

## Cis Regulatory Elements (CREs), a key for gene control

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To unravel the complexities of biological processes, the understanding of the intricate mechanisms of gene control is essential. Most of the regulatory elements are universal, however, substantial differences occur among elements assigned to particular tissues e.g. tissue/organ-specific promoters (Twyman 2003; Venter and Botha 2010). Plant regulatory sequences are located directly in the transcribed DNA strand or may be added during post-transcriptional modifications (Vaughn et al. 2012). Based on their structure, regulators are classified as *cis* sequences and *trans* factors. They are linear nucleotide fragments of non-coding DNA and have varied localization, orientation and activity in relation to genes (Venter and Botha, 2010) besides influencing how genes are expressed by interacting with various molecular factors. These sequences also determine when, where, and how much a gene is transcribed. Exploring CREs offers insights into genetic regulation and its implications for cellular function and development.

According to PLACE database, there are 469 *cis* regulatory elements present in plants. In several promoters, ACGT core sequence has been established as a functionally important *cis* element that frequently regulates gene expression in synergy with other *cis* elements. Promoter activity is largely affected by the copy number, inter motif distance, position, deletions or mutations in the core sequences of the *cis* regulatory regions. (Mehrotra et al. 2015). There are two main types of *cis* sequences – enhancers and silencers.

### Enhancer sequences

Plant enhancers enhance gene expression through cooperation with specific transcription factors and are located upstream or downstream of the promoter sequence at different, often considerable, distances (Mehrotra et al. 2011). Unlike promoters, enhancers lack the capacity for autonomous transcription initiation. They primarily regulate transcription burst frequency rather than the magnitude of messenger RNA (mRNA) biosynthesis (Haberle et al. 2018). Enhancers were also reported within the introns of the genes they regulate. For

instance, *AGAMOUS* (AG) in *Arabidopsis* (Sieburth and Meyerowitz, 1997.) and *knotted1* (*kn1*) (Inada et al. 2003) in maize.

### Silencers

These regulatory sequences are capable of silencing gene expression, but have been challenging to identify. Chromatin features potentially characteristic of silencing elements were recently found in genome wide studies. For example, CRM-gene chromatin loops in maize associated with H3K27me3 were coincident with significantly lower transcript abundances compared to CRM-gene chromatin loops tethered by H3K4me3 nucleosomes (Ricci et al. 2019)

### Insulator sequences

Insulators are a group of genetically different elements, inducing common effect which vary amongst species. It is hypothesized that they cause DNA strand looping or attach protein factors, which results in conformational changes and physical access barrier (Yang et al. 2011). In the gene borders, barrier insulators may be found which neutralize the position effect, and the influence of adjacent sequences on gene expression (Papadakis et al. 2004; Allen 2008), thus protecting genes against undesirable silencing by heterochromatin.

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