Cornell University
College of Veterinary Medicine

Baker Institute for Animal Health

DEDICATED TO THE STUDY OF VETERINARY INFECTIOUS DISEASES, IMMUNOLOGY, GENETICS, AND REPRODUCTION

What makes us human is not just our genes, but how we regulate them

Humans and chimpanzees share more than 99% of the same DNA. So why are we so vastly different from our closest primate relatives?

Scientists have long suspected that what make us human isn't just our genes, but how we regulate them. A new study from Dr. Charles Danko and colleagues at the Baker Institute and Cold Spring Harbor Laboratory provides strong support for this idea. In a study published in Nature Ecology and Evolution, they describe small differences between humans and chimps in regions of DNA called enhancers, which help turn on nearby genes. These changes point to specific ways that human and chimp evolution has diverged. They can also be explored further for their potential roles in inherited human diseases.

Danko used a technique call PRO-seq, developed by co-author John Lis, of Cornell University. The technique maps where the RNA polymerase – the molecular copy machine that copies DNA into RNA is sitting on the genome. PRO-seq gives a more precise picture of the genes that a cell is using at any given time. With the help of Baker Institute colleague Tait-Wojno, the team used this technique to analyze immune cells from humans, chimpanzees, and rhesus macaque monkeys.

When lots of enhancers target the same gene, Danko discovered that they undergo evolutionary changes together as a unit. This helps cells to protect themselves from mutations in individual enhancers, to ensure that important genes are transcribed at constant levels regardless of these mutations. "How the elements work together is important for understanding how they evolve," said Danko. "This is important for establishing differences between humans and chimpanzees."

With multiple enhancers affecting the same gene, the cells can protect itself from mutations in individual enhancers, ensuring that important genes are transcribed regardless of these mutations. The redundancy of the enhancers also frees them up to change and acquire new functions so that species can rapidly adapt to new situations.

Currently, the researchers are continuing to perfect this technique, allowing them to analyze difficult samples like primary tumors. Danko also plans to investigate how enhancers interact with each other by folding of DNA inside the cell.

Other collaborators on the paper include Dr. Adam Siepel of Cold Spring Harbor Laboratory and the Baker Institute's Drs. Elia Tait Wojno and Scott Coonrod.