BÖLÜM 2

Yaşlanma ve Kanser Fizyolojisi–İmmünolojisi–Genetiği

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GİRİŞ

Yaşlanma, organizmada zaman içinde meydana gelen biyolojik, fizyolojik ve moleküler düzeydeki değişikliklerle karakterize edilen kompleks bir süreçtir. Bu süreç, hücresel düzeyde onarılamayan DNA hasarları, telomer kısalması, mitokondriyal disfonksiyon, epigenetik düzenlemelerde bozulmalar ve hücresel senesans gibi çok sayıda biyolojik mekanizmayı içerir (1). Klinik olarak, yaşlanma ile birlikte bağışıklık sistemi işlevlerinde belirgin azalma (immünosenesans), kronik düşük düzeyli inflamasyon (inflammaging) ve rejeneratif kapasitede azalma ortaya çıkar (2). Kanser, genetik ve epigenetik düzensizliklerin bir sonucu olarak hücresel proliferasyonun kontrolsüz hale gelmesiyle gelişen bir hastalık grubudur. Giderek yaşlanan dünya nüfusunda, malignitelerin özellikle 65 yaş üstü bireylerde daha sık görülmesi, yaşlanma ve kanser arasındaki moleküler bağlantıların anlaşılmasını önemli kılmaktadır. Epidemiyolojik veriler, yeni tanı alan solid tümörlerin yaklaşık %60'ının 65 yaş üzeri bireylerde saptandığını göstermektedir (3). Ürolojik kanserler, özellikle prostat, mesane ve böbrek tümörleri yaşlı erkek bireylerde sık karşılaşılan malignitelerdir. Bu bölümde yaşlanma sürecine eşlik eden biyolojik değişimlerin kanser fizyolojisi, immün sistemi ve genetik regülasyon üzerindeki etkileri; ayrıca yaşlı bireylerde ürolojik kanserlerin özel durumu güncel kanıtlar ışığında detaylı olarak ele alınacaktır.

YAŞLANMA BİYOLOJİSİ VE KANSER

Yaşlanmanın moleküler temelleri, özellikle son yıllarda artan genomik, epigenetik ve proteomik çalışmalarla daha iyi anlaşılmaya başlanmıştır. López-Otín ve arkadaşlarının 2013 yılında tanımladığı yaşlanmanın dokuz temel biyolojik işareti (hallmarks of aging): "telomer kısalması, genomik instabilite, epigenetik değişiklikler, kayıp proteostaz, beslenme

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