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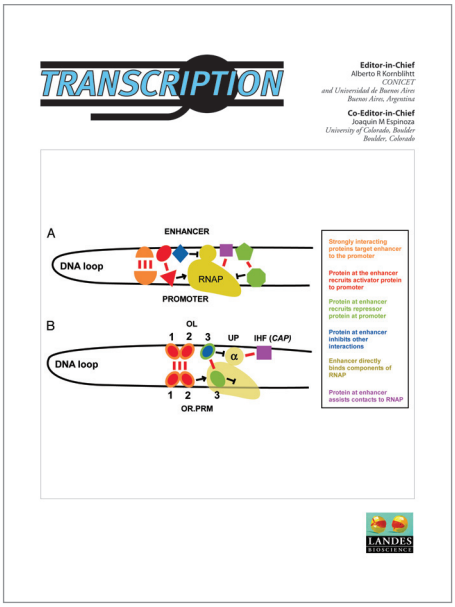
Landes Highlights

Promoterless transcription of DNA coligo templates by RNA polymerase III

Lodoe Lama, Christine I Seidl, and Kevin Ryan

Chemically synthesized DNA can carry small RNA (sRNA) sequence information but converting that information into sRNA is generally thought to require large double-stranded promoters in the context of plasmids, viruses, and genes. It was recently reported that circularized oligodeoxynucleotides (coligos) containing certain sequences and secondary structures can template the synthesis of sRNA by RNA polymerase III (RNAP III) in vitro and in human cells. The same team of researchers, headed by Dr Kevin Ryan, has now reported corroborating evidence that RNAP III is the sole polymerase responsible for coligo transcription. The use of immunoprecipitated RNAP III enabled experiments showing that coligo transcripts can be formed through transcription termination without subsequent 3′ end trimming. To better define the determinants of productive transcription, a structure-activity relationship study was performed using over 20 new coligos. The results showed that unpaired nucleotides in the coligo stem facilitate circumtranscription, but also that internal loops and bulges should be kept small to avoid secondary transcription initiation sites. A polymerase termination sequence embedded in the double-stranded region of a hairpin-encoding coligo stem was shown to antagonize transcription. Using lessons learned from new and old coligos, the authors demonstrate how to convert poorly transcribed coligos into productive templates. Their findings support the possibility that coligos may prove useful as chemically synthesized vectors for the ectopic expression of sRNA in human cells.
https://www.landesbioscience.com/journals/transcription/article/27913/



Reference

Lama L, Seidl CI, Ryan K. Transcription 2014; 5:In press; PMID:24531370; http://dx.doi.org/10.4161/trns.27913

Epigenetic loss of the PIWI/piRNA machinery in testicular tumorigenesis

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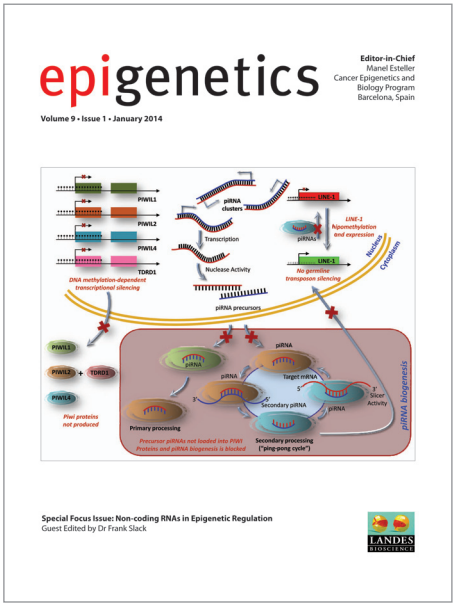
Although most cancer research has focused on mRNA, non-coding RNAs (ncRNAs) are also essential players in tumorigenesis. In addition to the well-recognized microRNAs, recent studies have also shown that epigenetic silencing by CpG island hypermethylation of other classes of ncRNAs, such as transcribed ultraconserved regions (T-UCRs) or small nucleolar RNAs (snoRNAs), also occurs in human neoplasia. A new study has looked at the putative existence of epigenetic aberrations in the activity of PIWI proteins, an Argonaute family protein subclass, and the small regulatory PIWI-interacting RNAs (piRNAs) in testicular cancer. The PIWI/piRNA pathway is known to play a critical role in male germline development. The research team, headed by Dr Manel Esteller, observed the existence of promoter CpG island hypermethylation-associated silencing of piwi-like protein encoding genes *PIWIL1*, *PIWIL2*, *PIWIL4*, and *TDRD1* (ecoding tudor-domain containing protein 1) in primary seminoma and non-seminoma testicular tumors, in addition to testicular germ cell tumor cell lines. Most importantly, these epigenetic lesions occurred in a context of piRNA downregulation and loss of DNA methylation of the LINE-1 repetitive sequences, one of the target genomic loci where the PIWI/piRNA machinery acts as a caretaker in non-transformed cells. The study data indicate that epigenetic disruption of the entire PIWI/piRNA pathway is indeed a hallmark for the development of testicular tumors.
https://www.landesbioscience.com/journals/epigenetics/article/27237/



