Taming wild animals with a single gene change, a genomic take on goat domestication

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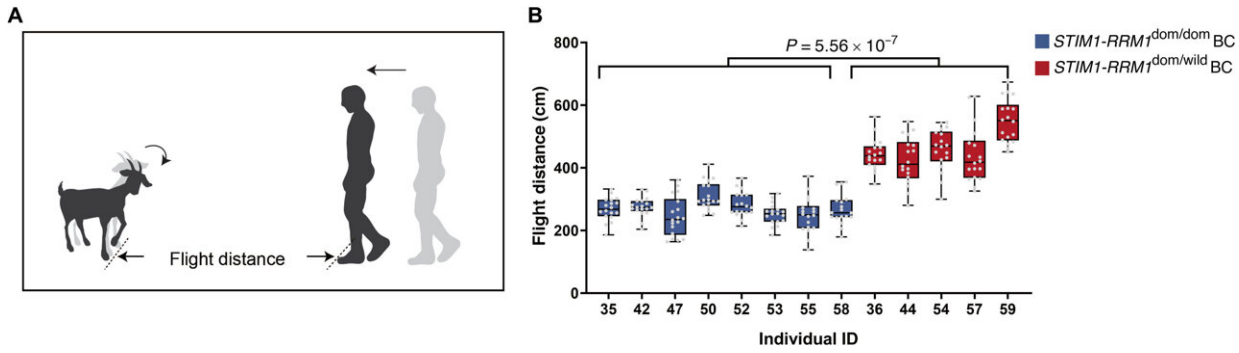

The association between the STIM1-RRM1 locus and tameness. (A) Schematic representation of FD test. The FD was measured when a standing idle goat started to move away from an approaching individual. (B) The FD of the ibex-goat hybrid individuals. The P value between the two groups was calculated by one-way ANOVA. Credit: *Science Advances* (2023). DOI: 10.1126/sciadv.adf4068

Domestication of animals may have a genetic component, according to research led by Northwest A&F University in China. In their paper, "A missense mutation in RRM1 contributes to animal tameness," published in *Science Advances*, the team makes a case for a single base pair substitution of gene RRM1 as the origin of animal tameness.

The current study builds on previous goat research by members of the team that initially discovered the genetic divergence of the

STIM1-RRM1 and MUC6 gene loci in a rare mtDNA haplogroup A around the point of goat domestication. If these genes in a set of early female goats are responsible for offspring with less fear and stress reactions, they would have either been selected intentionally by early goat farmers for breeding or may have simply better survived the stress of domestication.

The MUC6 gene enhances immune resistance to gastrointestinal pathogens, which would have made for healthier stock. STIM1 regulates calcium and glutamate receptor signals in the nervous system, with the implication of inducing reduced anxiety. RRM1 is involved in DNA synthesis, repair, and maintenance and has been linked to neural tube defects in mice and behavior disorders in humans.

Behavior tests of a wild-domestic hybrid goat population indicated that the locus under the most substantial artificial selection during domestication is the same as the one with the missense mutation of RRM1 in the early domestic goat ~6,500 years ago.

Goat domestication was investigated using a selection of genomes from 210 domestic goats from four continents, 24 wild bezoar ibex and 70 ancient goat genomes. The bezoar is a wild goat species native to the Caucasus and the Zagros Mountains of Iran, a potential location of early goat domestication. The researchers conducted a "flight distance" test, which is a measure of how close they could get to a wild goat before it ran away.

The top outlier associated with the skittishness of the goats was the STIM1-RRM1 locus, indicating that this locus represents a function with broad significance to goat domestication.

Genome editing of RRM1 to the variant type in mice showed increased tameness, sociability and reduced anxiety around humans. These

behavioral changes, induced by the change in RRM1, were sourced to altered activity of glutamatergic synapse and other synapse-related pathways. This suggests that the pathways involved in the RRM1 variant goats might be the same across many domesticated species.

At the end of any good study, more questions have been raised, and more research is needed. Here we have the prospect of a genetically induced tameness that could be leveraged in the domestication of currently wild animals, inviting them to the list of pets or livestock, or as a conservation strategy.

More information: Mingle Dou et al, A missense mutation in RRM1 contributes to animal tameness, *Science Advances* (2023). DOI: 10.1126/sciadv.adf4068