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ARTICLE

Conserved noncoding sequences conserve biological networks and influence genome evolution

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Abstract

Comparative genomics approaches have identified numerous conserved *cis*-regulatory sequences near genes in plant genomes. Despite the identification of these conserved noncoding sequences (CNSs), our knowledge of their functional importance and selection remains limited. Here, we used a combination of DNA methylome analysis, microarray expression analyses, and functional annotation to study these sequences in the model tree *Populus trichocarpa*. Methylation in CG contexts and non-CG contexts was lower in CNSs, particularly CNSs in the 5′-upstream regions of genes, compared with other sites in the genome. We observed that CNSs are enriched in genes with transcription and binding functions, and this also associated with syntenic genes and those from whole-genome duplications, suggesting that *cis*-regulatory sequences play a key role in genome evolution. We detected a significant positive correlation between CNS number and protein interactions, suggesting that CNSs may have roles in the evolution and maintenance of biological networks. The divergence of CNSs indicates that duplication–degeneration–complementation drives the subfunctionalization of a proportion of duplicated genes from whole-genome duplication. Furthermore, population genomics confirmed that most CNSs are under strong purifying selection and only a small subset of CNSs shows evidence of adaptive evolution. These findings provide a foundation for future studies exploring these key genomic features in the maintenance of biological networks, local adaptation, and transcription.

Introduction

Conserved noncoding sequences (CNSs), DNA sequences conserved across species, are under sequence constraint, probably due to their functional importance. One of the major remaining challenges in functional and evolutionary genomics is to determine the functional importance of many components of the genome, in particular CNSs located near protein-coding genes. Some of these CNSs are thought to be important regulatory sequences that are involved in diverse regulatory functions such as transcription initiation and processing of transcripts. (Haudry et al. 2013; Tompa et al. 2005). About 3% of vertebrate CNSs are under purifying selection, and most of these sequences function as *cis*-elements that regulate gene transcription in transgenic assays (Cooper et al. 2005; Sanges et al. 2006). During evolution, functional sequences are expected to be under selective constraints and diverge more slowly than non-functional sequences (Haudry et al. 2013). Researchers have proposed that CNSs repress the rearrangement of the surrounding genome, but do not drive retention of duplicate genes (Hufton et al. 2009). Therefore, comparative analyses of CNSs, based on phylogenetic footprinting of conserved DNA sequences, have been used to detect functional elements.

Genome-wide comparisons of ten dicot plants yielded large numbers of CNSs (Velde et al. 2016). These genomic DNA motifs (median size 15 bp) occur in different genic regions (5′-upstream, 5′-UTR, intron, 3′-UTR, 3′-downstream) and have different potential functions. Although the

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