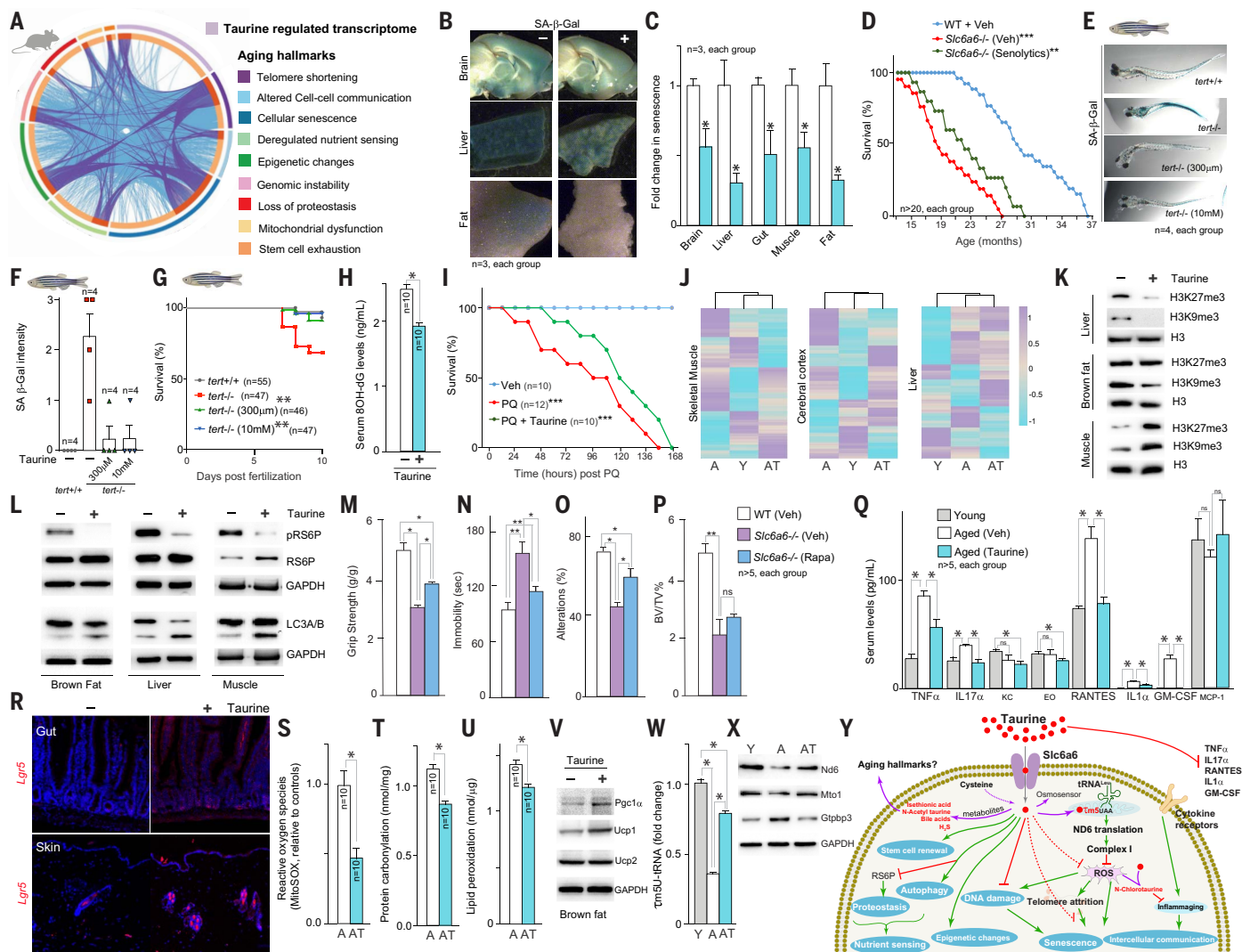


Fig. 3. Taurine regulation of healthy life span is associated with alterations in multiple aging hallmarks. (A) Circos plot representing a comparative analysis of a taurine-deficient transcriptome with the core gene signatures of nine aging hallmarks. (B and C) SA β -Gal staining (blue-stained cells) (B) and relative quantification of staining (C) in tissues collected from mice with or without taurine supplementation, as viewed with whole-mount imaging. (D) Life-span assay of congenitally taurine-deficient (*Slc6a6*^{-/-}) mice and littermate controls that received either vehicle or rapamycin (once daily for 6 weeks). (E to G) SA β -Gal staining photomicrographs (E), relative quantification of staining (F), and survival analysis (G) of telomerase-deficient [*tert*^{-/-}(G2)] zebrafish embryos with or without taurine supplementation (300 μ M or 10 mM) beginning at 2 dpf. (H) Serum 8-OH-dG concentrations in vehicle-treated (-) or taurine-treated (+) mice. (I) Kaplan-Meier survival curves for mice after paraquat (PQ) treatment, with or without prior taurine supplementation (T1000 for 1 month). Veh, vehicle. (J and K) Comparative DNA methylation levels of 2045 age-related CpG sites in the muscle, cerebral cortex, and liver (J) and changes in histone H3K27me3, H3K9me3, and H3 levels in the liver, brown fat, and muscle (K) of 4-month-old WT (young, Y), 16-month-old vehicle-treated WT (aged, A), and 16-month-old taurine-treated WT (aged-taurine, AT) mice. (L) Changes in phosphoribosomal S6 protein (pRS6P) and LC3A/B levels in the brown fat, liver, and muscle of vehicle- or taurine-treated aged mice. GAPDH, glyceraldehyde phosphate dehydrogenase. (M to

