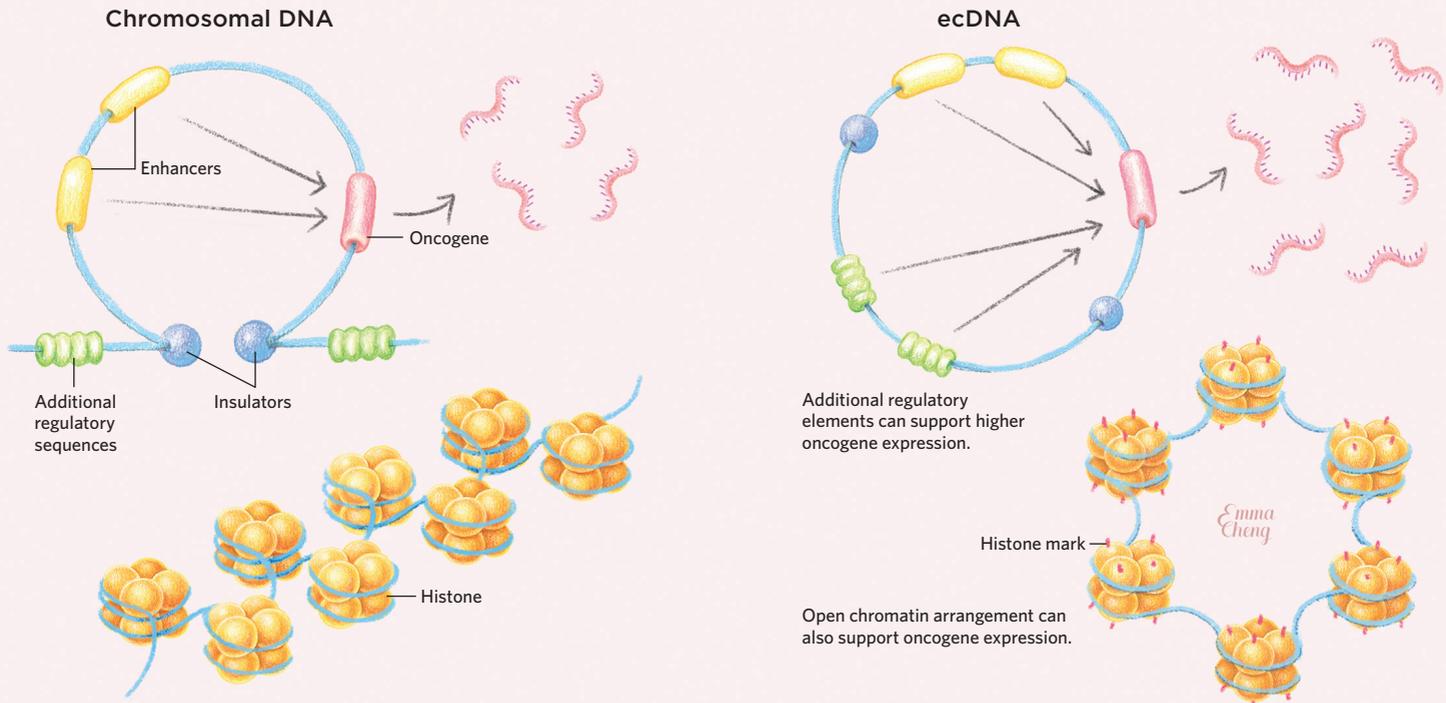


HOW ecDNAs MIGHT SUPPORT CANCEROUS GROWTH

The circular nature of ecDNAs can enable gene interactions that may support the increased transcription of oncogenes, as genetic elements normally found in distant parts of the genome may come together to interact. While insulators in the chromosomal DNA sit at the stem of a loop structure and ensure that regulatory sequences such as enhancers work only on their nearby target genes, the circular shape of ecDNA generates new interactions with additional regulatory sequences that would not normally occur on chromosomal DNA.



Additionally, ecDNAs tend to have a more-open chromatin structure than chromosomes that promotes increased gene expression. DNA is wound around histone cores into units of organization called nucleosomes. On chromosomes, some regions can become highly compacted, rendering the DNA inaccessible to the transcriptional machinery, but ecDNAs have an altered chromatin structure in which the nucleosomes do not compact, resulting in highly accessible DNA that is primed for transcription. Moreover, ecDNAs are loaded with active histone marks but have a paucity of repressive histone marks, promoting high levels of transcription.