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Synopsis

DARWIN AND NATURAL SELECTION:
ARE WE STILL EVOLVING?

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DARWIN AND NATURAL SELECTION: ARE WE STILL EVOLVING?

"A good definition of culture could be: anything that curbs natural selection." This is according to Jaume Bertranpetit, researcher at the Institute for Evolutionary Biology (CISC-UPF) in Barcelona and co-leader of this B·Debate session with Elena Bosch. If natural selection is the basic mechanism behind evolution as proposed by Darwin, and if human beings are deeply immersed in what we call culture, the question is: are we still evolving?

The short answer is yes, at least if we take into account the past thousands of years. Examples of genetic adaptations after the first humans left Africa can be seen in **lighter skin tone** to improve vitamin D production, **ability to digest milk** throughout our lives and **certain populations' adaptation to higher elevations**. New genetic tools are making it possible to explore other changes not by observing traits but through the marks natural selection leaves on the genome.

To discuss the latest advances in this field, several top international experts met for the debate entitled 'Natural Selection in Humans: Understanding our adaptations', organized by B·Debate –an initiative of Biocat and the "la Caixa" Foundation to promote scientific debate– and the Institute for Evolutionary Biology (CSIC-UPF) and Pompeu Fabra University (UPF).

CONCLUSIONS

- Genetic tools are allowing us to disentangle the marks left by natural selection in humans over the past thousands of years.
- Some of the more recent changes include lighter skin tone to take advantage of sunlight and adapting to life at higher elevations or specific diets.
- The immune system is one of the parts of the body that shows the most variation among populations, and could explain differences in response to infectious diseases, which varies widely in time and space, and in the frequency of autoimmune diseases.
- There are traits that seem to be changing, like a tendency to be taller. However, scientists doubt this is a mechanism of natural selection.

1. EVOLUTION AND GENOME ANALYSIS

"We're trying to get a more unified view of natural selection as seen from the National Geographic reports and what we see in genetics," explained Jaume Bertranpetit. To do so, laboratories all over the world are comparing millions and millions of pieces of data: they're looking for changes in the DNA sequence that are consistently different among today's populations and/or they are comparing our genetic information with that of our ancestors. Then they try to establish what has caused these changes, an advantage or simply chance: they are trying to figure out whether they were selected. And, if they were, why.

There are many changes that could take place and they aren't always easy to identify. Sometimes they are **specific mutations**, changes in a single gene that are beneficial depending on the context. This is what has allowed most of the modern population to **continue drinking milk without problems throughout their lives**: 10,000 years ago, one single genetic mutation (although it could have been several) allowed the body to manufacture lactase –the protein that allows us to digest milk- throughout life and not just as infants (as is common in nature). The advantage was important, taking into account that humans had already began raising livestock, and the mutation was selected in the European population to such an extent that **between 60% and 90% of the European population now carries this mutation**.

Sometimes, however, the mutations affect multiple genes, and it is the sum of their effects that accounts for the final result. This tends to be more complicated to study, and is what happens with **the change of skin tone**. As humans moved away from the equator and were exposed to less sunlight, their skin became lighter, very possibly to make the most of the available sun and continue producing vitamin D, which in generally very scarce in our diet.

On other occasions, the genetic "novelties" are "borrowed" from other species. Some of our genes come from **cross-breeding with other archaic humans such as Neanderthals or Denisovans.** This is known as introgression.

There are many mechanisms, and it is difficult to establish whether the results are truly due to natural selection. For Aida Andrés, researcher at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, "**It is clear that we have adapted to new environments since humans left Africa, although diversity is very limited overall**." Elena Bosch suggests the possibility that "Perhaps selection is there but we don't have the means to identify the changes or explain them." And she adds, "If we take into account all the laboratories working on this topic and the number of genes sequenced, we're not having much success. But **each sign is fascinating and fantastic**."

And there are quite a few. Here are some examples.

2. RECENT ADAPTATIONS: ELEVATION, FAT, INFECTIONS

"As humans migrated, they found themselves in different environments and had to adapt," explained Emilia Huerta-Sánchez, professor at the University of California, Merced, in the United States. **One of the adaptations can be seen in the inhabitants of Tibet**, used to living at high elevations where the air has considerably less oxygen than at sea level.

When other populations climb to higher elevations, their bodies react by producing more hemoglobin and red blood cells. This helps the blood transport more oxygen and compensate for the fact that there is less available (this is what many athletes look for when training at high elevations). This strategy, however, comes with its risks: the more cells in the blood, the thicker it is and the greater the risk of clots.

