

Comparative analysis of the domestic cat genome reveals genetic signatures underlying feline biology and domestication

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is known about the genetic changes that distinguish stic cat populations from their wild progenitors. Here we describe a high-quality domestic cat reference genome assembly and comparative inferences made with other cat breeds, wildcats, and other mammals. Based upon these comparisons, we identified positively selected genes enriched for genes involved in lipid metabolism that underpin adaptations to a hypercarnivorous diet. We also found positive selection signals within genes underlying sensory processes, especially those affecting vision and hearing in the carnivore lineage. We observed an evolutionary tradeoff between functional olfactory and vomeronasal receptor gene repertoires in the cat and dog genomes, with an expansion of the feline chemosensory system for detecting pheromones at the expense of odorant detection. Genomic regions harboring signatures of natural selection that distinguish domestic cats from their wild congeners are enriched in neural crest-related genes associated with behavior and reward in mouse models, as predicted by the domestication syndrome hypothesis. Our description of a previously unidentified allele for the gloving pigmentation pattern found in the Birman breed supports the hypothesis that cat breeds experienced strong selection on specific mutations drawn from random bred populations. Collectively, these findings provide insight into how the process of domestication altered the ancestral wildcat genome and build a resource for future disease mapping and phylogenomic studies across all members of the Felidae.

Felis catus | domestication | genome

he domestic cat (*Felis silvestris catus*) is a popular pet species, with as many as 600 million individuals worldwide (1). Cats and other members of Carnivora last shared a common ancestor with humans ~92 million years ago (2, 3). The cat family Felidae includes ~38 species that are widely distributed across the world, inhabiting diverse ecological niches that have resulted in divergent morphological and behavioral adaptations (4). The earliest archaeological evidence for human coexistence with cats dates to ~ 9.5 kya in Cyprus and ~ 5 kya in central China (5, 6), during periods when human populations adopted more agricultural lifestyles. Given their sustained beneficial role surrounding vermin control since the human transition to agriculture, any selective forces acting on cats may have been minimal subsequent to their domestication. Unlike many other domesticated mammals bred for food, herding, hunting, or security, most of the 30-40 cat breeds originated recently, within the past 150 y, largely due to selection for aesthetic rather than functional traits.

Previous studies have assessed breed differentiation (6, 7), phylogenetic origins of the domestic cat (8), and the extent of recent introgression between domestic cats and wildcats (9, 10). However, little is known regarding the impact of the domestication process within the genomes of modern cats and how this compares with genetic changes accompanying selection identified in other domesticated companion animal species. Here we describe, to our knowledge, mplete APPROVED

Significance

We present highlights of the first complete domestic cat reference genome, to our knowledge. We provide evolutionary assessments of the feline protein-coding genome, population genetic discoveries surrounding domestication, and a resource of domestic cat genetic variants. These analyses span broadly, from carnivore adaptations for hunting behavior to comparative odorant and chemical detection abilities between cats and dogs. We describe how segregating genetic variation in pigmentation phenotypes has reached fixation within a single breed, and also highlight the genomic differences between domestic cats and wildcats. Specifically, the signatures of selection in the domestic cat genome are linked to genes associated with gene knockout models affecting memory, fearconditioning behavior, and stimulus-reward learning, and potentially point to the processes by which cats became domesticated.

Cats are popular, but not as good as toads Abthor contributions: M.J.M., G.L., B.G., L.A.L., W.J.M., and W.C.W. designed research; M.J.M., G.L., B.G., P.M., L.W.H., D.C.K., B.W.D., C.A.D., C.S.B., K.B., G.W.C.T., M.W.H., M.M.-R., S.J.O., L.A.L., W.J.M., and W.C.W. performed research; M.J.M., G.L., B.G., B.L.A., S.M.J.S., D.C.K., B.W.D., C.A.D., J.Q., B.L.-G., T.M.-B., C.A., G.W.C.T., M.W.H., R.K.W., L.A.L., W.J.M., and W.C.W. contributed new reagents/analytic tools; M.J.M., G.L., B.G., R.K., B.W.D., J.Q., B.L.-G., T.M.-B., C.A., G.W.C.T., M.W.H., L.A.L., W.J.M., and W.C.W. analyzed data; and M.J.M., G.L., B.G., R.K., P.M., D.C.K., B.W.D., C.A.D., C.S.B., K.B., T.M.-B., M.W.H., L.A.L., W.J.M., and W.C.W. wrote the paper.

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