Genes contribute to behavior differences between fierce and friendly rats

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After many generations, rats bred for their bad attitude behave differently from those selected for a calm demeanor around humans. Research published November 7 in the journal *Genetics* identifies gene regions that contribute to differences between nasty and nice rats in their behavior and the activity of genes in the brain. These results may provide important clues as to which genes make tame animals like dogs behave so differently from their wild ancestors.

"Tameness is one trait that all domestic animals share. Whether it's pigs or cats or horses, domestication changed species that used to fear humans into animals that now tolerate and even trust us. This research is an important step in uncovering the genetic basis of such remarkable transformations," said co-author Henrike Heyne, of the Max Planck Institute for Evolutionary Anthropology and the University of Leipzig in Germany.

The rats in the study are descendents of an experiment initiated more than forty years ago by Dmitry K. Belyaev, who is famous for his work on experimental domestication of foxes. Belyaev and his colleagues collected around 200 wild rats and divided them into two groups. In one group, the rats selected for breeding were the most aggressive of the bunch—those most likely to attack or show fear towards an approaching human hand. In the second group, only the tamest rats were bred. After repeating this process for more than sixty generations, rodents in the two groups reacted to humans very differently.

"Rats from the tame group allow you to pick them up and will sometimes even approach your hand on their own. In contrast, the aggressive rats immediately attack you or try to escape," said co-author Frank Albert of the Max Planck Institute for Evolutionary Anthropology and the University of California, Los Angeles.

To find gene variants responsible for these heritable behavior differences, the researchers crossed rats from each of the two groups to create a population of hybrids. These hybrid animals showed a wide range of behaviors and inherited a random mix of genetic variants from the original tame and aggressive parent rats. By combining information on the genes and the behavior of each hybrid, the team identified eight regions of the genome that contributed to the variation in tameness.

Within these broad regions, Heyne and colleagues looked for specific genes of interest by analyzing their activity in the brain. Eleven of the genes within these regions carried variants that made them more active in the brains of aggressive rats compared to tame rats, or vice versa. For five of these genes, the team found additional evidence that the variants regulating activity of the gene were the same variants that influenced behavior.

These five genes may play key roles in shaping behavior in the two populations. Several of the genes are involved in nervous system development and one, *Slc17a7,* has previously been implicated in fear and stress behavior in mice. Further experiments will be required to determine which genes contribute significantly to tameness or aggression.

"These rats are one of those rich experimental resources that keeps providing new insights as our methods and technology advance," said Mark Johnston, Editor-in-Chief of *GENETICS.* "Thanks to the authors' excellent work and to Belyaev's foresight in 1972, we are finally starting

to understand the genetic details of a biological process that has been pivotal to human history."

More information: Genetic Influences on Brain Gene Expression in Rats Selected for Tameness and Aggression, Henrike O. Heyne, Susann Lautenschläger, Ronald Nelson, François Besnier, Maxime Rotival, Alexander Cagan, Rimma Kozhemyakina, Irina Z. Plyusnina, Lyudmila, Trut, Örjan Carlborg, Enrico Petretto, Leonid Kruglyak, Svante Pääbo, Torsten Schöneberg, and Frank W. Albert, *GENETICS*, November 2014 198:1277-1290; DOI: 10.1534/genetics.114.168948

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