P) Changes in muscle function (grip-strength test) (M), anxiety (tail suspension test) (N), memory (Y maze test) (O), and bone mass [bone volume divided by total volume percentage (BV/TV%)] (P) in 6-month-old *Slc6a6*^{-/-} mice and littermate controls that received either vehicle or rapamycin (once daily for 6 weeks). (Q) Serum levels of various cytokines in young mice, aged mice, and aged mice treated with taurine. EO, eotaxin; KC, keratinocyte cytokine. (R to V) In situ hybridization analysis of *Lgr5* expression in the gut and skin (R), levels of mitochondrial ROS (superoxide anion radicals, MitoSOX assay) in skeletal muscle mitochondria (S), protein carbonyl levels in the liver (T), lipid peroxidation levels in the liver (U), and Pgc1 α , Ucp1, and Ucp2 levels in the brown fat (V) of aged mice treated without or with taurine. (W and X) Changes in tRNA modification (W) and Nd6, Mto1, and Gtpbp3 protein levels in the liver (X) of young mice, aged mice, and aged mice treated with taurine. In (W), $n \geq 6$ mice in each group. (Y) Schematic representation of the effect of taurine and taurine-derived biomolecules (in red) on classical hallmarks of aging. For (K), (L), (V), and (X), Western blots are representative of at least three independent biological replicates. Statistical analysis details are as follows: For (D), (G), and (I), the OASIS software (<https://sbi.postech.ac.kr/oasis>) was used to calculate p values using a log rank test (the Mantel-Cox method), and for other panels, statistical analysis was performed with Graph Pad Prism 7 using Student's t test or one-way or two-way ANOVA. All values are means \pm SEM. ns indicates not significant. *** $p \leq 0.001$, ** $p \leq 0.01$, and * $p \leq 0.05$ are versus WT or control.

gene expression (fig. S5, R and S). To investigate whether taurine affects telomerase deficiency-induced deterioration in organismal health, we used a zebrafish model of telomerase deficiency (52). *tert*^{-/-}(G2) fish show an increase in senescence, and ~40% of them die within 10 days postfertilization (dpf) (52). Supplementing the medium used for *tert*^{-/-}(G2) fish with taurine, starting at 2 dpf, suppressed senescence (Fig. 3, E and F). Moreover, at concentrations of 300 μ M and 10 mM, taurine rescued lethality in *tert*^{-/-}(G2) zebrafish embryos (Fig. 3G).

Taurine suppresses DNA damage and improves the survival of mice after oxidative DNA damage

Aging is associated with genomic DNA lesions in multiple cell types (53). Taurine supplementation reduced serum 8-hydroxydeoxyguanosine (8-OH-dG) abundance, a measure of oxidative DNA damage (54), in aged mice (Fig. 3H). Conversely, DNA damage [measured as the abundance of phospho- γ -H2A histone family member X (H2Ax)] was increased in the muscle of taurine-deficient mice (fig. S5T). In a paraquat model of DNA damage-induced lethality, mice administered with paraquat without prior taurine supplementation died within 150 hours, but mice treated with taurine lived slightly longer (Fig. 3I). Thus, taurine supplementation suppressed DNA damage and improved the survival of mice after oxidative DNA damage.

Taurine affects epigenetic changes in the genome

Methylation at CpG sites and of histones changes with age and affects the state of chromatin, which affects DNA packaging and gene expression (55, 56). We therefore analyzed changes in methylation of 2045 CpG sites and measured two histone modifications [histone 3 lysine 9 trimethylation (H3K9me3) and histone 3 lysine 27 trimethylation (H3K27me3)] in multiple tissues obtained from untreated or taurine-treated middle-aged mice and compared them with those in tissues from young mice. Clustering analysis showed that the CpG methylation pattern in the muscle and cerebral cortex of taurine-treated old mice was more similar to that in young mice than to that in untreated old mice (Fig. 3J). However, the pattern in liver from taurine-supplemented mice was more similar to that in old mice than to that in young mice (Fig. 3J). Conversely, muscles from taurine-deficient mice showed changes in the amount of CpG site methylation, and the DNA methylation pattern of muscles in 70-week-old taurine-deficient mice was similar to that in 206-week-old WT mice (fig. S5U). Taurine treatment decreased the abundance of H3K9me3 in brown fat and liver but increased it in skeletal muscle; H3K27me3

abundance was suppressed in the liver, increased in muscle, and unaffected in brown fat (Fig. 3K). The varied changes in DNA and histone methylation indicate that taurine may affect chromatin conformation, which could contribute to altered transcription during aging.

