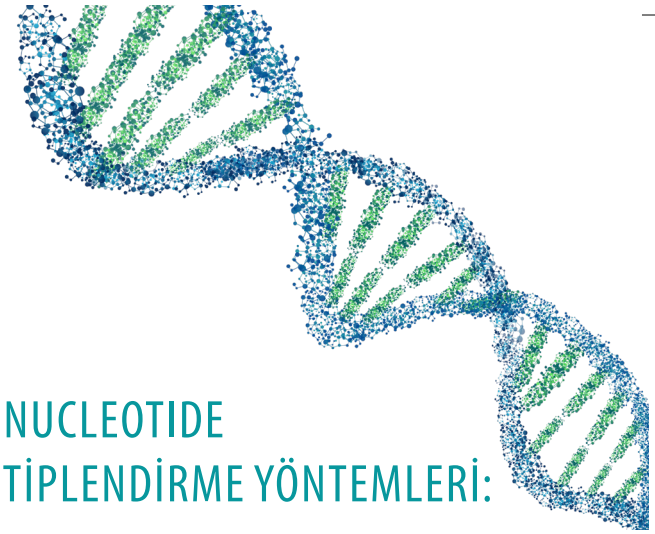

BÖLÜM 28

TEK NÜKLEOTİT POLİMORFİZM [SINGLE NUCLEOTIDE POLYMORPHISMS (SNP)] VE TEK LOKUS TİPLENDİRME YÖNTEMLERİ: PRENSİPLERİ, METODOLOJİ VE KULLANIM ALANLARI

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Polimorfizm, kişiler, gruplar veya popülasyonlar arası DNA dizisindeki farklılıklar olarak adlandırılmaktadır. DNA seviyesindeki polimorfizm, tek bir baz çifti değişimi, birçok baz çifti değişimi veya tekrarlanan dizilerdeki değişimler olmak üzere çeşitli varyasyonları içermektedir. DNA polimorfizm çeşitleri; tek nükleotit polimorfizmleri [single nucleotide polymorphisms, SNP)], restriction fragment length polymorphism (RFLP), değişken sayıda tandem tekrarlar [minisatellitler; variable numbers of tandem repeats (VNTR)] ve kısa tandem tekrarlar [mikrosatellitler; short tandem repeats (STR)] olarak sıralanabilir [1].

Polimorfizmlerin oluşma şekilleri tek nükleotit değişimi, delesyon ve insersiyon olarak özetlenebilir. Tek nükleotit değişimi DNA üzerinde her 2.000-2.500 bazda bir gözlemlenmektedir; bu değişim transisyon veya transversiyon yoluyla gerçekleşir. Transisyon bir pürin bazının diğer pürin bazına (A→G ya da G→A) ya da bir pirimidin bazının diğer pirimidin bazına (T→C ya da C→T) dönüşmesidir. Transversiyon ise bir pürin bazının (A, G) pirimidin bazlarından (C, T) birine dönüşmesidir. Delesyon ise DNA dizisinden nükleotidin silinmesi durumudur, sonucunda ilgili genin boyu kısalır. Gen eğer protein kodlayan bir gen ise proteinin amino asit dizisinde değişim olacağı için protein işlevini yitirecektir. İnsersiyon ise delesyonun tersidir; DNA dizisine nükleotit eklenmesiyle meydana gelir, insersiyon sonrası genin uzunluğu artar. Nükleotit eklenen gen protein kodlayan bir gen ise amino asit dizilimi değişeceği için ortaya çıkan protein delesyonda olduğu gibi işlevini yitirecektir. İnsersiyon ve delesyonlar ayrıca indel olarak da adlandırılmaktadır.

Tek Nükleotit Polimorfizmi

Tek nükleotit polimorfizmi [single nucleotide polymorphism (SNP)], en yaygın kalıtsal dizi varyasyonlarından biridir. Genomik düzeyde belirli bir pozisyonda tek bir nükleotidin değişmesinin neden olduğu bir DNA dizisi polimorfizmidir. Tek nükleotit baz değişikliği, bir geçiş (transisyon) mutasyonu, transversiyon mutasyonu, insersiyon veya

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emm-tiplendirme, PFGE veya MLST gibi diğer tiplendirme yöntemleriyle tamamlanmalıdır.

Tek lokus tiplendirme, Campylobacter flagellin B geninin (*flaB*) kısa değişken bölgesindeki (*short variable region*, SVR) nükleotit diziliminin tanımlanmasında ve epidemiyolojik çalışmalarda kullanılmaktadır. *Pulsed-field gel electrophoresis* en yüksek ayrım gücü olan teknik olsa da yapılan çalışmalar, *flaB*'nin SVR bölgesi dizilemesinin Campylobacter için hızlı ve tekrarlanabilir bir tiplendirme yöntemi olduğunu göstermiştir [56]. Ayrıca, *flaB* dizi tiplendirmenin, salgın izolatlarını ayırt etmek için MLST gibi diğer tiplendirme yöntemleri ile kombinasyonunun faydalı olduğu bildirilmiştir.

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