

tion and the onset of various age-associated pathologies. Recent observations in mice support the idea that removal of senescent cells can extend healthy life span (10, 11). These findings have led to the exploration of pharmacological approaches to induce selective death in senescent cells (senolysis).

Although it has been found that metabolism can influence cellular senescence, a general understanding of the links between metabolism, senescence, and aging is still in its early stages (12). Johmura *et al.* reveal that glutamine metabolism may contribute to the pathogenesis of age-related disorders (see the figure). They found that *GLS1* expression was up-regulated in multiple cell types in response to diverse senescent stimuli, and its depletion induced senolysis and improved various age-associated organ dysfunctions in mice. As a possible mechanism, the authors present evidence that senescent cells utilize glutamine to neutralize the intracellular acidosis that results from senescence-associated lysosomal dysfunction. Indeed, supplementation of ammonia could ablate the senolytic activity of *GLS1* inhibition. A number of interpretations are consistent with this finding, including the anabolic functions of ammonia that could then couple to the activity of the TCA cycle. More analysis of metabolic pathway activity in the presence of ammonia and supplementation with other nutrients might address this. These possibilities could be separate or interconnected metabolic mechanisms from those that involve nicotinamide adenine dinucleotide (NAD⁺), which along with mitochondrial metabolism are perhaps the most studied molecular features associated with aging (13). Given the pleotropic roles of glutamine metabolism,

more work is needed to better define the metabolic requirements of senescent cells.

The general molecular traits of senescent cells and their contribution to aging and related diseases remain open questions (14). The identification of *GLS1* as a senolytic target confirms metabolism as a major regulator of aging, thus providing some rationale for how therapeutics that target metabolism might achieve specificity for senescent cells as anti-aging agents. *GLS1* is an attractive target for anti-aging therapies because clinical studies for cancer indications have so far established safety (4). Much attention has been focused on the use of dietary supplementation or possibly metformin or rapamycin use to manipulate aging. These efforts have included increasing NAD⁺ concentrations and altering mitochondrial metabolism, which, although promising, may not be the entire picture (13). The findings of Johmura *et al.* suggest a complementary strategy, although more research is needed. ■

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J.W.L. advises Restoration Foodworks, Nanocare Technologies, and Raphael Pharmaceuticals.

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CULTURAL EVOLUTION

Behavioral convergence in humans and animals

Local ecology combines with culture to produce behavioral variation in hunter-gatherers

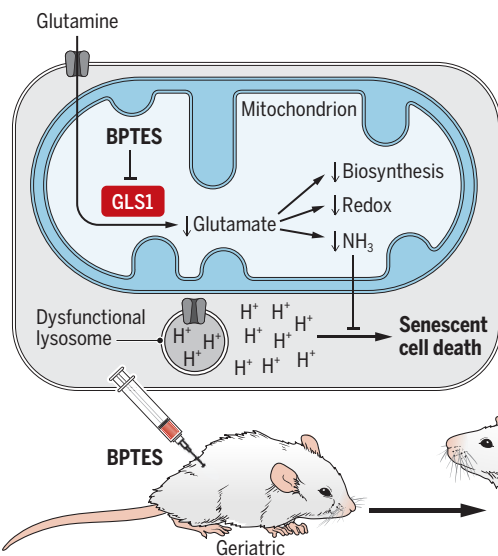
By Kim Hill and Robert Boyd

Over the 20th century, the social sciences developed without taking much notice of humans' nature as products of evolution. In the 1970s this attitude was challenged by behavioral biologists (1, 2) who asserted that general principles concerning the behavior of life forms must also be relevant to understanding human behavior. They argued that because human cognition and emotions had evolved by natural selection, these behavior-generating mechanisms should generally shape behavior so that it maximizes biological fitness. Not all social scientists agreed. Cultural anthropologists, in particular, were mostly aghast at the rigidly scientific and overtly biological nature of this perspective, viewing it as blatantly flawed (3). They claimed that differences between and within human societies were mainly due to variant cultural belief systems. On page 292 of this issue, Barsbai *et al.* (4) show that adaptation to local ecological conditions is an important determinant of variation in human behavior in traditional societies.

