What's driving specific patterns of gene expression among cell types?

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(PhysOrg.com) -- Providing another tool to help to understand gene regulation on a global scale, a nationwide research team has identified and mapped 55,000 enhancers, short regions of DNA that act to enhance or boost the expression of genes. The map, which will be published March 18 in the advance on-line edition of the journal *Nature*, will help scientists understand how cells control expression of genes specific to their particular cell type.

"Our studies show that enhancers play much more prominent role than previously appreciated in cell-type-specific gene expression, helping to explain what causes cells to differentiate into liver or brain or skin cells, or why these cells might become cancerous," said principal investigator Bing Ren, PhD, associate professor of Cellular and Molecular Medicine at the University of California, San Diego School of Medicine and head of the Laboratory of Gene Regulation at the Ludwig Institute for Cancer Research (LICR).

Nearly all cells in the human body have the exact same genome, but different cells have vastly different roles in development, normal tissue function and disease. The diversity between cells is mainly caused by differences in gene expression - the process through which a protein, or other molecule encoded by a gene is produced.

Enhancers are one of several types of regulatory elements, along with promoters and insulators, which are scattered across the genome and act to assemble proteins that regulate the transcription of individual genes.

"Expanding the knowledge of enhancers is critical for understanding the mechanisms that control gene expression. As only two percent of the genome encodes proteins, there is so much left to discover about what was once considered non-coding 'junk DNA' and how that other 98 percent contributes to human disease," said Ren.

By systematically analyzing more than 14 million DNA probes corresponding to the entire human genome, the team - including scientists from UC San Diego, MIT, the Broad Institute of MIT and Harvard, the National Institutes of Allergy and Infectious Disease, the University of Wisconsin and Duke University - created a new genomic-scale map of enhancers.

The research team has performed a type of genome-wide analysis called ChIP-chip analysis to locate promoters, enhancers, insulators and other regulatory DNA sequences for each gene, using this approach to identify these elements in multiple cell types and investigate their roles in gene expression. ChIP-chip is used to localize protein binding sites that may help identify functional elements of the genome.

"Using this process, we described signatures, or distinguishing patterns, on histone proteins that enabled us to distinguish promoters and enhancers in the genome," said Ren. "In our analyses, we were surprised to find that the chromatin signatures at promoter sites were similar across all cells. However, we found that enhancers are marked with highly cell-type specific modification patterns. These patterns suggested that enhancers are of primary importance in the differentiation of specific cell types."

Using previously described chromatin signatures for enhancers, the scientists mapped 55,000 elements that differentiate gene expression in cervical cancer, leukemia and embryonic stem cells, among others.

Regulatory modifications that determine gene expression are part of what's known as the epigenome - a second "dimension" to the genome that determines fundamental biological processes. Ren heads The San Diego Epigenome Center at the LICR at UC San Diego, one of four centers in the country called Reference Epigenome Mapping

Centers (REMC) as part of an overall five-year, $190 million program funded by the National Institutes of Health.

Source: University of California - San Diego (news : web)