Reference

Ferreira HJ, Heyn H, Garcia Del Muro X, Vidal A, Larriba S, Muñoz C, Villanueva A, Esteller M. Epigenetics 2013; 9:113-8; PMID:24247010; http://dx.doi.org/10.4161/epi.27237

A common exon is important for IRES activity in different HIV-1 transcripts

Terra-Dawn M Plank, James T Whitehurst, Regina Cencic, Jerry Pelletier, and Jeffrey S Kieft

Alternative splicing of the human immunodeficiency virus 1 (HIV-1) RNA transcripts produces mRNAs encoding nine different viral proteins. The leader of each contains a common non-coding exon at the 5′ end. Previous studies have shown that the leaders from the common exon-containing transcripts gag, nef, vif, vpr, and vpu can direct protein synthesis through internal ribosome entry sites (IRESs) with varying efficiencies. In a recent study, Dr Jeffrey Kieft and colleagues explored whether the common exon acts as an IRES element in the context of all the 5′ leaders or if each harbors a distinct IRES. The authors also studied the relationship between the IRESs and initiation codon selection. They found that the common exon adopts a similar conformation in every leader explored and that the sequence and structure is required for IRES activity. Each leader used a scanning mechanism for start codon identification. Together, the study data point to a model in which the common exon on HIV-1 transcripts acts as the ribosome landing pad, recruiting preinitiation complexes upstream of the initiation codon, followed by scanning to each transcript's initiator AUG. The results demonstrate how a single RNA structural element, grafted onto different transcripts by alternative splicing, can serve to provide a common function to an otherwise diverse family of mRNAs.

https://www.landesbioscience.com/journals/translation/article/27694/

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Plank T-DM, Whitehurst JT, Cencic R, Pelletier J, Kieft JS. Translation 2014; 2:e27694; http://dx.doi.org/10.4161/trla.27694

Nematode endogenous small RNA pathways

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The discovery of small RNA (sRNA) silencing pathways has greatly expanded our knowledge of gene regulation. sRNAs have been presumed to play a role in every field of biology because they affect many biological processes via regulation of gene expression and chromatin remodeling. Well-known examples of affected processes include development, fertility, and genome stability. A recent review by Dr L Basten Snoek and colleagues has looked at the role of the three main endogenous sRNA silencing pathways in *Caenorhabditis elegans*: microRNAs, endogenous small interfering RNAs, and PIWI-interacting RNAs. The authors provide an overview on how these pathways function, and discuss research on other nematode species providing insights into the evolution of these sRNA pathways. In understanding the differences between the endogenous sRNA pathways and their evolution, a more comprehensive picture is formed of the functions and effects of sRNAs.

https://www.landesbioscience.com/journals/worm/article/28234/

Reference

Hoogstrate SW, Volkers RJM, Sterken MG, Kammenga JE, Snoek LB. Worm 2014; 3:e28234; http://dx.doi.org/10.4161/worm.28234