

## Bölüm 13

# EPIGENETİK MEKANİZMALAR VE KANSER İLİŞKİSİ

Bahadır BATAR<sup>1</sup>

### GİRİŞ

Bir vücudun tüm hücreleri temel olarak aynı genlere sahip olsa da, genomun ifadesini düzenleyen ve farklı gelişim evrelerinde ve yetişkin dokularında hücreSEL farklılaşmada rol oynayan epigenetik bilgidir. Bu epigenetik bilgi, kromatin bileşeninin kovalent modifikasyonları olarak saklanır<sup>1</sup>. Epigenetik bilgi genin nükleotit dizisini etkilemeden bir genin transkripsiyonunu ve fonksiyonunu etkiler.

Epigenetik modifikasyonlar nispeten mitotik ve/veya mayotik olarak kalıtılsaldır. Bununla birlikte, DNA metilasyonu durumunda mitotik kalıtım iyi kanıtlanmış olmasına rağmen, histon asetilasyonu gibi bazı translasyon sonrası (post-translasyonel) değişiklikler söz konusu olduğunda durum çok net görünmemektedir<sup>2-4</sup>. Daha da önemlisi, epigenetik modifikasyonlar sperm ve oositlerin öncüleri olan primordial germ hücrelerinde (PGC'ler) sıfırlanır<sup>5</sup>. Epigenetik modifikasyonlar genetik materyali değiştirmede için, bu epigenetik yeniden programlama, ebeveynlerden kalıtılan genomik bilgilerin dokunulmadan kalmasını sağlar.

Kanser hem genetik hem de epigenetik bir hastalıktır. Genetik değişikliklerin ve mutasyonların birikmesi ve kromatin yapısındaki genel değişiklikler kanserin başlamasına ve ilerlemesine katkıda bulunur. Genetik ve epigenetik değişiklikler arasında bir etkileşim vardır. Örneğin, kromatini düzenleyen enzimleri kodlayan genler yetişkin ve pediatrik kanserlerde en sık mutasyona uğramış genler arasındadır ve bu mutasyonlar epigenomdaki değişiklikler ile ilişkilidir<sup>6</sup>. Bunun aksine, DNA metilasyonu sitozini deaminasyona daha duyarlı hale getirerek C>T transversiyon mutasyonlarına yol açar. Gerçekten de metillenmiş CpG bölgelerinde

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## Sonuç

Kanser ile ilişkili epigenetik değişikliklerin moleküler düzeyde fonksiyonel sonuçlarının anlaşılması önemlidir. Bu tür değişikliklerin en net etkisi gen ifadesi üzerinedir. Bununla birlikte, epigenetik modifikasyonların kromatinin yapısını nasıl değiştirdiği ve transkripsiyon faktörlerinin bağlanması ve histon modifikasyonları gibi diğer epigenetik değişikliklerle ilişkili olup olmadıkları hakkında daha fazla bilgi edinmek de önemlidir.

Kanser epigenetiği ile ilgili bilimsel araştırmalardaki ilerlemeler kişiselleştirilmiş tedavilere ve klinik uygulamalara giden yolu açacaktır. Epigenetik modifikasyonlar hastalığın prognozu ve tedavisi için yararlı biyobelirteçler haline gelecektir.

**Anahtar Kelimeler:** Asetilasyon, Epigenetik, Kanser, Metilasyon

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