Taurine modulates nutrient sensing and proteostasis pathways

Aging cells have a reduced ability to sense nutrients and maintain proteostasis (57). We assessed changes in nutrient sensing by measuring the phosphorylation of ribosomal S6 protein (RS6P), a key regulator of ribosomal function, and proteostasis by measuring changes in abundance ratio of isoforms A and B of the light chain 3 (LC3A/B), an autophagy marker. Taurine supplementation decreased phosphorylation of RS6P in the liver, brown fat, and skeletal muscle (Fig. 3L). Phosphorylation of RS6P was increased in the muscle of taurine-deficient mice (fig. S5V). Taurine-supplemented mice had more autophagy (as judged by LC3A/B abundance) in the liver, brown fat, and skeletal muscle, whereas it was decreased in taurine-deficient mice (Fig. 3L and fig. S5V). To test whether an increase in phosphorylation of RS6P and a decrease in autophagy contribute to the compromised health span in taurine-deficient mice, we treated *Slc6a6*^{-/-} mice with or without rapamycin [8 mg per kg body weight intraperitoneally once daily (58) for 6 weeks], which inhibits phosphorylation of RS6P and increases autophagy. Compared with control mice, rapamycin-treated taurine-deficient mice showed improved muscle-, anxiety-, and memory-related parameters but not increased bone mass (Fig. 3, M to P). Thus, the effects of taurine supplementation on nutrient sensing and proteostasis pathways contribute to its beneficial effects on several health parameters.

Taurine effects on inflammatory cytokines

Intercellular communication is compromised with age (59). One example is the accumulation of proinflammatory and other cytokines (59). Serum concentrations of tumor necrosis factor- α (TNF α), interleukin-17 α (IL-17 α), RANTES (regulated upon activation, normal T cell expressed and presumably secreted), IL-1 α , and granulocyte-macrophage colony-stimulating factor (GM-CSF) were increased in middle-aged mice compared with young mice, but taurine-treated middle-aged mice had amounts of these cytokines that were similar to those in young control animals (Fig. 3Q). These results, together with the observation that the ratio of myeloid cells to lymphoid cells was significantly decreased in taurine-supplemented mice (Fig. 2K), indicates that sustained taurine concentrations help prevent the proinflammatory state that is observed during aging.

Positive effects of taurine on the health of stem cells or their renewal

Aging reduces the ability of tissues to regenerate after injury. This is linked to defects in tissue-specific stem cells (60). We analyzed changes in the number of stem cell populations in the gut epithelium and hair follicles obtained from untreated and taurine-treated middle-aged mice through staining for the gene encoding leucine-rich repeat-containing G protein-coupled receptor 5 (*Lgr5*), which is a wntless-related integration site (Wnt) target gene expressed in the stem or progenitor cells (61). The numbers of *Lgr5*⁺ cells in these two tissues were increased by taurine supplementation (Fig. 3R). Conversely, the numbers of *Lgr5*⁺ cells in the gut epithelium and hair follicles were decreased in taurine-deficient mice compared with control mice (fig. S5W). Thus, taurine supplementation may increase the regenerative capacity of some tissues by increasing the number of resident stem cells.

Taurine promotion of mitochondrial health

Compromised mitochondrial biogenesis and oxidative capacity leads to progressive accumulation of reactive oxygen species (ROS)-mediated damage that contributes to aging (62). ROS accumulation in mitochondria isolated from the muscle of taurine-treated middle-aged mice was decreased compared with that in the muscle of control mice (Fig. 3S), whereas it was increased in the muscle of taurine-deficient mice (fig. S6A). Measurement of lipid peroxidation and protein carbonylation, two indirect markers of ROS-induced molecular damage, in the liver showed a decrease (of ~22 and ~11%, respectively) in taurine-supplemented mice compared with control mice (Fig. 3, T and U). Assessment of the abundance of peroxisome proliferator-activated receptor- γ coactivator 1 α (Pgc1 α), a key regulator of mitochondrial biogenesis, and uncoupling protein 1 (Ucp1), which uncouples mitochondrial fuel oxidation and respiration from adenosine triphosphate (ATP) production (63), in brown fat showed increased amounts in taurine-treated middle-aged mice, and their abundance was decreased in taurine-deficient mice (Fig. 3V and fig. S6B). These results indicate that taurine promotion of mitochondrial homeostasis may contribute to its effect on health.

