

Genomic Medicine: Understanding Genome Engineering, a Focus on Genome Regulation



Each cell in the body has a complete copy of all the genes within your DNA. The cells that make muscle, for example, still contain the genes of a liver cell or neurons, the main cell type of the nervous system. But genes are not all turned on at the same time. To carry out their own unique functions, our cells turn certain genes on or off in different patterns to make a muscle cell look and act different from a liver cell, a skin cell or a neuron.

Genome regulation is the process of controlling which genes in a cell's DNA are turned on (expressed) or off (repressed). The patterns in which genes are turned on or off causes each cell type to contain different sets of proteins, making that cell specialized to do its specific job.

Our cells often regulate gene expression by relying on zinc finger proteins which are small, highly abundant proteins that help turn specific genes on or off by binding to unique sequences of DNA, enabling a cell to differentiate the targeted gene from thousands of others. The family of zinc finger proteins (ZFPs) are among the most common regulatory proteins in the human genome.

Scientists are studying genome regulation as a complement to genome editing which uses specific technologies to create permanent change to the translation of genetic code of a cell by correcting, disabling, removing, or modifying a person's DNA. Genome editing technologies could be leveraged to switch specific genes on or off using ZFPs, to develop new therapeutic approaches. Examples of genome engineering technologies are zinc finger proteins (ZFPs); clustered, regularly interspaced, short palindromic repeat (CRISPR)/CRISPR-associated-9 (CRISPR/Cas9); and transcription activator-like effector nucleases (TALENs). All three of these technologies can be designed to target specific stretches of DNA within the human genome. Scientists are working to apply these approaches to develop medicines that can specifically target diseased cells without harming healthy cells.

One approach, as mentioned above, uses special zinc finger proteins which are engineered to precisely express or repress whichever gene they are designed to target. In this approach, ZFPs are coupled with transcription factor (TF) proteins that control the efficiency of transcription from gene to protein. The coupling of ZFPs to these domains yield ZFP-TFs that can be used to regulate the expression of select genes. ZFP-TFs can selectively repress (down-regulate) or activate (upregulate) the expression of key genes, including those involved in brain function. By using adeno-associated viruses (AAVs), which can be engineered to transport the ZFP-TFs to specific cells within the body without causing diseases, the goal is a one-time administration that is designed to have a long-term result for the person who received the treatment.

ZFP-TF technology can be designed to target any genome sequence and are tunable, meaning they can turn up or turn down the expression of a gene to a precise level. This highly customized approach may help develop treatments for challenging genetic conditions by slowing disease progression or restoring healthy gene expression. Currently, this technology is being studied as a potential therapy for diseases of the central nervous system including amyotrophic lateral sclerosis, Huntington's disease and Alzheimer's disease.

Learn More

For more information on genomic medicines, including genome regulation, visit the website below. If you or a family member have a genetic-related condition, your physician or a genetics professional can help you understand if a genomic medicine approach is right for you, or help you find an appropriate clinical trial.

National Institutes of Health, Human Genome Research Institute | [Genome.gov](https://www.genome.gov)

