

# BÖLÜM 10

## Kodlamayan RNA'lar

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### Giriş

Çok uzun zamandan beri, sadece mesajcı RNA (mRNA), taşıyıcı RNA (tRNA) ve ribozomal rRNA (rRNA) gibi housekeeping RNA'ların, DNA üzerinde bulunan genlerin fonksiyonel birimleri olan proteinlerine dönüştürülmesinde aracı moleküller olarak görev aldıkları düşünülmekteydi (1). Hatta 2000'li yılların başına kadar bilim insanları çalışmalarını çoğunlukla mRNA üzerine yoğunlaştırmıştı. Ancak yaklaşık 25 yıl önce mikroRNA'ların (miRNA) keşfedilmesiyle beraber bu algı değişti. Ürünü fonksiyonel bir proteine dönüşmeyen RNA transkriptlerinin, yani 'kodlamayan RNA'ların' hücrede birçok genin ifadesinin değişiminden hücrenin kaderinin belirlenmesine kadar birçok sürece etki ettikleri artık biliniyor. Biz de bu kitap bölümünde kodlamayan RNA'ları tanımlayarak, bu RNA'ların biyo-oluşum sürecinden ve hücrede aktif bir şekilde rol oynadıkları mekanizmalardan bahsettik.

### 1. Kodlamayan RNA'lar (ncRNA)

Eskiden beri RNA'ların temel işlevlerinin, DNA üzerinde bulunan genlerin proteine dönüşmesi için birer mesajcı olarak davranmak olduğu düşünülüyordu. Ancak bu görüş, küçük kodlamayan RNA'lardan olan miRNA'ların, yaklaşık

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circRNA'lara ilk olarak 1976 yılında bitkileri enfeksiyona sebep olan patojen bir viroid türünde rastlanmış (108), daha sonra circRNA'lar 1979 yılında HeLa hücrelerinin elektron mikroskopuyla görüntülenmesiyle tespit edilmiş (109), RNA-seq verileri ve biyoinformatik biliminin de gelişmesiyle daha sonra yapılan çalışmalarda ise circRNA'ların ökaryotik canlılarda endojen olarak sentezlenen bir RNA splays ürünü olduğu ortaya çıkarılmıştır (109, 110). Fazla miktarda ve farklı şekillerde üretildiği bilinen circRNA'ların hücrede birçok gelişimsel sürece katkı sağlamalarının yanı sıra, RNA-protein etkileşimleri, alternatif splaysın düzenlenmesi, miRNA'ların fonksiyonlarının sürdürülmesi gibi süreçlerde de önemli rolleri olduğu bilinmektedir (111).

## Sonuç

Kodlamayan RNA'lar, genel itibariyle birçok düzenleyici RNA'lara ek olarak, housekeeping olarak isimlendirilen RNA'ları da içerirler. Düzenleyici RNA'lar boyutlarına göre kısa ve uzun olarak sınıflandırılmıştır. Bu RNA'lar işlevsel bir protein üretmemelerine rağmen, hücrede mRNA ve tRNA'ların işlenmesinde görev alan ribonükleoprotein kompleksleri oluştururlar. Ek olarak prokaryotlarda ve ökaryotlarda 3 boyutlu yapıları sayesinde gen ifadesinin düzenlenmesinde rol alırlar. Yine hücre döngüsünün düzenlenmesinde, apoptoz yolağında, hücre kaderinin belirlenmesinde de rolleri olduğu bilinmektedir. Özellikle miRNA'ların ifadeleri birçok tümör baskılayıcı ve onkogenlerin ifadelerini etkilemelerinden dolayı kanser oluşumu ve ilerlemesi gibi süreçlerde rol aldıklarına dair birçok veri bulunmaktadır. ncRNA'ların hücrede birçok metabolik yolakta görev aldıkları bilinmektedir ve genom boyu analiz teknolojilerinin gelişmesi, genomik dizileme sonuçlarının ileri biyoinformatik araçlarla analiz edilmesi yeni birçok ncRNA'nın keşfedilmesine imkan tanımaktadır. Sonuç olarak, ncRNA'ların hücredeki birçok süreçte rol alan potansiyel işlevlerini düşündüğümüzde, hücrede meydana gelen olaylara nasıl etki ettiklerinin ve aksiyon mekanizmalarının açığa kavuşturulması sayesinde kanser dahil birçok genetik hastalığın teşhis ve tedavisinde büyük çaplı potansiyellerinin olacağını belirtmek gerekir.

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