BÖLÜM 3

KEMİRGENLERDE DENEYSEL SEPSİS MODELLERİ

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1. GİRİŞ

Sepsis, enfeksiyonun tetiklediği düzensiz konak yanıtı sonucu ortaya çıkan, organ disfonksiyonu ile seyreden ve yüksek mortaliteye neden olan kompleks bir sendromdur. Dünya Sağlık Örgütü ve Sepsis-3 konsensusu, sepsisi enfeksiyona bağlı organ disfonksiyonu olarak tanımlamaktadır (1). Küresel ölçekte, sepsis yılda yaklaşık 48,9 milyon vakayı ve 11 milyona yakın ölümü beraberinde getirmektedir. Bu rakamlar, toplam küresel ölümlerin yaklaşık beşte birine denk gelmektedir (2).

Klinikte sepsis, oldukça heterojen bir tablo sergiler. Hastaların yaşları, komorbiditeleri, enfeksiyonun kaynağı, kullanılan antibiyotikler ve yoğun bakım koşulları sepsisin seyrini belirgin şekilde etkiler. Dolayısıyla insan sepsisinde gözlemlenen heterojenite, deneysel çalışmaların tasarımını da doğrudan zorlaştırmaktadır. Bu bağlamda, hayvan modelleri, sepsisin temel mekanizmalarının anlaşılması, immün yanıtın farklı evrelerinin araştırılması ve yeni tedavi stratejilerinin preklinik düzeyde test edilmesi için vazgeçilmez araçlardır (3). Kemirgenler (özellikle fare ve sıçan), sepsis çalışmalarında yaygın olarak kullanılan deney hayvanlarıdır. Bunun başlıca nedenleri arasında genetik homojenite, ucuz maliyet, hızlı üreme döngüsü, immün sistem hakkında kapsamlı bilgi birikimi ve deneysel protokollere kolay adaptasyonları yer almaktadır. Ayrıca transgenik ve knockout farelerin geliştirilmesi, belirli genlerin ve sinyal yolaklarının sepsis patofizyolojisindeki rollerinin incelenmesini mümkün kılmıştır (4).

Bu kitap bölümünde, kemirgenlerde kullanılan deneysel sepsis modelleri detaylı şekilde ele alınacak, avantaj ve dezavantajları tartışılacak, ayrıca gelecekteki perspektifler değerlendirilecektir.

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