Tibetans, however, don't have high hemoglobin levels. Why don't their bodies react in the same way? The answer seems to be in the EPAS1 gene, among others. Scientists believe a mutation of the gene, widespread among this population, changes this response and protects them against thickening blood. "**This adaptation seems to have come from introgression of the Denisovans**," Huerta-Sánchez explained and published (it has hardly ever been found beyond the Tibetan and Denisovan populations). "**And it seems to have continued being selected for the past 3,000 years**," added Anna di Rienzo, professor at the University of Chicago. What isn't totally clear are the genetic traits that allow them to work at high elevations. Some could be associated with the EPAS1 gene, which has many functions. These seem to include ones that help increase the number of blood vessels (capillaries) in muscles.

Another example of a recent adaptation can be seen in the Inuit population, the native inhabitants of Greenland. Given their environment, for many years they have eaten "a diet low in carbohydrates and very high in proteins and omega-3 fatty acids (found in fish and marine mammals)," said Rasmus Nielsen, professor at the University of California, Berkeley. The "consequences" can be seen in their genome: **a selection has occurred in the genes responsible for synthesizing fatty acids**. Their bodies produce fewer of their own to compensate for the huge amounts they consume. This is why "**we can't directly extrapolate the theoretical benefits of their diet to other populations**."

There are more examples that consistently demonstrate recent adaptations: in areas where **malaria** is endemic, most of the population bears a mutation of the hemoglobin gene that

causes sickle-cell anemia. The risk is compensated because this variant protects against infection.

Bertranpetit's group showed that **pygmies** on the Andaman Islands, in the Indian Ocean, had been selected to be shorter, which when there are no predators has certain metabolic advantages. And his team also participated in describing **how the plague helped select** the genomes of many Europeans, those most resistant to the infection.

If there is one thing subject to evolution, it seems to be our defenses.

3. THE IMMUNE SYSTEM AND NATURAL SELECTION

"**Infections have been a huge cause of mortality in humans practically until just *yesterday***," said Lluis Quintana-Murci, director of the Institut Pasteur in Paris. "Immune responses to them vary among individuals, and among populations, too," he continued.

In 2016, his team published a revealing paper. They took defense cells from Africans and Europeans and exposed them to different bacterial and viral products. In studying their response, they saw that **the African cells were three times more powerful**. Hundreds of genes were expressed differently and changes in the genetic sequence –some inherited from the Neanderthals- explained most of these differences. Does this mean Africans have better defenses? Not necessarily. The hypothesis is that Europeans, as they were in contact with fewer pathogens, adapted by relaxing their defenses. And that could explain their lower rate of autoimmune diseases. It is a question of balancing risk and reward.

There are also individual differences. As explained Mihai G. Netea, head of the Experimental Medicine Laboratory at Radboud University Nijmegen Medical Center, in the Netherlands, "Some (non-immunodepressed) patients beat a Candida infection in just 1-2 days, while it takes others more than 10."

In an attempt to explain this, "**several consortia have been set up to study what is a healthy immune response and how it varies among individuals and populations**," explained Quintana-Murci. These groups will analyze genetic and epigenetic aspects —including the role of the microbiome— and will also do exhaustive interviews to determine hereditary influence and that of the environment.

4. THE DEBATE: ARE WE STILL EVOLVING?

"**Cultural innovations keep genetic mutations alive that in other times wouldn't be allowed**," said Elena Bosch, professor at Pompeu Fabra University and the

Institute for Evolutionary Biology and co-leader of this B·Debate. For Laurent Excoffier, professor at the Institute of Ecology and Evolution at the University of Bern, Switzerland, "It will be difficult to find clear, non-polygenic examples of natural selection in places that are not extreme." Beyond these locations, are we still adapting? "We don't know. We have to keep looking," said Bertranpetit.

Recently, however, curious data has appeared. There seem to **be signs of selection pointing to tallness in northern Europe**, and a selection that favors individuals that are blonde and have blue eyes. Is that adaptation? For Bertranpetit, this "**isn't natural selection but possibly sexual selection**". Sexual selection is another mechanism —also proposed by Darwin— of selection that takes into account what is most "attractive", not what is most "appropriate". "The problem is that these are hypotheses, and we don't have a way to differentiate between the two mechanisms," he said.

Another controversial paper found that **reproductive success seems to be greater in people who carry genes that predict a lower level of education**. This would imply a small trend towards there being fewer people predisposed to being more intelligent. And leads to Quintana-Murci's question: "What do we say when the topic of eugenics comes up?"

The answer was conclusive and unanimous: more education is necessary.