

## TRANSKRİPSİYON

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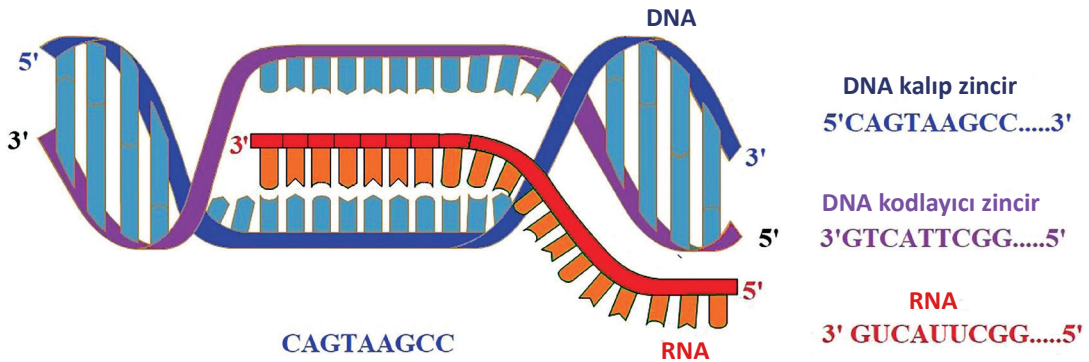
## 22.1. Giriş

Gen ekspresyonunun ilk aşaması olan transkripsiyon, RNA polimeraz enziminin katalizlediği bir reaksiyonda transkripsiyon faktörleri olarak adlandırılan bir dizi aksesuar proteinin katılımı ile DNA çift sarmalındaki genetik bilginin RNA molekülüne kopyalandığı süreçtir. DNA, hücre çekirdeğindeki genetik materyali bir referans veya şablon olarak güvenli ve stabil bir şekilde depolar. Transkripsiyonun gerçekleşeceği DNA parçasında sadece tek bir DNA zinciri kalıp olarak görev yapmaktadır. DNA'nın iki tamamlayıcı zinciri yazım sırasındaki işlevlerine göre belirlenir. Transkripsiyon faktörleri hızlandırıcı (enhancer) ve promotör dizileri olarak adlandırılan spesifik DNA dizilerine bağlanarak transkripsiyon bölgesinde RNA polimeraz'ın işlev görmesinde görev alırlar. Bu şekilde transkripsiyon faktörleri ve RNA polimeraz transkripsiyon başlatma kompleksi olarak adlandırılan bir kompleks oluştururlar. Bu kompleks, transkripsiyonu başlatır ve RNA polimeraz, orijinal DNA zincirine tamamlayıcı bazları eşleştirerek mRNA sentezini başlatır. mRNA molekülünün sentezi tamamlandığında transkripsiyon

sonlandırılır. Genin yeni oluşturulmuş mRNA kopyaları, daha sonra, protein sentezinde kalıp olarak görev alır.

RNA sentezinde kalıp görevi gören DNA zincirine kalıp zincir denir. Kalıbın tamamlayıcısı olan DNA zincirine kodlayıcı veya kalıp olmayan zincir adı verilir. RNA kalıp zincirin tamamlayıcısı olarak sentezlenir ve kodlayıcı (kalıp olmayan) zincirle aynı diziyi içerir (Timin yerine Urasil) (Şekil 22.1).

RNA sentezi RNA polimeraz enzimi tarafından katalize edilir. Transkripsiyon, RNA polimerazın "promotör" adı verilen genin hemen yakınındaki özgül, değişken dizilere bağlanması ile başlar. Promotörler, DNA üzerinde ilgili genin transkripsiyon başlangıç noktasına yakın bölgelerde ilk ekzondan önce yer alırlar (Şekil 2). RNA polimeraz, promotör dizisinden itibaren terminatör (sonlandırıcı) bölgeye ulaşana kadar DNA kalıbı boyunca RNA sentezleyerek hareket eder. Promotörden terminasyon bölgesine kadar uzanan bu hareket bir "transkripsiyon birimi" olarak tanımlanır. Bir transkripsiyon birimi bir (monosistron) veya daha fazla gen (polisistron) içerebilir.



Şekil 22.1. Transkripsiyon. RNA yazılımı kalıp zincirin tamamlayıcısı olarak sentezlenir ve kodlayıcı (kalıp olmayan) zincirle aynı diziyi içerir (Timin yerine Urasil ile).

