

Bölüm 8

KANSER İLİŞKİLİ SİNYAL İLETİ YOLAKLARI

Beslen GÖKSOY¹

GİRİŞ

Hücre sinyali basit bir terimle hücre içi veya hücreler arası iletişim kurulması ve bu iletişim sonucu hücrelerin birbirleriyle ilişki kurmasıdır. Hücrelerin büyüme, çoğalma, farklılaşma ve yaşamını sürdürmesi için bu sinyallere ihtiyacı vardır. Çoğu zaman bu olaylar, hedef molekülün kinaz aktivitesi içeren enzimler tarafından fosforilasyonunu yoluyla meydana gelir. Bir ligand (büyüme faktörü, hormon, sitokin gibi) reseptörüne bağlandığında fosforilasyon ve kinaz aktivitesi ile sinyal yolağını başlatır. Böylece transkripsiyon faktörlerinin oluştuğu çekirdeğe iletilmesini sağlayan bir dizi fosforilasyon olayının gerçekleşmesine izin veren bir sinyalleme kaskadı aktif hale gelir. Sonunda gen ekspresyonunda değişikliklere ve hücre tarafından biyolojik bir yanıtın üretilmesi gerçekleşir¹.

Sinyal yollarının bilinmesi klinik açıdan özellikle kanser tanı ve tedavisinde önemli bir yere sahiptir. 2018 yılında Kanser Genom Atlası tarafından 9125 tümörde toplam 33 farklı kanserde sinyal yolları detaylandırılmış ve tümörlerin %89'unun en az bir sinyal yolağında değişikliğe sahip olduğu, %57'sinin ise şu anda mevcut olan ilaçlar tarafından potansiyel olarak hedeflenebilen en az bir değişikliğe sahip olduğu belirtilmiştir². Hücre sinyali kapsamını, ayrıntılı mekanizmalarını ve birlikte oluşumunu anlama ile bu yollardaki onkojenik değişiklikler hasta bakımını iyileştirebilecek yeni terapötik yaklaşımların geliştirilmesi için kritik öneme sahiptir. Bu bölümde kanser sinyalizasyonunda önemli olan kilometre taşlarının birkaçı tartışılacaktır.

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sinyal iletiminin düzensizliği bulunur. Tüm kanserlerin nasıl geliştiğini açıklamak ve hatta aynı kanser içinde farklı kanserlerin nasıl geliştiğini açıklamak yeterli olmasa da ortak olan, önemli sinyal yollarının düzensizliğidir. Sinyal yollarının nasıl işlev gördüğünün daha fazla anlaşılması, yeni terapötik yaklaşımların geliştirilmesine yol açabilir. Kanser kök hücrelerinin epigenetik karakterlerini ve ilgili sinyal yollarını tanımlamak, kemo-dirençli farklı kanserlere karşı terapötik yolların geliştirilmesine katkıda bulunabilir¹⁰⁰.

Anahtar Kelimeler: kanser; sinyal yolları; TGF- β ; MAPK; JAK/STAT; PI3K; WNT

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