Bölüm 2

HÜCRE ÖLÜMÜNE GENEL BAKIŞ VE GÜNCEL HÜCRE ÖLÜMÜ MEKANİZMALARI

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GİRİŞ

Vücudumuzda yaşam döngüsünü tamamlayıp sağlıklı yaşlanmış hücreler ve hasar görmüş hücreler de dahil olmak üzere günde milyonlarca hücre yerlerine sağlıklı yeni hücrelerin gelmesi amacıyla ölmektedir. Hücre ölümü, ölü ya da ölmekte olan hücre tanımını ve hücre ölümü çeşitlerini bilimsel çalışma ve yayınlanan bilimsel makalelere dayandırarak sınıflandıran ve bu sınıflandırmayı seriler halinde güncel bilgiler ışığında yayınlayan bir "Hücre Ölümü Adlandırma Komitesi- The Nomenclature Committee on Cell Death (NCCD) mevcuttur. Komisyonun amacı hücre ölümü alanında devam eden bilimsel çalışmaların çıktılarını göz önünde tutarak hücre ölümü konusunda kabul görmüş bir isimlendirme ve sınıflandırma sağlamaktır (1). Bu amaç doğrultusunda farklı hücre ölümü çeşitleri farklı açılardan (örneğin morfolojik, biyokimyasal, fonksiyonel ve terapötik uygulamalar) değerlendirilmektedir ve bu konuda araştırmacılar arasında tartışma ve görüş paylaşımı ortamı yaratılmıştır. Böylece ortak bir dil ile oluşturulmuş esnek kavramlar geliştirilmiştir ve hücre ölümü çalışan bilim insanları arasında iletişim kurulması sağlanmıştır (2). Komite 2005 yılından bu yana beş derleme makale yayınlamıştır (1–5). Komitenin 2005 ve 2009 yıllarında yayınlanan derlemelerinde hücre ölümü litetratüründeki kavramlardan ve hücre ölümünün sınıflandırılmasından bahsedilmiştir (2,5). Bir sonraki derleme makalesinde ise (4) ise hücre ölümü alt tiplerinin moleküler düzeyde meydana gelen süreçleri açıklanmıştır. 2015 yılındaki derlemede komite hücre ölümüne farklı bir bakış açısı kazandırmak adına hücre ölümünü "gerekli" (essential) ya da "yardımcı" (accessory) yönden değerlendirmiştir. Bir diğer deyişle hücre ölümü mekanizmalarınınsırasıyla etiyolojik ve morfolojik /biyokimyasal yönden ne şekilde meydana geldiği özetlenmiştir (3). Komitenin 2018 yılında yayınladıkları son derlemede ise hücre ölümünün moleküler mekanizmalarına derinlemesine değinilmiştir (1). Bu kitap bölümde hücre ölümü araştırmalarının sonuçlarını içeren güncel literatür bulguları derlenmiştir ve hücre ölümü alanında yapılan çalışmalar özetlenmiştir.

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bu süreçlerin her zaman hücrenin "ölümü" ile sonuçlanmayan süreçler olduğu vurgulanmaktadır. Regüle edilen (regulated) hücre ölümü süreçlerine benzer morfolojik ve biyokimyasal özellikler göstermekle beraber sözkonusu olaylar sonucunda hücrelerin ölümü gerçekleşmeyebilmektedir (1).

1. Hücresel Senesens (Cellular senescence)

Senesens-ilişkili sekretuvar fenotip (SASP- senescence-associated secretory phenotype) de dahil olmak üzere, hücrelerin geridönüşümsüz bir şekilde spesifik olarak morfolojik ve biyokimyasal bazı özelliklerinde kayıp meydana gelmesi sonucunda gelişir ve regüle edilen (regulated) hücre ölümü çeşidi değildir (112,113).

2. Mitotik Katastrof (Mitotic catastrophe)

Mitotik katastrof, fazla miktarda meydana gelen DNA hasarı, mitotik süreçle ilgili problemler ve mitotik kontrol noktalarının yetersizliği nedeniyle mitozu tamamlayamayan hücrelerin çoğalmasını ve hayatta kalmasını engelleyen onkosupresif bir mekanizmadır (114,115). Regüle edilen (regulated) hücre ölümü çeşidi değildir. Endojen (DNA replikasyon mekanizması sırasında meydana gelen stres ve DNA replikasyonunda veya kromozom ayrılması sırasında rol alan faktörlerin düzensiz aktivitesi) ve egzojen (ksenobiyotikler) tetikleyiciler tarafından indüklenebilen bir süreçtir (116,117). Örneğin; mitotik katastrof süreci sonucunda regüle edilen bir hücre çeşidi olan "mitotik ölüm" diye adlandırılan bir süreçle hücreler ölebilmektedir.

Anahtar Kelimeler: Hücre Ölümü, Sınıflandırma, Programlı, Ani gelişen

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