核酸生物学院重点实验室学术报告

Systematic Analysis of Differential Transcription Factor Binding to Non-Coding Variants in the Human Genome

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报告摘要： A large number of sequence variants have been linked to complex human traits and diseases, but deciphering their biological function remains a daunting challenge especially for the non-protein-coding variants. To fill this gap, we have systematically assessed the differential binding of transcription factors (TF) to different alleles of non-coding variants in the human genome. Using an ultra-high throughput multiplex protein-DNA binding assay, we examined the binding of 270 human TFs to 95,886 common sequence variants within the 110 type 2 diabetes (T2D) risk loci. We then employed a machine-learning approach to derive computational models to predict differential DNA binding of 124 TFs to other common non-coding variants in the human genome. We showed that the newly derived models outperformed current position-weight matrices (PWM) in describing TF binding to non-coding variants, and facilitated discovery of potential causal variants and dysregulated molecular pathways in human diseases.

[1] **J. Yan**, et al. Transcription factor binding in human cells occurs in dense clusters formed around cohesin anchor sites, *Cell* 154(4) (2013) 801-13.
[2] A. Jolma*, **J. Yan***, et al. DNA-binding specificities of human transcription factors, *Cell* 152(1-2) (2013) 327-39.
[3] **J. Yan**, et al. Histone H3 lysine 4 monomethylation modulates long-range chromatin interactions at enhancers, *Cell Research* 28(2) (2018) 204-220.