Further investigations could pave the way to a more complete understanding of the genetics and metabolomics of cell growth in yeast and the underlying mechanisms relevant to other settings in which cells face challenging conditions, such as cancer progression and the evolution of drug resistance.

Reference

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Evolutionary Medicine of Skin Cancer Risk among Europeans

The proclivity of Spaniards to bask in regions like the Costa del Sol while their northern European counterparts must stay under cover to protect their paler skin or risk skin cancer is due in large part to the pigment-producing qualities of the MC1R gene locus. The MC1R gene, expressed in skin and hair follicle cells, is more diverse in Eurasian populations compared with African populations.

Now, a team of researchers led by Santos Alonso (Martínez-Cadenas et al. 2013) has examined the evolutionary selective pressure for MC1R among a large population of Spaniards in comparison with their northern European counterparts as well as individuals with melanoma. Using data from the 1,000 Genomes Project as well as samples from different regions of Spain, the authors show that selection for the MC1R locus is strong in south Europeans, but this is not the case for northern Europeans.

Two evolutionary selective processes seem to be acting on MC1R in southern Europeans. On one hand, there is selective pressure to maintain at high frequencies the ancestral form of the gene, which is also the one most common in Africans. But simultaneously, one gene variant seems to be favored in south Europeans. This gene variant, called the V60L allele, has been associated before with red/blond hair and fair skin.

World frequency distribution of V60L is confined mostly to Europe and the Near East but mostly absent in East Asia and Africa, indicating that the first appearance of the V60L mutation occurred some time after modern humans left Africa but before dispersal throughout Europe. Fair skin depigmentation could be a useful change for the adaptation of humans to this new environment. Traditionally, depigmentation had been hypothetically explained as a function of the need for humans to synthesize vitamin D in areas of reduced sunlight (compared with Africa). "We have not proved that this is the underlying reason for the signature of positive selection on V60L, but our data adds support to this view, although this point needs to be further explored," says Santos Alonso, senior author of the paper.

Interestingly, the same V60L allele has been associated with increased risk of melanoma, the most dangerous of skin cancers. "This indicates," says Saioa López, one of the two main authors of the paper, "that the increase in fitness for the population as a consequence of depigmentation has had a collateral damage consequence for the individual's health. This can be reconciled if we assume that melanoma is typically a post-reproductive disease, and consequently should have little effect on the individual's genetic contribution to the next generation. It constitutes a kind of evolutionary 'buy now, pay later' trade-off."

Reference

Martínez-Cadenas C, López S, Ribas G, et al. (15 co-authors). 2013. Simultaneous purifying selection on the ancestral *MC1R* allele and positive selection on the melanoma-risk allele V60L in South Europeans. *Mol Biol Evol.* 30:2654–2665.

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Genetic Study Pushes Back Timeline for First Significant Human Population Expansion

About 10,000 years ago, the Neolithic age ushered in one of the most dramatic periods of human cultural and technological transition, where independently, different world populations developed the domestication of plants and animals. The hunter-gatherers gave rise to herders and farmers. Changes to a more sedentary lifestyle and larger settlements

are widely thought to have contributed to a worldwide human population explosion, from an estimated 4–6 million people to 60–70 million by 4,000 BC.

Now, researchers Aimé et al. (2013) have challenged this assumption using a large set of populations from diverse geographical regions (20 different genomic regions and mitochondrial DNA of individuals from 66 African and Eurasian populations) and compared their genetic results with archeological findings. The dispersal and expansion of Neolithic culture from the Middle East has recently been associated with the distribution of human genetic markers.

The authors conclude that the first significant expansion of human populations appears to be much older than the emergence of farming and herding, dating back to the Paleolithic (60,000–80,000 years ago) rather than Neolithic age. Therefore, hunter-gatherer populations were able to thrive with cultural and social advances that allowed for the expansion. The authors also speculate that this Paleolithic human population expansion may be linked to the emergence of newer, more advanced hunting technologies or a rapid environmental change to dryer climates.

Finally, they also suggest that strong Paleolithic expansions may have favored the emergence of sedentary farming in some populations during the Neolithic. Indeed, the authors also demonstrate that the populations who adopted a sedentary farming lifestyle during the Neolithic had previously experienced the strongest Paleolithic expansions. Conversely, contemporary nomadic herder populations in Eurasia experienced moderate Paleolithic expansions, and no expansions were detected for nomadic hunter-gatherers in Africa. "Human populations could have started to increase in Paleolithic times, and strong Paleolithic expansions in some populations may have ultimately favored their shift toward agriculture during the Neolithic," said Aimé.

Reference

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X Doesn't Always Mark the Spot

Research from the University of Bath has found a greater number of "escaping genes" on the X chromosome than have been previously detected, with implications for the understanding of mental impairment in humans.

Human females, unlike males, have two copies of the X chromosome. This double dose of the X chromosome presents an interesting genetic conundrum: namely, what happens to the genes on this extra chromosome? If all of the genes were to be expressed, then females would have twice the dose of the genes' products compared with males.

To compensate for this extra set of genes in females, a process called X-Chromosome Inactivation switches off one entire X chromosome and its complement of genes, shriveling it up like a raisin so that the genes can't be expressed.

However, this process is not perfect, and some genes are able to escape this "silencing." These escaping genes are of interest because in about one in a thousand births of girls, the newborn inherits a further copy of the X chromosome, making them XXX rather than simply XX. The very high level of expression of the genes that have escaped X-chromosome inactivation can have serious consequences, including growth abnormalities and mental impairment.

Zhang et al. (2013) have carried out a unique study that has built on previous understanding in this area. Unlike previous research that compared X-chromosome inactivation between mice and humans, this study looked within the human species at two different groups, Europeans and Yorubans from Africa, with interesting results (Zhang et al. 2013).

The study found that 114 genes on the X chromosome had escaped X-chromosome inactivation, including 76 that had not been previously identified.

Co-author Professor Hurst said, "The genes we have identified are located in areas of the X chromosome where we expected to find escaping genes. We have now found that there are also great variations between the two populations we studied, and between individuals within these populations. This level of variation matches what we see in women with three X chromosomes: some appear normal, but some are profoundly affected."

In some individuals, up to 80 genes were shown to escape. The genes that were most variable in escape were also shown to be the fastest evolving. Previous research has found that escaping genes undergo stronger purification selection—the process of selective removal of genes that are deleterious or harmful—but the current evidence didn't confirm this.

The work has implications for understanding genetic diseases. Hurst commented that "importantly, our research could tie in the sorts of genes that escape X-chromosome inactivation with the symptoms of having too many X chromosomes, in that the genes we found were commonly those previously associated with mental impairment, the most common symptom of XXX syndrome."