16. BÖLÜM

GENOM DÜZENLEME VE TEDAVİLERİN GELECEĞİ

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GİRİŞ

Genom düzenleme; tedavisi olmayan birçok hastalığın özellikle kanser ve tek gen hastalıklarının tedavisinin umut ışığı ve yarınları olma potansiyeline sahiptir (1,2). Genom düzenlemenin tedavi olarak kullanılma çabaları 1970'lere dayansa da (3) geçişte yaşanan trajik sonlu denemelerden dolayı günümüze kadar büyük ilerlemeler kaydedilememiştir. Genetik tedavi denemelerinin ilk zamanlarında ağır kombine immün yetmezlik (SCID) hastaları üzerinde yapılan iki farklı çalışmada; bazı hastaların kliniklerinde en fazla orta düzey ilerleme olurken çoğunda klinik tabloda ilerleme kaydedilememiş ve çalışmalardan birinde tedaviye bağlı sekonder lösemi nedenli ölümler yaşanmıştır (4-7). Yaklaşık aynı zamanlarda yapılan başka bir çalışmada ise ornitin transkarbamilaz eksikliği olan bir hasta tedavi edilmek istenmiş fakat tedavide kullanılan vektör nedenli multiorgan yetmezliği gelişmiş ve hasta ex olmuştur (8).

Temel olarak genom düzenleme ve genetik tedaviler; monogenik veya kompleks genetik hastalıkları tedavi etmek için mutant genin destrükte edildiği veya yerine yeni bir dizi yerleştirildiği yöntemler bütünüdür (9). Genetik tedavilerin ilk ve en önemli aşaması DNA'da çift dal kırığı ile hasar oluşturup bu hasarın hücre tamir mekanizmaları ile tamir edilmesidir (10, 11)(Şekil-1). DNA'da oluşan çift dal kırıkları hücre için ölümcül olduğu için çeşitli mekanizmalar ile hızlıca tamir edilmektedir. Çift dal DNA kırığı homolog rekombinasyon (HR) veya non homolog rekombinasyon (NHR) ile tamir edilmekte ve hücre tarafından hangi yöntemin seçileceği hücrenin hangi fazda olduğu ile

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lar ve DNA toksisitesi aşılması gereken sorunlar olarak karşımızda dursa da mükemmel CRISPR sistemleri geliştirmeye yönelik artan çabalar çözümleri kısa sürede önümüze getirecektir. Bu gelişmeler yarının tıbbi tedavilerin çok daha iyi yerlerde olacağını düşündürmekte ve geleceğe umutla bakabilmemizi sağlamaktadır.

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