We next investigated how taurine affects cellular mechanisms during aging (24). One pool of cytosolic taurine is actively transported into mitochondria, where it is conjugated to the uridine residue at the wobble position of tRNA^{Leu}(UUA), forming 5-taurinomethyluridine-tRNA^{Leu}(UUA) (τ m5U-tRNA) (64). τ m5U modification is specific to mitochondrial tRNAs (64) and promotes the translation of NADH-ubiquinone oxidoreductase chain 6 protein (ND6), an electron transport chain complex I subunit (64). We therefore measured whether

τ m5U tRNA modification changed during aging in mice. The τ m5U content of tRNAs was reduced by >60% in aged liver compared with young liver; in taurine-supplemented mice, the τ m5U content of tRNAs was reduced by only about 20% (Fig. 3W and fig. S6C). Consistent with the role of τ m5U-tRNA^{Leu} in promoting the translation of ND6, amounts of this protein were decreased in aged mice compared with young mice and were increased by taurine supplementation (Fig. 3X and fig. S6D). Taurine supplementation, however, did not affect the translation of nuclear DNA-encoded mitochondrial oxidative phosphorylation (OXPHOS) proteins in aged mice (fig. S6E). We conducted experiments on worms to test whether regulation of organismal health by taurine requires complex I activity. Taurine increased the motility of control worms, which is indicative of better health status (65), but failed to do so in rotenone-treated worms (fig. S6F), suggesting that increasing mitochondrial complex I activity is a mechanism by which taurine promotes health. The aforementioned analyses of molecular and cellular features of aging hallmarks show that during aging, taurine supplementation may impart health benefits by affecting such features in various cells or tissues (Fig. 3Y).

Lower circulating taurine and its metabolites in humans are associated with multiple age-associated pathologies

To determine whether blood levels of taurine-pathway metabolites (taurine, hypotaurine, and *N*-acetyltaurine) are associated with health variables in humans, we performed an association analysis of circulating taurine metabolite levels with >50 clinical risk factors in 11,966 subjects of the EPIC-Norfolk study (fig. S7, A and B) (66). We found that higher blood taurine and hypotaurine levels were associated with lower body mass index (BMI) and waist-to-hip ratio as well as less abdominal obesity (Fig. 4A). Furthermore, higher levels of taurine metabolites were associated with a lower prevalence of type 2 diabetes and lower glucose levels (Fig. 4A). Also, higher taurine and hypotaurine levels were associated with lower levels of the inflammation marker C-reactive protein (CRP). For liver- and lipid-related traits such as aspartate aminotransferase (AST) and blood cholesterol, we found positive associations with taurine levels but negative associations with those of its precursor hypotaurine (Fig. 4A). Blood cell parameters like hemoglobin, platelets, and WBC count correlated positively with the three taurine metabolites (Fig. 4A). Association does not establish causation, but these results are consistent with taurine deficiency contributing to human aging.

A bout of exercise increases abundance of taurine and its metabolites

We next investigated whether blood levels of taurine-pathway metabolites respond to ex-

ercise, which improves many health- and aging-related variables (67, 68). Specifically, we analyzed concentrations of taurine-pathway metabolites in serum before and after a graded exercise test in male athletes (sprinters, endurance runners, and natural bodybuilders) and sedentary individuals (fig. S7C). Taurine levels significantly increased (1.16-fold) in response to a graded cycle exercise test in all the investigated athlete groups ($p_{\text{bodybuilding}} = 0.046$, $p_{\text{endurance}} = 0.0021$, $p_{\text{sprint}} = 0.0017$) (Fig. 4B) and tended to be higher in the sedentary subjects, although the change was not significant ($p_{\text{sedentary}} = 0.067$) (Fig. 4B). Levels of hypotaurine were significantly increased 1.36-fold in response to exercise in all subjects (Fig. 4C). Levels of *N*-acetyltaurine were significantly increased by 1.18- and 1.28-fold in endurance athletes ($p = 0.027$) and sprinters ($p = 0.0016$), respectively, and tended to be elevated in bodybuilders and sedentary subjects, although the change was not significant ($p_{\text{bodybuilders}} = 0.054$, $p_{\text{sedentary}} = 0.067$) (Fig. 4D). These results are consistent with the notion that an increase in taurine and taurine-related metabolites might mediate some of the health benefits of exercise.

