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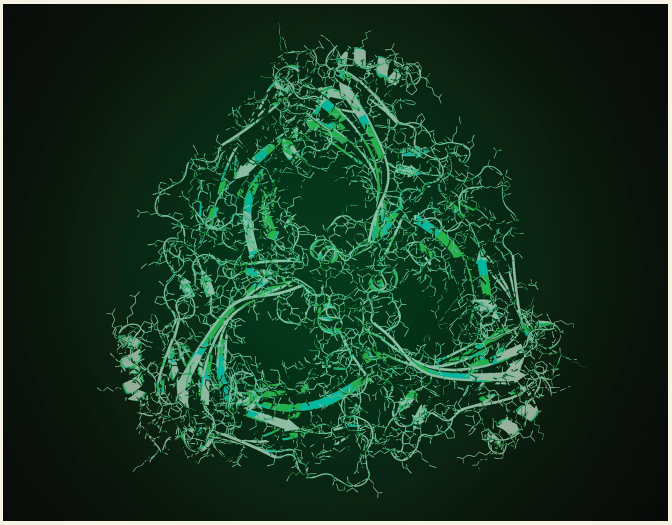
Tau clearance and aggregation in degenerative brain disease

Frontotemporal lobar degeneration (FTLD) is a common cause of dementia. Due to the toxic accumulation of tau in central neurons, both Alzheimer's disease (AD) and FTLD are considered tauopathies, but FTLD neurons lack the amyloid β found in AD. Through experiments with cells and mice, Jung-A Woo et al. (pp. 5006–5015) found that in FTLD the G protein-coupled receptor signaling protein β-arrestin2 is part of a positive feedback loop with tau, in which the proteins amplify each other to fuel neurodegeneration. Furthermore, the authors found that elevated β-arrestin2 inhibits tau clearance and promotes tau aggregation by impairing the function of p62/SQSTM1, a cargo protein involved in autophagy. The authors also present findings demonstrating that genetic ablation of β-arrestin2 reverses tau pathology and restores brain plasticity in transgenic mice. Because p62-mediated autophagy is carried out by the oligomerized form of β-arrestin2, the study represents a proof of concept for novel treatments of tauopathies such as FTLD and AD using small-molecule inhibitors designed specifically to target β-arrestin2 oligomerization, according to the authors. — T.J.



β-Arrestin2 oligomer, which impairs tau clearance in FTLD. Image courtesy of Cynthia Greco and Eric Lewandowski (University of South Florida, Tampa, FL).

Cannabis and false memories

The main psychoactive constituent of cannabis has been associated with memory impairments. However, relatively little is known about the effects of cannabis on the generation of false memories. Lilian Kloft et al. (pp. 4585–4589) conducted a double-blind, randomized, placebo-controlled study of false memory in 64 healthy, occasional cannabis users. In each experiment, the participants inhaled the vapor of a single dose of cannabis or a placebo and then performed memory tasks immediately afterward and 1 week later. In the first experiment, cannabis-intoxicated individuals showed an increase in the false recognition of words that had not been previously presented. In two separate virtual reality experiments, the participants witnessed a fight or perpetrated a theft. The participants were then exposed to misinformation about the scenarios through suggestive questions during an interview or through the testimony of a second virtual witness. The authors report that cannabis appeared to increase false memories for misinformation while subjects were intoxicated, but not 1 week later. According to the authors, the findings carry implications for the questioning of cannabis-intoxicated eyewitnesses and suspects during investigative interviews. — J.W.

Gender inequality in STEM publishing

Gender inequality in STEM academic positions has been documented across disciplines, but the extent of disparities in academic publishing remains unclear. Using data from the Web of Science database, Junming Huang, Alexander Gates, et al. (pp. 4609–4616) examined the publication history of 1.5 million gender-identified authors who published their last articles between 1955 and 2010. The authors found that women represented 12% of active authors in 1955, increasing to 35% by 2005. On average, men published 13 articles during their careers, whereas women published 10 articles, and male scientists received 30% more citations than female scientists. Although the authors found that an increase in the number of women academics has increased the publishing gender gap, they also found that men and women publish a comparable number of articles per

year and have equivalent total citations for the same total number of publications. The authors determined that gender differences in academic publishing are mostly related to the rate of women leaving academia, as female scientists were almost 20% more likely than male scientists to leave academia each year throughout their careers; the dropout rate accounted for 67% of the gender differences in publications. The findings underscore the importance of retention of female scientists at all career stages, according to the authors. — M.S.

