Single nucleotide variants affecting binding of transcription factors at DNA and inheritance of polygenic features.

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Abstract

Up to 90% of variants associated with various individual human traits are located out of protein coding regions and probably affect regulation of transcription activity. Functional annotation of individual genome variants helps to assess the risk of pathologies for carriers. Mechanistically such variants change the affinity of protein transcription factors to their cognate binding sites. Most of regulatory interactions in the human genome are still unexplored, but this area develops fast owing to the progress in the experimental and related computational methods.

We processed in silico the published results of tens of thousands of high-throughput chromatin immunoprecipitation (ChIP-Seq) experiments in various human cell types and developed a number of databases, such as the database of characteristic motifs of DNA sequences that bind certain regulatory proteins (http://hocomoco.autosome.ru), and the ADASTRA database (https ://adastra.autosome.ru) of allele-specific binding of transcription factors. We show how the developed tools and databases can be used to studyindividual variants in genome-wide association studies in samples of carriers of various inherited diseases.