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Human Enhancement with the Loss of an Enhancer

A similar search for human-specific DNA deletions in primate genomes found some fascinating candidates. Recalling that the loss of an inhibitor is equivalent to the gain of an activator (think about the Wnt pathway or the double-negative gate in sea urchin blastomeres), McLean and colleagues (2011) uncovered 510 sequences that are present in the genomes of chimpanzees and other mammals but not in humans. One of these deletions is in the forebrain enhancer of the *GADD45G* gene. This gene encodes a growth suppressor that is normally expressed in the ventral forebrain region of chimpanzees and mice, but not humans. When a reporter gene is joined to a chimpanzee *GADD45G* enhancer and inserted into a mouse embryo, the reporter gene is expressed in the mouse brain. However, when joined to a human *GADD45G* enhancer (which is lacking specific regions of the primate enhancer), the reporter gene is not expressed in the mouse brain. This provides evidence that in humans, uniquely, the *GADD45G* enhancer *does* act to suppress a suppressor of brain growth (the *GADD45G* gene).

Literature Cited

McLean, C. Y. and 12 others. 2011. Human-specific loss of regulatory DNA and the evolution of human-specific traits. *Nature* 471: 216–219.
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