### 22.3. Kaynaklar

- Lodish H, Berk A, Zipursky SL, Matsudaira P, Baltimore D, Darnell J. Bacterial transcription initiation (chapter 10.2). *Molecular cell biology*, 4. Edition. 2000
- Bell SP, Learned RM, Jantzen HM, Tjian R. (1988). Functional cooperativity between transcription factors UBF1 and SLI mediates human ribosomal RNA synthesis. *Science* 1998; 241:1192-7.
- Blanco JA. The role of the TATA-binding protein in the assembly and function of the multisubunit yeast RNA polymerase III transcription factor, TFIIB. *Cell* 1992; 71: 1055-64.
- Bogenhagen DF, Sakonju S, Brown DD. A control region in the center of the 5S RNA gene directs specific initiation of transcription: II. The 3' border of the region. *Cell* 1980; 19: 27-35.
- Burke TW, Kadonaga JT. Drosophila TFIID binds to a conserved downstream basal promoter element that is present in many TATA-box-deficient promoters. *Genes Dev* 1996; 10: 711-24.
- Butler JE, Kadonaga JT. The RNA polymerase II core promoter: a key component in the regulation of gene expression. *Genes Dev* 2002; 16: 2583-92.
- Campbell EA, Korzheva N, Mustaev A, Murakami K, Nair S, Goldfarb A, Darst SA. (2001). Structural mechanism for rifampicin inhibition of bacterial RNA polymerase. *Cell* 2001;104:901-12.
- Canella D, Praz V, Reina JH, Cousin P, Hernandez N. Defining the RNA polymerase III transcriptome: genome-wide localization of the RNA polymerase III transcription machinery in human cells. *Genome Res* 2010; 20: 710-21.
- Cramer P, Bushnell DA, Fu J, Gnatt AL, Maier-Davis B, Thompson NE, Burgess RR, Edwards AM, David PR, Kornberg RD. Architecture of RNA polymerase II and implications for the transcription mechanism. *Science* 2000; 288(5466): 640-9.
- Doi RH, Wang LF. Multiple prokaryotic RNA polymerase sigma factors. *Microbiol. Rev.* 1986; 50: 227-43.
- Egloff S, Murphy S. Cracking the RNA polymerase II CTD code. *Trends Genet* 2008; 24: 280-8.
- Galli G, Hofstetter H, Birnstiel ML. Two conserved sequence blocks within eukaryotic tRNA genes are major promoter elements. *Nature* 1981; 294: 626-31.
- Geiduschek EP, Tocchini-Valentini GP. Transcription by RNA polymerase III. *Annu. Rev Biochem* 1988; 57: 873-914.
- Grummt I. Life on a planet of its own: regulation of RNA polymerase I transcription in the nucleolus. *Genes Dev* 2003;17: 1691-702.
- Hartzog GA, Quan TK. (2008). Just the FACTs: Histone H2B ubiquitylation and nucleosome dynamics. *Mol Cell* 2008; 31: 2-4.
- Helmann JD, Chamberlin M. Structure and function of bacterial sigma factors. *Ann Rev Biochem* 1998; 57: 839-72.
- Kassavatis GA, Braun BR, Nguyen LH, Geiduschek EP. S. cerevisiae TFIIB is the transcription initiation factor proper of RNA polymerase III while TFIIA and TFIIC are assembly factors. *Cell* 1990; 60: 235-45.
- Kassavatis GA, Joazeiro CA, Pisano M, Geiduschek EP, Colbert T, Hahn S, Knutson BA, Hahn S. Yeast Rrn7 and human TAFIB are TFIIB-related RNA polymerase I general transcription factors. *Science* 2011; 333: 1637-40.
- Kassavatis GA, Letts GA, Geiduschek EP (1999). A minimal RNA polymerase III transcription system. *EMBO J* 1999; 18: 5042-51.
- Korzheva N, Mustaev A, Kozlov M, Malhotra A, Nikiforov V, Goldfarb A, Darst SA. A structural model of transcription elongation. *Science* 2000; 289: 619-25.
- Kuhn CD, Geiger SR, Baumli S, Gartmann M, Gerber J, Jennebach S, Mielke T, Tschochner H, Beckmann R, Cramer P. Functional architecture of RNA polymerase I. *Cell* 2007;13 L: 1260-73.
- Kulich D, Lee J, Lomakin I, Nowicka B, Das A, Darst S, Normet K, Borukhov S. The functional role of basic patch, a structural element of Escherichia coli transcript cleavage factors GreA and GreB. *J Biol Chem.* 2000; 275(17):12789-98.
- Kunkel GR, Pederson T. Upstream elements required for efficient transcription of a human U6 RNA gene resemble those of U1 and U2 genes even though a different polymerase is used. *Genes Dev* 1988; 2: 196-204.
- Lee DN, Phung L, Stewart J, Landick R. Transcription pausing by E. coli RNA polymerase is modulated by downstream DNA sequences. *J Biol Chem* 1990; 265: 15145-53.
- Lesnik EA, Sampath R, Levene HB, Henderson TJ, McNeil JA, Ecker DJ. Prediction of rho-independent transcriptional terminators in E. coli. *Nucleic Acids Res* 2001; 29: 3583-94.
- Liu X, Bushnell DA, Wang D, Calero G, Kornberg RD. Structure of an RNA polymerase II-TFIIB complex and the transcription initiation mechanism. *Science* 2011; 327: 206-9.

