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KOLOKVIJ

Prof. Boris Lenhard

Institute of Clinical Sciences, Faculty of Medicine, Imperial College London

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Promoter classes and promoter grammars in vertebrate genomes

Cap analysis of gene expression (CAGE) is a high-throughput method for transcriptome analysis that provides a single base-pair resolution map of transcription start sites (TSS) and their relative usage. It has led to the discovery of different classes of vertebrate promoters with respect to TSS distribution, associated with distinct underlying genomic features and gene functions. By applying CAGE to a developmental time course of zebrafish (Danio rerio), we found that thousands of promoters in the genome are utilized differently throughout embryonic development and have established sequence and chromatin determinants that produce different readouts from the same promoter in the oocyte and the developing embryo (Haberle et al Nature 2014). We introduced a novel method for detecting variability in TSS usage within promoter between different contexts and successfully decoupled maternal and zygotic determinants of TSS selection that drive the dynamic change of promoter shape. While maternal selection requires an A/T-rich (W-box) motif at a fixed upstream position and produces composite sharp promoter architecture, the zygotic selection is restricted to a region defined by the position of the first downstream nucleosome with the dominant TSS aligned precisely to nucleosome positioning signal. We conclude that the type of the promoter is not an inherent property of the genomic locus, but depends on the regulatory context, and uses different, overlapping sets of instructions even at ubiquitously expressed promoters.