11.
BÖLÜM

MikroRNA'ların Meme Kanserinin Tanı ve Takibinde Kullanımı

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GİRİŞ

MikroRNA'lar (miRNA'lar), normal hücresel süreçlerde ve hastalık süreçlerinde kritik işlevlere sahip transkripsiyon sonrası gen ifadelerini düzenleyen, 19 ila 25 nükleotid uzunluğunda evrimsel olarak korunmuş kısa RNA moleküleridir (1). MiRNA'lar başlangıçta RNA polimeraz II ve çeşitli transkripsiyon faktörleri tarafından birincil miRNA (pri-miRNA) transkripti olarak işlenir. Devamında, pri-miRNA'lar, öncü miRNA'lar (pre-miRNA'lar) üretmek için nükleer bir RNaz III enzimi olan Drosha tarafından işlenir. Öncü miRNA'lar çekirdekten sitoplazmaya taşınır ve burada başka bir RNaz III ailesine ait endonükleaz olan Dicer tarafından 22 baz çifti (bp) içeren miRNA dupleksleri haline getirilirler. Olgun miRNA'lar daha sonra miRNA dupleksleri'nden çözülür ve susturma kompleksine (RISC) yüklenir (**Şekil 1**). MiRNA-RISC kompleksi, hedef mRNA'nın proteine translasyonunu bloke edebilir ve/veya hedef mRNA transkriptinin degradasyonunu (bozunmasını) indükleyerek gen ifadelerini düzenlerler. Genel olarak miRNA'lar, mRNA'ların 3' kodlanmayan bölgelerine (3'-UTR) bağlanıp ve mRNA translasyonunu baskılar (2). miRNA'lar, kontrolsüz hücre bölünmesini teşvik

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si önemlidir. Bunun yanında, tedavi amaçlı kullanılacak miRNA modülatörlerinin (inhibitör ya da mimikler) kanser hücrelerine iletilmek üzere daha stabil hale getirilmeleri ve taşınma araçlarının (lipozom, vs) ve dağıtım stratejilerinin multidisipliner çalışma yöntemleriyle optimize edilmesi gerekir. Sonuç olarak, miRNA bazlı tedavilerdeki ilerleme, meme kanseri tedavisinde devrim yaratma ve kişiselleştirme potansiyeline sahip olmak beraber, klinik olarak tedavi amaçlı uygulamalarına geçilmeden önce etki mekanizmaların *in vivo* koşullarda daha detaylı araştırılmalı ve miRNA temelli tedavi uygulamalarının biyolojik sonuçları hakkında daha derinlemesine bilgi sahibi olunması gerekmektedir.

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