- Martinez E, Chiang CM, Ge H, Roeder RG. TATA-binding protein associated factors in TFIID function through the initiator to direct basal transcription from a TATA-less class II promoter. *EMBO J* 1994; 13: 3115-26.
- Mathews DA, Olson WM. What is new in the nucleolus? *EMBO Rep* 2006; 7: 870-3.
- Muller F, Demeny MA, Tora L. New problems in RNA polymerase II transcription initiation: matching the diversity of core promoters with a variety of promoter recognition factors. *J Biol Chem* 2007; 282: 14685-9.
- Naidu S, Friedrich J, Russell J, Zomerdijk JC. TAFIB is a TFIIB-like component of the basal transcription machinery for RNA polymerase I. *Science* 2011; 333: 1640-2.
- Nikolov DB, Burley SK. RNA polymerase II transcription initiation: a structural view. *Proc Natl Acad Sci USA* 1997; 94: 15-22.
- Nikolov DB, Hu SH, Lin J, Gasch A, Hoffmann A, Horikoshi M, Chua NH, Roeder RG, Burley SK. Crystal structure of TFIID TATA-box binding protein. *Nature* 1992; 360: 40-6.
- Paule MR, White RJ. Survey and summary: transcription by RNA polymerases I and III. *Nucleic Acids Res* 2000; 28: 1283-98.
- Pieler T, Hamm J, Roeder RG. The 5S gene internal control region is composed of three distinct sequence elements, organized as two functional domains with variable spacing. *Cell* 1987; 48: 91-100.
- Poortinga G, Sharkey K, Hung S, Holloway TP, Quin J, Robb E, Wong LH, Thomas WG, Stefanovsky V, Moss T, Rothblum L, Hannan KM, McArthur GA, Pearson RB, Hannan RD. UBF levels determine the number of active rRNA genes in mammals. *J Cell Biol* 2008; 183: 1259-74.
- Purves WK, Sadava DE, Orians GH, Heller HC. *Transcription: DNA-directed RNA synthesis. Life: the science of biology* (7. edition). 2004.
- Reece JB, Urry LA, Cain ML, Wasserman SA, Minorsky PV, Jackson RB. *Transcription is the DNA-directed synthesis of RNA: A closer look. Campbell biology* (10. edition). 2011.
- Reynolds R, Bermadez-Cruz RM, Chamberlin MJ. Parameters affecting transcription termination by *E. coli* RNA polymerase. I. Analysis of 13 rho-independent terminators. *J Mol Biol* 1992; 224, 31-51.
- Rice GA, Kane CM, Chamberlin M. Footprinting analysis of mammalian RNA polymerase II along its transcript: an alternative view of transcription elongation. *Proc Natl Acad Sci USA* 1991; 88: 4245-81.
- Sakonju S, Bogenhagen DF, Brown DD. A control region in the center of the 5S RNA gene directs specific initiation of transcription: I. The 5' border of the region. *Cell* 1980; 19: 13-25.
- Schramm L, Hernandez N. Recruitment of RNA polymerase III to its target promoters. *Genes Dev* 2002; 16: 2593-620.
- Seith LA, Sigurdsson S, Svejstrup JQ. (2010). Transcript elongation by RNA polymerase II. *Annu. Rev Biochem* 2010; 79, 271-293.
- Singer VL, Wobbe CR, Struhl K. A wide variety of DNA sequences can functionally replace a yeast TATA element for transcriptional activation. *Genes Dev* 1990; 4: 636-45.
- Smale ST, Baltimore D. The "initiator" as a transcription control element. *Cell* 1989; 57: 103-13.
- Smale ST, Jain A, Kaufmann J, Emami KH, Lo K, Garraway IP. The initiator element: a paradigm for core promoter heterogeneity within metazoan protein-coding genes. *Cold Spring Harb Symp Quant Biol.* 1998; 63: 21-31.
- Smale ST, Kadonaga JT. The RNA polymerase II core promoter. *Annu. Rev. Biochem* 2003;72: 449-79.
- Sprouse RO, Karpova TA, Mueller F, Dasgupta A, McNally JG, Auble DT. Regulation of TATA-binding protein dynamics in living yeast cells. *Proc Nat Acad Sci USA* 2008; 105: 13304-8.
- Travers AA, Burgess RR. Cyclic reuse of the RNA polymerase sigma factor. *Nature* 1969; 222: 537-40.
- von Hippel PH. An integrated model of the transcription complex in elongation, termination, and editing. *Science* 1998; 281: 660-5.
- Wang D, Meier TI, Chan CL, Feng G, Lee DN, Landick R. Discontinuous movements of DNA and RNA in RNA polymerase accompany formation of a paused transcription complex. *Cell* 1995; 81: 341-50.
- Woychik NA, Hampsey M. The RNA polymerase II machinery: structure illuminates function. *Cell* 2002; 108: 453-63.
- Young RA. RNA polymerase II. *Annu Rev Biochem* 1991; 60: 689-715.
- Zhang G, Campbell EA, Zhang EA, Minakhin L, Richter C, Severinov K, Darst SA. Crystal structure of *Thermus aquaticus* core RNA polymerase at 3.3 Å resolution. *Cell* 1999; 98: 811-24.
- Zhang Y, Sikes ML, Beyer AL, Schneider DA. The Pafl complex is required for efficient transcription elongation by RNA polymerase I. *Proc Natl Acad Sci USA* 2009; 106: 2153-8.