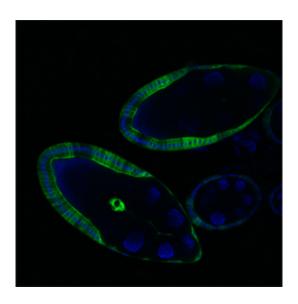


Scientists shed light on the 'dark matter' of DNA

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In each cell, thousands of regulatory regions control which genes are active at any time. Scientists at the Research Institute of Molecular Pathology (IMP) in Vienna have developed a method that reliably detects these regions and measures their activity. The new technology is published online by *Science* this week.

Genome sequences store the information about an organism's development in the DNA's four-letter alphabet. Genes carry the instruction for proteins, which are the building blocks of our bodies. However, genes make up only a minority of the entire genome sequence



- roughly two percent in humans. The remainder was once dismissed as "junk", mostly because its function remained elusive. "Dark matter" might be more appropriate, but gradually light is being shed on this part of the genome, too.

Far from being useless, the non-coding part of DNA contains so-called regulatory regions or enhancers that determine when and where each gene is expressed. This regulation ensures that each gene is only active in appropriate cell-types and tissues, e.g. haemoglobin in red blood cell precursors, digestive enzymes in the stomach, or ion channels in neurons. If gene regulation fails, cells express the wrong genes and acquire inappropriate functions such as the ability to divide and proliferate, leading to diseases such as cancer.

Despite the importance of gene regulatory regions, scientists have been limited in their ability to study them on a genome-wide scale. Their identification relied on indirect means, which were error prone and required tedious experiments for validating and quantifying enhancer activities..

Alexander Stark and his team at the IMP in Vienna now closed this gap with the development of a new technology called STARR-seq (self-transcribing active regulatory region sequencing), published online by *Science* this week. STARR-seq allows the direct identification of <u>DNA</u> sequences that function as enhancers and simultaneously measures their activity quantitatively in entire genomes.

Applying their technology to Drosophila cells, the IMP-scientists surprisingly find that the strongest enhancers reside in both regulatory genes that determine the respective cell-types as well as in broadly active "housekeeping" genes that are required for basic cell survival in most or all cells. In addition, they find several enhancers for each active gene, which might provide redundancy to ensure robustness of gene regulation.



The new method combines advanced sequencing technology and highly specialized know-how in bio-computing. It is a powerful tool which, according to Alexander Stark, will prove immensely valuable in the future. "STARR-seq is like a magic microscope that lets us zoom in on the regulatory regions of DNA. It will be crucial to study gene regulation and how it is encoded in the genome – both during normal development and when it goes wrong in disease."

The paper "STARR-seq Reports Genome-Wide Quantitative Enhancer Activity Maps Revealing Complex cis-Regulation of Transcription" by Cosmas Arnold et al. is published online by *Science* on January 17, 2013.

More information: Arnold, C. et al., STARR-seq Reports Genome-Wide Quantitative Enhancer Activity Maps Revealing Complex cis-Regulation of Transcription. *Science*, January 17, 2013.

Provided by Research Institute of Molecular Pathology

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