The sample analyzed by Barsbai *et al.* consists of 339 hunter-gatherer societies that are most appropriate for comparison because their members' lives and livelihoods are intimately constrained by the natural world. The authors show that variation in hunter-gatherer patterns for 15 behavioral variables statistically converges on the same characteristics that are most common in birds and mammals in the same local regions of the world. These traits include diet composition, mobility patterns, paternal invest-

School of Human Evolution and Social Change, Institute of Human Origins, Arizona State University, Tempe, AZ 85287, USA. Email: kim.hill@asu.edu, robert.t.boyd@gmail.com

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Glutamine in senescence

Senescent cells up-regulate the expression of glutaminase 1 (*GLS1*), which mediates glutaminolysis. This promotes senescent cell survival, possibly by producing ammonia (NH₃), which may neutralize the acidic intracellular pH that results from senescence-associated lysosomal dysfunction. In geriatric mice, bis-2-(5-phenylacetamido-1,3,4-thiadiazol-2-yl)ethyl sulfide (BPTES) administration cleared senescent cells and improved various age-related disorders.

- ↓ Glomerulosclerosis
- ↓ Kidney, liver dysfunction
- ↓ Lung fibrosis
- ↓ Adipose atrophy

ment, divorce rates, social group size, and social stratification. In other words, in places where hunter-gatherers are more polygynous, there also tend to be more polygynous bird and mammal species. These patterns appear to be driven by ecological and habitat similarity, not by locational proximity per se. Not only are hunter-gatherers behaviorally similar in similar ecologies, but even mammals and birds in those ecologies tend to exhibit the same behavioral regularities as do the human populations. Hence, the study appears to validate the basic premise of the evolutionary perspective called “human behavioral ecology” (5, 6).

However, it is a mistake to conclude from this that culture is unimportant.



Penan hunter-gatherers from Borneo extracting sago palm starch, their dietary staple. The Penan were one of 339 societies around the world showing convergence in behavioral patterns with bird and mammal species living in the same habitats (Barsbai *et al.*, this issue).

Beginning in the 1980s, researchers in human behavioral sciences developed a sophisticated, scientific, evolutionary theory accounting for the role of culture in human behavior (7, 8). These scientists provided both theoretical and empirical evidence that social learning was a prime determinant of human behavioral variation. The affective and cognitive mechanisms that underpin social learning are adaptations and are in large part responsible for our species' spectacular ecological success, but they also create historical patterns absent in other species and lead to outcomes not predicted by theories developed for non-cultural creatures.

Barsbai *et al.* show convincingly that ecological factors explain much variation in hu-

man behavior, but so too does cultural history. For example, Mathew and Perreault (9) studied the causes of variation among 172 native American groups in western North America. Like Barsbai *et al.*, they found that ecological factors explained a substantial amount of variation, particularly in behaviors related to subsistence and technology. But the variation in subsistence-related behaviors was equally well explained by the linguistic distance between groups, which proved to be an even better explanation than ecological factors for the variation in political organization, religious practice, and kinship organization. Moreover, the effect of cultural history seems to persist for hundreds or even thousands of years.

Cultural evolution can also lead to outcomes not predicted by the evolutionary mechanisms applied to other species. Barsbai *et al.* show that variation in human residential group size has the same relationship to ecology as in other species. However, human foragers are much more cooperative than other primates (10), and sometimes they cooperate in groups numbering hundreds of individuals in communal foraging, construction of shared capital facilities, and warfare (11). No other vertebrate cooperates on these scales. Exactly why this is the case is controversial, but it seems likely that culturally transmitted social norms play an important role.

Culture and genes are linked in a tight coevolutionary embrace, and this leads to

complex patterns of genetic and cultural coadaptation. For example, Henrich has recently argued (12) that the extent to which people are embedded in networks of kin obligation is a function of both ecological factors (cooperative intensive agriculture) and cultural history (church edicts against kin marriage and collective property institutions), and that variations in the intensity of kin-network embeddedness ultimately transformed human psychology into that observed today in “WEIRD” (Western, educated, industrialized, rich, democratic) societies, where individualism is paramount, rather than the psychology of traditional societies, where collectivism and kin-group favoritism predominate. Experiments show that the cognitive, emotional, and psychological effects of these different cultural histories are profound, and imply that findings from Western modern societies may often be irrelevant to predicting behavior in non-Western and traditional societies. Likewise, the spread of monogamy in modern societies, despite increasing wealth stratification, appears to be a puzzle that requires both adaptive modeling (13) and a recognition that monogamous social norms substantially increased cooperation with societies, and this norm can spread by group competition and cultural imitation (12). Coevolution between genes and culture in different ecologies may lead to uniquely human patterns not anticipated by animal studies. These examples illustrate just how complex human behavioral studies will become when the social sciences fully integrate an adaptive evolutionary view with a view of human behavioral variation in terms of cultural social norms. So far, a complete theory that predicts when culture will override fitness maximizing ecological adaptation and vice versa is not available. That will be the challenge for the next generation of social scientists, as an “either/or” view is replaced with an integrated evolutionary theory of human behavior. ■

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Kim Hill and Robert Boyd

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