Taurine supplementation improves health parameters in middle-aged nonhuman primates

To test whether taurine has health and anti-aging effects in nonhuman primates, we fed aged rhesus monkeys (15 \pm 1.5 years old, equivalent to 45 to 50 years old in humans) control solution or taurine [250 mg per kg body weight (T250), equivalent to T1000 in mice] at 10:00 am once daily for 6 months and then measured the health variables (fig. S7D). Before the start of taurine supplementation, body weight and bone density were not significantly different in the two groups of aged monkeys (fig. S7, E and F). Three hours after oral feeding, serum taurine concentrations in taurine-fed monkeys were about twice (65.4 \pm 10.1 ng/ml) that in controls (35.1 \pm 7.3 ng/ml). Monkeys that received taurine gained 0.75 kg less body weight, and their fat percentage tended to be lower compared with that of controls (Fig. 4E). In-life dual-energy x-ray absorptiometry (DEXA) analysis after 6 months of taurine treatment showed that taurine increased bone density and content in the lumbar spine (L1 to L4) and legs, but not in the head, in taurine-treated monkeys compared with control monkeys (Fig. 4F and fig. S7, G and H). Serum markers of bone formation (osteocalcin) increased, whereas those of resorption [C-terminal telopeptide of type 1 collagen (Ctx)] decreased about 16 weeks after the start of treatment; these levels were maintained until the end of the dosing period (fig. S7, I and J). Taurine treatment reduced fasting blood glucose concentrations by 19% (Fig. 4G). Taurine also reduced the serum concentrations of liver damage markers AST and alanine transaminase (ALT)

by ~36 and 20%, respectively (Fig. 4, H and I). Numbers of WBCs, monocytes, and granulocytes, which increase with age, were decreased by ~50% in taurine-treated monkeys compared with control monkeys (Fig. 4, J to L). Consistent with the beneficial effect of taurine on the mitochondrial health observed in worms and mice, indirect markers of ROS-induced molecular damage—DNA 8OH-dG, lipid peroxide, and protein carbonyl concentrations—were decreased by ~36, 11, and 20%, respectively, in the sera of taurine-supplemented monkeys (Fig. 4, M to O). Thus, taurine has beneficial effects on most tested health parameters (body weight, bone, glucose, liver, and immunophenotype) in nonhuman primates.

Discussion

Taurine abundance decreases in blood and tissues during aging. We found that a reversal of this decline through taurine supplementation increased markers of healthy life span in worms and mice as well as health span in monkeys, which identifies taurine deficiency as a driver of aging in these species. In mice, the effect of taurine supplementation on healthy life span was greater in females than in males, indicating that sex-specific pathways may mediate taurine action. The optimal dose of taurine to maximize its efficacy differed depending on the physiological functions tested, which was possibly due to a wide variation in the uptake rate, synthesis, and metabolism of taurine in different biological fluids and tissues (24, 69–76).

Taurine appeared to affect all the established hallmarks of aging. Although we do not yet know the initial events that taurine elicits, we provide evidence for the suppressed taurinylation of mitochondrial tRNAs during aging in mitochondrial dysfunction, a prominent feature of aging. It is also possible that other taurine-derived biomolecules besides τ m5U-tRNA may directly or indirectly affect mitochondrial homeostasis or other aging features. Indeed, taurine contributes to the production of several other biomolecules, depending on the cell type or types that affect, or can potentially affect, aging (24). These molecules include *N*-chlorotaurine (77), hydrogen sulfide (H₂S) (78), isethionnic acid (24), *N*-acetyltaurine (79), and 5-taurinomethyl-2-thiouridine (τ m5s2U)-tRNA^{Lys} (24). We propose that a combination of taurine and taurine-derived biomolecules may delay aging by affecting various aging hallmarks in distinct cells and tissues.

The effects of taurine intervention on aging and congenital taurine deficiency in a mouse model are largely consistent, except for body weight accrual and glucose homeostasis (Fig. 2 and fig. S5). The concentrations of taurine in the serum and tissues of congenitally taurine-deficient mice are more severely reduced than in the biological fluids and tissues of aged

