BÖLÜM 1

ADAMTS GEN AİLESİ VE KANSER

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GİRİŞ

Kanser, tüm dünyada, kalp ve damar hastalıklarının ardından %23'lük oranla tüm ölümlerin ikinci en sık nedeni olarak karşımıza çıkmakta ve bu nedenle 21. Yüzyılın en yaygın epidemilerinden biri olarak değerlendirilmektedir [1, 2]. Ne yazık ki, son yıllarda tanı ve tedavi modalitelerindeki tüm ilerlemelere rağmen hemen hemen tüm kanserlerde arzu edilen sağkalım oranlarına ulaşılamamıştır. Dolayısıyla, mevcut tanısal ve terapötik yöntemlerin dışında alternatif ve hedefe yönelik efektif yaklaşımlar bir zorunluluk haline gelmiştir. Bu perspektiften hareketle, son yıllardaki klinik çalışmaların birçoğunda kanserin moleküler ve genetik temeli primer araştırma odağı olmuştur.

Bilindiği üzere, karsinogenez, hücre siklus kontrolü, programlı hücre ölümü (apopitozis), anjiyogenez ve hücre dışı matriks yeniden modellenmesi gibi hücresel ve hücreler arası birçok karmaşık süreçlerdeki normal dışı fonksiyonlar ve bozukluklar ile karakterizedir. Bunlar arasında, hücre dışı matriks karmaşık moleküler süreçlerin gerçekleştiği ve daha birçoğunun keşfedilmeyi beklediği bilinmeyenlerle dolu bir dünyadır. Normalde, hücre dışı matriks hücrelere mekanik destek sağlamanın yanı sıra embriyogenez, hücre migrasyonu, hücreler arası etkileşim, hemostaz, apopitoz ve yara iyileşmesi gibi pek çok fizyolojik süreçlerde önemli rollere sahip hücrelerarası bir kompartmandır. Bütün bu kompleks olaylar zinciri hücre dışı matrikste etki gösteren proteolitik ve anti-proteolitik moleküllerin belirli bir denge içerisinde karşılıklı etkileşimleri sayesinde sorunsuz yürütülür. Örneğin, kanser hücrelerinin hücre dışına yayılımının ve metastazının ilk ve en önemli basamaklarından biri olan hücre dışı matriks invazyonu bu zıt etkili proteinler tarafından önlenir. Bu yüzden, hücre dışı matrikste meydana gelen yapısal bozulmalar ve anormal fonksiyonlar kanser gelişiminde çok kritik önem taşır. Hücre dışı matriksteki yapısal bozulmalar gibi anjiyogenezis ve diğer birçok

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