RNA regulates transcription via hybrid-triplex formation

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Triplexes are triple-helical geometries comprising all-DNA, all-RNA, or mixed molecules. They are formed within the same strand or comprise two or three individual strands with intermolecular hydrogen bonds across the nucleobases. Such bonds expand the common Watson-Crick base-pairing including Hoogsteen interactions between a homopurinic strand and a third strand containing CT-only (or CU-only, in case of RNA) or AG-only bases. Recently, hybrid RNA-DNA triplexes were proposed as mediators of long non-coding RNA (lncRNA) function in chromatin architecture and gene expression. Two studies demonstrated that triplex formation at the promoter site of designed artificial transcription units can inhibit or enhance the observed transcription rate of the fluorogenic aptamer Broccoli, providing clues that support triplex-mediated lncRNA function. In fact, the up- or down-regulation was dictated by triplex motif, triplex position, and homopurinic location (i.e., template or sense strand). These new rule set was used to develop logic gates and a threshold gate, using triplex forming RNAs as inputs, and the transcription rate as output. To further study triplex function in cells, triplex targets were identified in E.coli genome and transferred into artificial transcription units. Quite remarkably, the different configurations previously tested with designed sequences, confirmed the effect of hybrid triplexes on transcription. The proposed system to study triplexes is expected to shed some light on these elusive structures, especially in the context of non-coding RNAs.