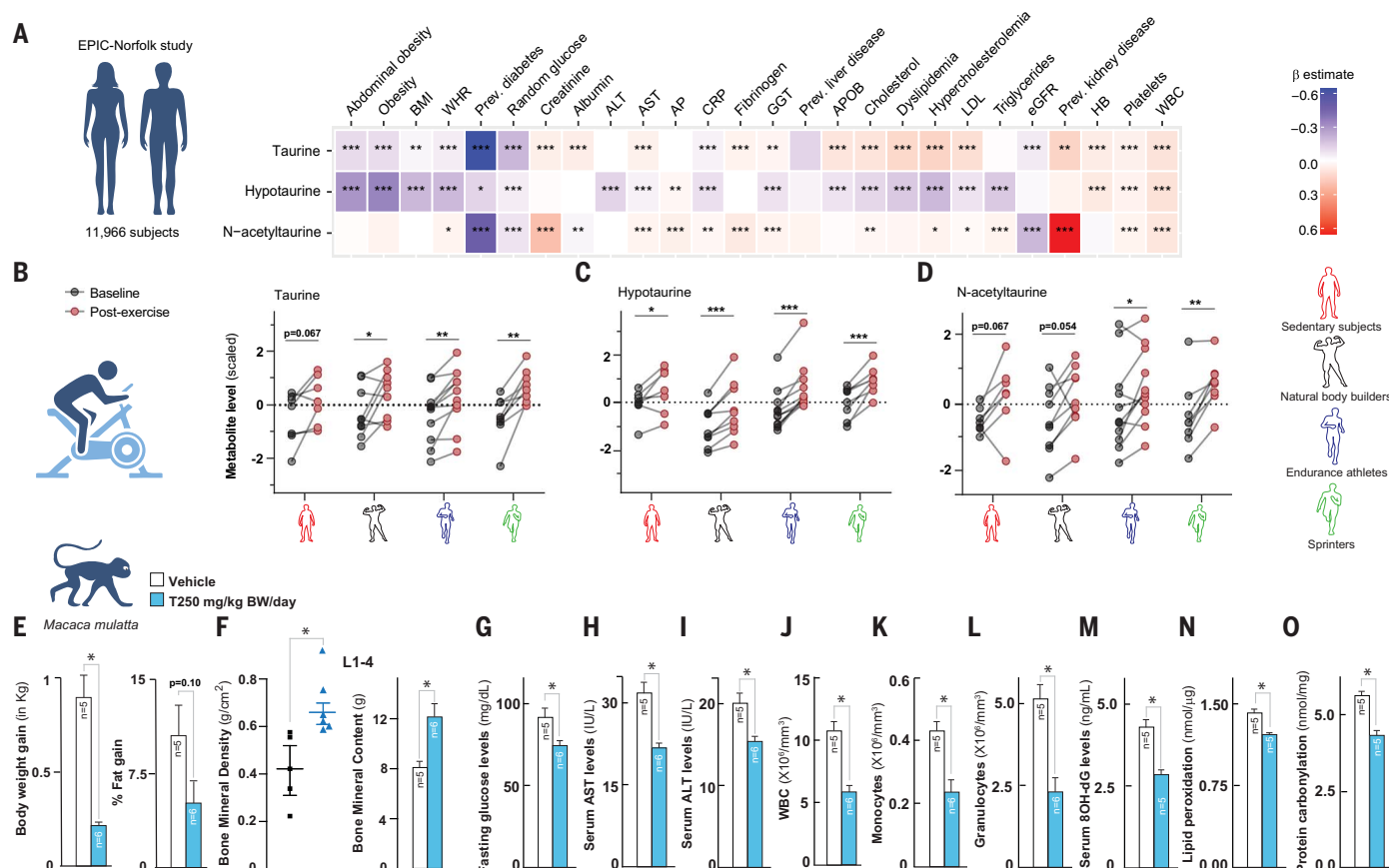


Fig. 4. Taurine pathway affects health span in primates. (A) Heatmap showing the results from linear regression models for assessing the associations between clinical risk factors and taurine-related metabolites (taurine, hypotaurine, and N-acetyltaurine) in blood from 11,966 subjects in the EPIC-Norfolk study. Effect size and direction of these associations are given by the β estimates resulting from these regression models. A negative β estimate (blue color) indicates an inverse association, where higher levels of a metabolite correlated with lower levels of a clinical parameter. A positive β estimate (red color) indicates a positive association, where higher levels of a metabolite correlated with higher levels of a clinical parameter. For example, as shown in blue, higher levels of taurine correlated with a lower prevalence of type 2 diabetes. Taurine-related metabolites were measured using an untargeted metabolomics approach (Metabolon HD4 platform). Data were extracted from the open-access web server located at <https://omicscience.org/apps/mwasdisease/>. AP, alkaline phosphatase; APOB, apolipoprotein B; eGFR, estimated glomerular filtration rate; GGT, γ -glutamyl transferase; HB, hemoglobin; LDL, low-density lipoprotein; WHR, waist-to-hip ratio. (B to D) Serum taurine (B), hypotaurine (C), and N-acetyltaurine (D) levels at fasted rest (baseline) and 5 min after a maximum graded exercise test (postexercise) in three groups of competitive athletes and healthy sedentary subjects. Metabolite levels are provided as z-scores, that is,

relative to the mean of measured levels with mean = 0 and standard deviation = 1. (E to O) Body-weight gain in kilograms and percent fat gain (E); bone mineral density and content in the lumbar spine (L1 to L4) (bone) (F); fasting glucose levels (pancreas function) (G); serum AST and ALT levels (liver dysfunction markers) [(H) and (I)]; WBC, monocyte, and granulocyte numbers (immunophenotyping in blood) [(J) to (L)]; and serum 8-OH-dG, lipid peroxide, and protein carbonyl levels (indirect markers of ROS-induced molecular damages) [(M) to (O)] in 15-year-old monkeys orally fed once daily with vehicle (T0) or taurine (T250) for 6 months. Statistical analysis details are as follows: For (A), summary statistics, including standardized regression coefficients (β estimates) and nominal p values, on a relevant subset of 26 clinical traits and three taurine-related metabolites were extracted from a web server. Regression coefficients and nominal p values were plotted in a heatmap using R version 4.1.0. For the exercise cohort in [(B) to (D)], differences between baseline and postexercise metabolite levels were analyzed per subject group using a paired-sample t test. Batch corrections were done using R version 4.1.0; the graphs were prepared using GraphPad Prism. For [(E) to (O)], statistical analysis was performed with Graph Pad Prism 7 using Student's t test or one-way or two-way ANOVA. All values are means \pm SEM. $p \leq 0.001$ ***, $p \leq 0.01$ **, and $p \leq 0.05$ * are versus WT or control.

