Bağırsak Mikrobiyotası ve Ateroskleroz Riski: Mekanizmalar ile ilgili Güncel Anlayış

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1. Giriş

İnsan bağırsağında, konağın normal işleyişi için gerekli olan çok sayıda komensal ve ortak yaşayan mikroorganizma bulunur (Aron-Wisnewsky ve diğerleri 2012; Bäckhed ve diğerleri. 2004; Cani ve diğerleri. 2012; Cox ve Blaser 2013; den Besten ve diğerleri. 2013; Le Chatelier ve diğerleri. 2013; Nicholson ve diğerleri. 2005; Tremaroli ve Bäckhed 2012). Bağırsak mikrobiyotası olarak adlandırılan bakteri, arke, mantar, virüs ve diğer protozoonlardan oluşan bağırsağın kolonizasyonu, milyonlarca yıl boyunca meydana gelen ortak evrimsel bir sürecin sonucudur (Aron-Wisnewsky ve diğerleri 2012; Bäckhed ve diğerleri. 2004; Cani ve diğerleri. 2012; Cox ve Blaser 2013; den Besten ve diğerleri. 2013; Le Chatelier ve diğerleri. 2013; Nicholson ve diğerleri. 2005; Tremaroli ve Bäckhed 2012). Bu organizmalar konaktan besin alırlar, kompleks karbonhidratların sindiriminde konakçıya yardımcı olurlar, bağışıklık sistemini hassas bir şekilde düzenlerler, metabolik ve enerji homeostazını korurlar, fırsatçı patojenlere karşı koruma sağlarlar ve hatta nörogelişime yardımcı olurlar (Aron-Wisnewsky ve diğerleri 2012; Bäckhed ve diğerleri. 2004; Cani ve diğerleri. 2012; Cox ve Blaser 2013; den Besten ve diğerleri. 2013; Le Chatelier ve diğerleri. 2013; Nicholson ve diğerleri. 2005; Tremaroli ve Bäckhed 2012). İlginç bir şekilde, doğumdan önce steril olan bağırsak, erken kolonize edicileri, doğum sırasında annenin fiziksel teması yoluyla edinir (Palmer ve ark. 2007; Dominguez-Bello ve ark. 2010). Bağırsağın barındırdığı trilyonlarca mikroorganizmanın çoğu, bileşimleri sindirim sistemi boyunca değişen zorunlu anaeroblardır (Aron-Wisnewsky ve ark. 2012; Fouhy ve ark. 2012). Yüksek verimli dizileme (HTS: high throughput sequencing) çalışmalarının ve biyoinformatik araçların geliştirilmesi; yaş, cinsiyet, genetik yapı ve çevresel etkilere dayalı olarak bağırsak mikrobiyotasının bileşiminde bireyler arası farklılıkları aydınlatmada devrim niteliğinde olmuştur (Fouhy ve diğerleri 2012; Li ve diğerleri 2014; Parkhill 2013; Santiago ve diğerleri 2014). Mikrobiyotadan elde edilen metabolitlerin taranması, metatranskriptomikler ve metaproteomikler gibi çeşitli modern yaklaşımlar; bağırsak mikrobiyomunu ve onun ateroskleroz ile ilişkisini daha iyi anlamak için büyük bir veri havuzundan yararlanmanın yollarını sağlar (Nicholson ve ark. 2005; Gosalbes ve

TMAO seviyelerini azaltarak ve hepatik safra asidi neo-sentezini artırarak TMAO'ya bağlı aterosklerozu zayıflattığını bulmuşlardır (Chen ve ark. 2016).

8 Sonuç

Ateroskleroz multifaktöriyel kronik inflamatuar bir hastalıktır. Bu nedenle, kesin altta yatan mekanizmaları aydınlatmak zordur. Bununla birlikte, son bulgular, bağırsak mikrobiyotası ile ateroskleroz da dahil olmak üzere çok sayıda metabolik hastalığın patogenezi arasında bir bağlantı olduğunu göstermiştir. Çalışmalar, mikrobiyotanın; plak gelişimi, bağışıklık sistemini aktive etme, lipid ve kolesterol metabolizmasını değiştirme, arter duvarında iltihaplanmaya neden olma ve bakteriyel metabolitlerin üretimi gibi çoklu mekanizmalar yoluyla aterosklerozu etkileyebileceğini göstermektedir. Bağırsak mikrobiyota transplantasyonu ile ilgili deneysel çalışmalar ile insanlarda ve farelerde bağırsak mikrobiyotasının kompozisyonunun analizi, spesifik bağırsak mikrobiyal suşlarının bolluğunun değişmesinin aterojenez ile ilişkili olduğunu göstermektedir. Çeşitli hayvan modellerinde yapılan son araştırmalar; prebiyotikler, probiyotikler, antibiyotikler ve bağırsak mikrobiyotasını hedef alan küçük moleküller kullanılarak ateroskleroz gelişiminin başarılı terapötik manipülasyonunu bildirmiştir. Bununla birlikte, klinik ortamında kardiovasküler hastalıklar için bağırsak mikrobiyota hedefli tedavinin rutin uygulamasını görmeden önce, uzun bir yol katedilmesi gerekmektedir. Disbiyoz ve ateroskleroz arasında kesin ilişkiler kurmak için büyük prospektif klinik çalışmaların garanti edildiği bir aşamadayız. Ek olarak, bağırsak mikrobiyomunu hedef alan terapötikleri uygulamadan önce hastalıkla ilişkili temel bakteri taksonlarını ve metabolitleri belirlemek önemlidir.

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