ALZHEIMER HASTALIĞINDA NHE6: ENDOZOMAL PH DÜZENLENMESİ VE MOLEKÜLER MEKANİZMALAR

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ÖNSÖZ

Alzheimer hastalığı, genetik yatkınlık, hücre içi protein trafiği, endozomal-lizozomal işlevler ve nörodejeneratif süreçlerin birbiriyle etkileşimi sonucunda gelişen kompleks bir hastalıktır. Son yıllarda yapılan çalışmalar, endozomal pH dengesinin ve bu dengenin düzenlenmesinde görev alan proteinlerin Alzheimer hastalığının moleküler mekanizmalarının anlaşılmasında önemli bir yere sahip olduğunu göstermektedir.

Bu kitap, "NHE6 Gen Modülasyonunun Alzheimer ile İlişkili Genlerin Anlatımı Üzerine Etkisinin Araştırılması" başlıklı doktora tez çalışmam temel alınarak hazırlanmıştır. Kitapta Alzheimer hastalığının temel klinik, patolojik ve genetik özelliklerinin yanı sıra endolizozomal sistem, hücre içi pH düzenlenmesi ve *SLC9A6* geni tarafından kodlanan NHE6 proteininin hücresel işlevleri ele alınmıştır. Ayrıca NHE6'nın Christianson sendromu, epilepsi, Parkinson hastalığı ve Alzheimer hastalığı ile ilişkisi değerlendirilmiş; NHE6 ve endozomal pH düzenlenmesinin terapötik hedef olarak taşıdığı potansiyel, mevcut literatür bulguları çerçevesinde tartışılmıştır.

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Dr. İrem Gülfem Akın

KISALTMALAR

Kısaltmalar	**Açıklama**
Aβ	: Amiloid-beta
AEP	: Asparaginil endopeptidaz
AH	: Alzheimer hastalığı
AMPA	: α-Amino-3-hidroksi-5-metil-4 izoksazolpropiyonik asit
AMPAR	: AMPA reseptörü
AP2	: Adaptör protein kompleksi 2
ApoE	: Apolipoprotein E
ApoE4	: Apolipoprotein E4
APP	: Amiloid öncü protein
AT2	: Anjiyotensin II tip 2 reseptörü
BACE1	: Beta-bölgesi APP parçalayıcı enzim 1
BDNF	: Beyin kaynaklı nörotrofik faktör
BOS	: Beyin omurilik sıvısı
CKIε	: Kazein kinaz 1 epsilon
CME	: Klatrin aracılı endositoz
CSNK1E	: Kazein kinaz 1 epsilon geni
DNA	: Deoksiribonükleik asit
EE	: Erken endozom
eNHE	: Endozomal Na^+/H^+ değiştirici
FDA	: Amerika Birleşik Devletleri Gıda ve İlaç Dairesi
GABA	: Gama-aminobütirik asit
GDP	: Guanozin difosfat
GTP	: Guanozin-5'-trifosfat
HDAC	: Histon deasetilaz
HDAC4	: Histon deasetilaz 4
HEK293	: İnsan embriyonik böbrek 293 hücreleri
IGF1	: İnsülin benzeri büyüme faktörü 1
IRS	: İnsülin reseptörü substratı
IRS1	: İnsülin reseptörü substrat 1 geni

KEGG : *"Kyoto Encyclopedia of Genes and Genomes"*
LE : Geç endozom
LTP : Uzun süreli potansiyasyon
MRG : Manyetik rezonans görüntüleme
MSS : Merkezi sinir sistemi
NFT : Nörofibriler yumak
NHE : Na^+/H^+ değiştirici
NHE6 : Na^+/H^+ değiştirici 6
NMDAR : N-metil-D-aspartat reseptörü
PET : Pozitron emisyon tomografisi
PH : Parkinson hastalığı
PHF : Eşleşmiş sarmal filament
pHi : Hücre içi pH
pHo : Hücre dışı pH
PSEN1 : Presenilin 1 geni
PSEN2 : Presenilin 2 geni
PSD95 : Postsinaptik yoğunluk proteini 95
pTrkB : Fosforile TrkB
RACK1 : Aktive protein kinaz C reseptörü 1
RE : Geri dönüşüm endozomu
RNA : Ribonükleik asit
SE : Sinyal endozomları
SLC9A6 : *"SLC9A6 solute carrier family 9 member A6 "* geni
SNARE : Çözünür NSF bağlanma proteini reseptörü
SNP : Tek nükleotid polimorfizmi
SV2 : Sinaptik vezikül proteini 2
TM : Transmembran
TrkB : Tropomiyozin reseptör kinaz B
V-ATPaz : Vakuoler tip H^+-ATPaz
βCTF : Karboksil-terminal APP parçacığı

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