rodents and humans (23, 27, 80). However, in the liver, the concentrations of α m5U, a downstream conjugate of taurine, were similarly affected. Thus, during early life, taurine appears to be essential for homeostasis in several organ systems, and its deficiency during development may compromise these functions postnatally. Consistent with this hypothesis, organisms have a three- to fourfold higher taurine concentration in embryonic tissues than in

adult tissues; moreover, taurine deficiency during development leads to growth retardation, blindness, and osteoporosis (25, 81), and its supplementation during gestation increased bone mass postnatally (fig. S5X). This role of taurine in embryonic tissues that affects postnatal phenotypes would be consistent with the theory of the developmental origin of aging phenotypes (82, 83). It is possible that developmental or postnatal changes in taurine me-

tabolism might affect the rate of aging during late life, and adjusting this endogenous machinery might extend healthy life span.

In humans, lower levels of taurine-pathway metabolites were associated with multiple age-associated diseases, such as obesity, diabetes, and inflammation (Fig. 4A). In the FinnGen database (Freeze R5), polymorphisms in the taurine biosynthesis gene, *CSAD*, are associated with hypertension (fig. S7K), and *SLC6A4*

mutations cause retinal degeneration and cardiomyopathy (26, 84). However, taurine supplementation in subjects with metabolic abnormalities does not affect BMI (85). Furthermore, our results, together with those of previous studies (86, 87), show that taurine concentrations increase in healthy men after acute endurance exercise and after 24 weeks of exercise training in obese individuals. Although the mechanisms that increase blood taurine concentrations after exercise are unclear, these results suggest that some of the health benefits of exercise may be explained by an increase in blood taurine concentrations.

A limitation of our study is that we have not tested the effect of taurine in male monkeys, and our association studies in humans did not distinguish between sexes. Nevertheless, together with our supplementation studies in 15-year-old monkeys, the results presented in this work suggest that an increase in taurine concentrations or its actions may have the potential to suppress the decline in biological functions that occurs during human aging.

Reversal of taurine deficiency during aging may be a promising antiaging strategy. Given that taurine has no known toxic effects in humans (though rarely used in concentrations used here), can be administered orally, and affects all the major hallmarks of aging, human trials are warranted to examine whether taurine supplementation increases healthy life span in humans.

Methods summary

Life-span analysis

Mice

Life-span analysis was performed in middle-aged mice that were administered once-daily oral taurine supplementation with or without other interventions.

Yeast

RLS of yeast was assessed on nutrient-rich YPD plates or on a synthetic medium with or without taurine.

Worms

The life span of worms was assessed on agar plates supplemented with taurine or without.

Health-span analysis

The functions and health of various organs in middle-aged mice and monkeys were assessed after taurine supplementation and included the following: body weight; fat-pad weight; bone histology and μ CT or DEXA measurements of bone; rotarod, wire-hang, and grip-strength tests of neuromuscular strength; glucose and insulin tolerance tests of glucose homeostasis; tail suspension, light-dark box, and Y maze tests of behavior; GI transit tests; energy expenditure tests; and blood counts of immune cells. Aging hallmarks were assessed

in WT middle-aged mice supplemented with taurine, taurine-deficient mice, telomerase-deficient zebrafish, and worms. This analysis included assessments of senescence through SA β -Gal staining, SASP markers, irradiation, and senolytic intervention in taurine-deficient mice; DNA damage by using molecular markers and paraquat-induced lethality assays; telomere function by using telomerase expression in mice and zebrafishes and in telomerase-deficient zebrafishes; epigenetic changes based on CpG and histone methylations; nutrient sensing and proteostasis through phospho-RS6P measurements, autophagy marker analysis through LC3A/B abundance, and rapamycin intervention in taurine-deficient mice; and mitochondrial function through ROS measurements. In addition, electron transport chain assessments, Western blotting of OXPHOS proteins, and rotenone assays were performed in worms; stem cells were assessed using *Lgr5* in situ hybridization; and cytokine levels were measured in the blood. A human association analysis of taurine-pathway metabolites with health variables was performed in individuals from the EPIC-Norfolk study. Effect size and direction of these associations are given by the β estimates resulting from these regression models. A negative β estimate indicates an inverse association, where higher levels of a metabolite correlated with lower levels of a clinical parameter. A positive β estimate indicates a positive association, where higher levels of a metabolite correlated with higher levels of a clinical parameter. The effect of exercise on serum levels of taurine-pathway metabolites in humans was assessed before and after an endurance exercise test in athletes (sprinters, body builders, and marathon runners) and sedentary individuals. A detailed account of the methods and statistical analyses used in this study is provided in the supplementary materials.