Maternal age and offspring reproductive success

Aging patterns vary across individuals of various species, but it is unclear how maternal age at the time of an individual's birth influences the patterns. To measure the senescence and reproductive success of female offspring born to mothers of different ages, Svenja Kroeger et al. (pp. 4809–4814) examined a population of wild yellow-bellied marmots living at two different elevations in the Colorado East River Valley. The data comprised of 656 observations made between 1967 and 2014 of 218 female marmots born to 97 different mothers. Compared with female offspring born to younger mothers, those born to older mothers had greater annual reproductive success and greater lifetime reproductive success. However, compared with high-elevation environments, in low-elevation environments the reproductive success of female offspring born to older mothers decreased faster with age. In harsh high-elevation environments, female offspring born to older mothers tended to have shortened lifespans and died before reaching an age where senescent decreases are perceivable. Further, being born into a large litter negatively influenced the annual reproductive success of female offspring born to older mothers compared with those born to younger mothers. The findings suggest that maternal age, litter size, and environmental factors influence reproductive performance and senescence, according to the authors. — M.S.

Yellow-bellied marmot at the Rocky Mountain Biological Laboratory in Crested Butte, Colorado.

Symbolic behavior in modern humans

Symbolic behavior was essential to the evolution of modern humans, but it is unclear how such behavior evolved. Kristian Tylén et al. (pp. 4578–4584) conducted five experiments using engraved ochre and ostrich eggshell fragments from South Africa's Blombos Cave and Diepkloof Rock Shelter dating to between 52,000 and 109,000 years ago. The authors asked 296 participants in Aarhus, Denmark, to detect patterns presented to one eye while vivid, flickering colors were presented to the other eye. The participants were quicker to identify young patterns than old patterns. When participants were presented with two patterns and asked which was more likely to have been intentionally made by a human, they more often chose the young pattern than the old pattern. When participants saw a pattern for 3 seconds before it disappeared, they were able to reproduce young patterns more accurately than old patterns. Further, when participants were asked to determine which of two patterns came from the same site as a target pattern, they more accurately recognized young patterns than old patterns as belonging to a specific site. The findings suggest that the engravings were created with aesthetic intention and evolved to become easier to remember and replicate, according to the authors. — M.S.

Fragment of engraved ostrich eggshell from the Diepkloof Rock Shelter (Western Cape, South Africa) dating back circa 60,000 years. Image reprinted from P.-J. Texier *et al.*, A Howiesons Poort tradition of engraving ostrich eggshell containers dated to 60,000 years ago at Diepkloof Rock Shelter, South Africa. *Proc. Natl. Acad. Sci. U.S.A.* 107, 6180–6185 (2010).

Immune gene activity in young adults and late-life health

The health of older individuals varies depending on demographic and social factors. Little is known about the biological underpinnings or molecular precursors of late-life health disparities, partly due to the lack of relevant population health studies in young individuals. Steven Cole et al. (pp. 4601–4608) analyzed whole-blood transcriptome data from an ethnically diverse, nationally representative sample of 1,069 young adults in the United States. The authors examined the relationship between gene expression patterns and demographic, sociodemographic, and biobehavioral factors. Each sociodemographic factor analyzed was associated with variation in the expression of hundreds of genes across the genome. The authors also found sociodemographic-related variation in the activity of a prespecified set of 19 proinflammatory genes and 32 genes involved in type 1 interferon responses, which help defend against viral infections. The expression of inflammation-related genes varied most strongly with biobehavioral factors, such as body mass index and smoking, whereas variation in the activity of interferon-related genes was linked most strongly with individual demographic factors, such as sex and race/ethnicity. Taken together, the findings suggest that the activity of genes involved in inflammation and antiviral responses could help explain social and demographic disparities in chronic diseases that emerge decades later. According to the authors, early interventions aimed at reducing immune risk factors for chronic disease may help mitigate late-life health disparities. — J.W.