Bölüm 8

SMA GENETİĞİ

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GİRİŞ

Spinal müsküler atrofi olarak tanımlanan SMA, omurilikteki motor nöronların dejenerasyonu ile karakterize, ilerleyici proksimal kas zayıflığına neden olan otozomal resesif sinir-kas hastalığıdır. Motor nöronlar için hayati öneme sahip SMN1 (survival motor neuron) genindeki mutasyonlar ve özellikle delesyonlar nedeniyle SMN gen ürününün yetersizliği ve/veya işlevsizliği sonucu meydana gelen bir hastalıktır. SMA hastalığı, çocukluk çağı ölümlerinin en yaygın kalıtsal nedeni olarak dikkat çekmekte olup tahmini görülme sıklığı; 6.000 -10.000 canlı doğumda 1 olup, taşıyıcılık sıklığı 1/50 düzeyindedir.

SMN1 genindeki mutasyonlar, 4 grupta toplanan tüm SMA tiplerinin birinci derecede sorumlusudur. Yedek veya *backup* gen olarak tanımlanan SMN2 geninin kopya sayısı ise, hastalığın şiddeti konusunda belirleyici olup hangi SMA tipinin ortaya çıkacağını belirler.

SMN1 ve SMN2 genlerinin her ikisi de, hayatta kalma motor nöronu (SMN) proteini adı verilen bir proteinin yapımı için genetik bilgi sağlar. Normalde, çoğu fonksiyonel SMN proteini SMN1 geninden üretilirken, küçük bir miktar da SMN2 geninden üretilir. SMN2 geninden alternatif splayzing ile üretilen SMN proteininin birkaç farklı versiyonu bulunur, ancak yalnızca bir versiyon işlevsel fakat miktar olarak sadece %10 düzeyinde katkı sağlar. Üretilen diğer versiyonlar ise görece daha küçüktür ve çabuk bozulur. SMN proteini, motor nöronların bakımı için önemli olan, SMN kompleksi adı verilen bir grup proteinden biridir. Spinal müsküler atrofisi olan çoğu insanda, SMN protein üretimini bozan SMN1 geninin bir parçası eksiktir. SMN proteininin eksikliği, motor nöron ölümüne neden olarak beyin-kas sinyal iletimi kesintiye uğrayarak ilgili kas/kas grubunun dejenerasyonuna neden olur

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