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ACKNOWLEDGMENTS

We thank D. Renn for histology, H. Liu for genotyping, S. Surender for monkey experiments, and G. Karsenty and V. Mahajan for facilities. V.K.Y. dedicates this study to the memory of his mother, Bhagwati Devi, for showing the path of perseverance. **Funding:** This work was funded by a Nathan Shock Center of Excellence in the Basic Biology of Aging Project Grant (V.K.Y.); National Institutes of Health (NIH) R01HD107574 (V.K.Y.); Wellcome 098051 (V.K.Y.); Deutsche Forschungsgemeinschaft (DFG) 450149205-TRR333/1 (P.B., H.W.); NIH P30AG013280 (M.K.); NIH T32AG066574 (M.G.K.); Institut National Du Cancer (INCa) PLBIO21-228 (M.G.F.); Science and Engineering Research Board (SERB) STR/2019/00064 (A.M.); Department of Biotechnology (DBT) BT/PR40325/BTIS/137/1/2020 (B.K.B.); a Longevity Impetus Grant (A.K.); Academy of Finland Center of Excellence in Complex Disease Genetics grant nos. 312074, 336824, and 352793 (A.P.); The Sigrid Juselius Foundation (A.P.); a Larry L. Hillblom Foundation Fellowship (M.C.); Victorian Cancer Agency (VCA) Fellowship nos. ECRF21036 (S.M.) and MCRF21002 (B.P.); and a DBT Ramalingaswamy Fellowship (V.K.Y.). **Author contributions:** Conceptualization: V.K.Y.; Investigation: P.S., K.G., S.M., D.S., M.A.Y., M.C., B.L.B., A.N., S.L.S., A.Ri., E.M.V., A.F., T.N., A.J., J.D., J.Z.W., C.Q.N., M.M., M.G.K., K.S., S.J.C., S.R., S.K., A.Ra., P.B., M.S., F.I., G.d.L., A.G., R.S., C.K., A.S.C., A.S., N.C., B.K.B., P.N., V.V., A.M.A., V.K.Y.; Analysis and interpretation: D.S., P.S., M.C., K.G., S.M., M.A.Y., B.L.B., A.N., S.L.S., A.Ri., E.M.V., A.F., T.N., A.J., J.D., J.Z.W., C.Q.N., M.M., M.G.K., K.S., S.J.C., S.R., A.Ra., P.B., M.S., F.I., G.d.L., A.G., R.S., C.K., A.S.C., A.S., N.C., B.K.B., P.N., A.M., N.S., V.V., A.P., B.K.K., C.S., K.L.T., M.P., A.T.P., A.K., M.G.F., J.K.A., G.J.L., A.M.A., G.K., M.K., H.W., B.P., V.K.Y.; Funding acquisition: V.K.Y.; Project administration: V.K.Y., H.W., B.P., M.K., G.K.; Supervision: V.K.Y., H.W., G.K., B.P., M.K., A.M., B.K.B., S.G., M.G.F., M.C.; Writing – original draft: V.K.Y.;

Writing – review and editing: V.K.Y., H.W., M.A.Y., B.P., G.K., M.K., D.S., A.M., P.S., M.C., K.G., S.M. **Competing interests:** Columbia University has filed provisional patent applications on which V.K.Y. is listed as an inventor. The remaining authors declare no competing interests. **Data and materials availability:** All data are available in the main text or the supplementary materials. The codes used for data analysis are stored publicly at github main_taurine.R at https://github.com/stemangiola/singh_et_al_taurine_bone/blob/master/main_taurine.R. Sequencing scaled counts have been deposited at Zenodo (88).

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SUPPLEMENTARY MATERIALS

science.org/doi/10.1126/science.abn9257
Materials and Methods

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MDAR Reproducibility Checklist

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Submitted 1 January 2022; resubmitted 20 September 2022
Accepted 14 April 2023
[10.1126/science.abn9257](https://doi.org/10.1126/science.abn9257)

Taurine deficiency as a driver of aging

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Science, **380** (6649), eabn9257.
DOI: 10.1126/science.abn9257

Editor's summary

Aging is associated with physiological changes that range in scale from organelles to organ systems, but we are still working to understand the molecular basis for these changes. Studying various animals, Singh *et al.* found that the amount of the semi-essential amino acid taurine in circulation decreased with age (see the Perspective by McGaunn and Baur). Supplementation with taurine slowed key markers of aging such as increased DNA damage, telomerase deficiency, impaired mitochondrial function, and cellular senescence. Loss of taurine in humans was associated with aging-related diseases, and concentrations of taurine and its metabolites increased in response to exercise. Taurine supplementation improved life span in mice and health span in monkeys. —L. Bryan Ray

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