MAPPING THE TRANSCRIPTIONAL NETWORK IN STEM CELLS REGULATED BY REST

LAWRENCE W. STANTON
stantonl@gis.a-star.edu.sg

Genome Institute of Singapore, 60 Biopolis Street, #02-01, Genome, Singapore 138672

Abstract

REST (RE1 silencing transcription factor) is a protein that regulates neuronal gene expression. REST binds to a highly conserved 21-bp RE1 element and recruits co-repressors to repress transcription. Recently REST was found to be expressed in embryonic stem cell (ESC) and was identified as a direct target of Nanog and Oct4, two transcription factors critical in maintaining the pluripotency and self-renewal of ESC. We are interested in understanding the role that REST plays in ESC. We have identified hundreds of targets genes directly regulated by REST in ESC by performing comprehensive chromatin immunoprecipitation (ChIP)-on-chip experiments. A computational approach was used to identify ∼900 RE1 elements within the mouse genome. We then constructed an oligonucleotide array that contained unique probes for all these RE1 sites for our ChIPon-chip experiments. Our results showed that REST binds to $>$ 500 RE1 elements. We are now assessing REST occupancy by a comprehensive sequencing based ChIP method (ChIP-PET) for a more unbiased search for REST targets. Using these two different methods, we are able to identify REST targets at the genome-wide level, which will provide us with a clearer picture of the role of REST in the regulatory network that controls ESC differentiation.