BÖLÜM 8

İLAÇ DİRENÇLİLİĞİNDE WNT/B-KATENİN SİNYALİZASYONU VE GSTP1 ARASINDAKİ METABOLİK ETKİLEŞİM

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GİRİŞ

Kemoterapide ilaç dirençliliği, tedavi etkinliğini ve hasta sonuçlarını önemli ölçüde engelleyen kritik bir konudur. Kanser hücreleri, antikanser ilaçlara yanıt olarak evrimleşip adapte oldukça, ilaç direncinin mekanizmalarını ve etkilerini anlamak, tedavi stratejilerini optimize etmek için büyük önem taşımaktadır.

Kanser hücreleri, tedavi rejimlerini önemli ölçüde karmaşıklaştıran, tedavilere hem içsel (intrinsic resistance) hem de edinilmiş direnç (acquired resistance) gösterir. İçsel direnç, belirli tümör hücrelerinin terapötik ajanlara karşı direnç gösterme konusunda önceden var olan yeteneklerini ifade ederken; edinilmiş direnç, tedavinin kendisi tarafından indüklenen adaptasyonlar nedeniyle tedavi sonrası ortaya çıkar (1,2). Bu dirençlere çeşitli mekanizmalar katkıda bulunur. Bu mekanizmalar arasında genellikle ilaç metabolizmasındaki değişiklikler, ATP bağlayıcı kaset taşıyıcıları aracılığıyla artan ilaç efluksu, ilaç hedeflerindeki değişiklikler, artan DNA onarım kapasitesi ve apoptozdan kaçınma yer alır (3,4).

Kanserde ilaç direncinin ortaya çıkması, yalnızca kemoterapinin başarısızlığına yol açmaz, aynı zamanda kötü prognoz sonuçlarıyla da ilişkilendirilir (2,5). Kanserde ilaç direnç mekanizmaları, tedavilere verilen hücresel yanıtları önemli ölçüde bozan genetik mutasyonları ve epigenetik değişiklikleri içerir ve bu da tedavinin kalıcı olmamasına ve tümörlerin yeniden nüksetmesine katkı-

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DOI: 10.37609/akya.3862.c1433

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