Study shows pre-human ancestors adapted to metabolize ethanol long before humans learned about fermentation

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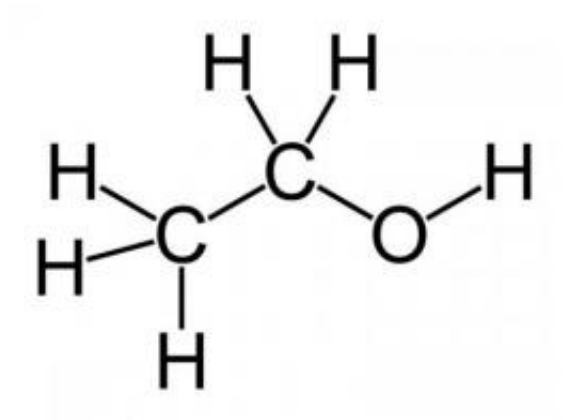

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(Phys.org)—A team of researchers in the U.S. has found evidence to support the notion that our pre-human ancestors were able to metabolize ethanol long before our later ancestors learned to take advantage of fermentation—to create alcoholic beverages. In their paper published in *Proceedings of the National Academy of Sciences*, the team describes how they genetically sequenced proteins from modern primates and used what they found to work backwards to discover just how long ago our ancestors have been able to metabolize ethanol.

Humans have been consuming beverages that make them tipsy, drunk

and/or sick for a very long time, of that there is little doubt. But why do we have the ability to metabolize ethanol in the first place? That's what the team set out to answer. They began by sequencing an enzyme called ADH4—it's what's responsible for allowing us to metabolize ethanol. Other primates have it as well, but not all metabolize ethanol as well as we do. By sequencing ADH4 found in a 28 mammal species including 17 that were primates, the team was able to create a family tree of sorts based on ethanol metabolizing ability. The team then tested those sequences for their metabolizing ability by synthesizing nine kinds of the ADH4 enzyme. Doing so showed the researchers that most early primates had very little ability to metabolize ethanol for most of their early history.

Then, about 10 million years ago, some of the ancestors of modern humans suddenly were able to do a much better job of it, while others that diverged and led to apes such as orangutans, did not. This discovery led the team to wonder what might have occurred to cause this to come about. They note that other evidence has shown that around this same time, the planet cooled slightly, making life a little more difficult for our tree dwelling ancestors. They suggest they began climbing down out of the trees to eat the fruit that fell, which gave them a food advantage and a reason for developing the ability to metabolize ethanol—otherwise they would have become too drunk from eating the fermenting fruit to defend themselves or live otherwise normal lives. If true, the theory would also offer a major clue as to why our ancestors became terrestrial.

More information: Hominids adapted to metabolize ethanol long before human-directed fermentation, *PNAS*, Matthew A. Carrigan, DOI: 10.1073/pnas.1404167111

Abstract
Paleogenetics is an emerging field that resurrects ancestral proteins from now-extinct organisms to test, in the laboratory, models of protein

function based on natural history and Darwinian evolution. Here, we resurrect digestive alcohol dehydrogenases (ADH4) from our primate ancestors to explore the history of primate–ethanol interactions. The evolving catalytic properties of these resurrected enzymes show that our ape ancestors gained a digestive dehydrogenase enzyme capable of metabolizing ethanol near the time that they began using the forest floor, about 10 million y ago. The ADH4 enzyme in our more ancient and arboreal ancestors did not efficiently oxidize ethanol. This change suggests that exposure to dietary sources of ethanol increased in hominids during the early stages of our adaptation to a terrestrial lifestyle. Because fruit collected from the forest floor is expected to contain higher concentrations of fermenting yeast and ethanol than similar fruits hanging on trees, this transition may also be the first time our ancestors were exposed to (and adapted to) substantial amounts of dietary ethanol