PARKIN Mutation

Mutations in the parkin gene (PARK2;OMIM #600116) [1) 2)], are the most common genetic risk factors for early-onset Parkinson's disease (EOPD) [3) 4) 5) 6) 7) 8) 9) 10) 11) 12) 13)].

Kunath et al., propose that Parkinson's patients with PARKIN mutations may benefit most from a cell replacement therapy because (i) they often lack synucleinopathy, and (ii) their neurodegeneration is often confined to the nigrostriatal pathway. While patients with PARKIN mutations exhibit clinical signs of Parkinson's, post-mortem studies to date indicate the majority lack Lewy bodies suggesting the nigral dopaminergic neurons are lost in a cell autonomous manner independent of α-synuclein mechanisms. Furthermore, these patients are usually younger, slow-progressing, and typically do not suffer from complex non-nigral symptoms that are unlikely to be ameliorated by a cell replacement therapy. Transplantation of dopaminergic cells into the putamen of these patients will provide neurons with wild-type PARKIN expression to re-innervate the striatum. The focal nature of PARKIN-mediated neurodegeneration and lack of active synucleinopathy in most young-onset cases makes these patients ideal candidates for a dopaminergic cell replacement therapy. Strategies to improve the outcome of cell replacement therapies for sporadic Parkinson's include the use of adjunct therapeutics that target α-synuclein spreading and the use of genetically engineered grafts that are resistant to synucleinopathy [14)].

References

1)
Kitada T, Asakawa S, Hattori N, et al. Mutations in the parkin gene cause autosomal recessive juvenile parkinsonism. Nature. 1998 Apr 9;392(6676):605–608.
2)
Hedrich K, Eskelson C, Wilmot B, et al. Distribution, type, and origin of Parkin mutations: Review and case studies. Mov Disord. 2004 Oct;19(10):1146–1157.
3)
Lucking CB, Durr A, Bonifati V, et al. Association between early-onset Parkinson's disease and mutations in the parkin gene. French Parkinson's Disease Genetics Study Group. N Engl J Med. 2000 May 25;342(21):1560–1567.
4)
Hedrich K, Marder K, Harris J, et al. Evaluation of 50 probands with early-onset Parkinson's disease for Parkin mutations. Neurology. 2002 Apr 23;58(8):1239–1246.
5)
Abbas N, Lucking CB, Ricard S, et al. A wide variety of mutations in the parkin gene are responsible for autosomal recessive parkinsonism in Europe. French Parkinson's Disease Genetics Study Group and the European Consortium on Genetic Susceptibility in Parkinson's Disease. Hum Mol Genet. 1999 Apr;8(4):567–574.
6)
Periquet M, Latouche M, Lohmann E, et al. Parkin mutations are frequent in patients with isolated early-onset parkinsonism. Brain. 2003 Jun;126(Pt 6):1271–1278.
7)
Lohmann E, Periquet M, Bonifati V, et al. How much phenotypic variation can be attributed to parkin genotype? Ann Neurol. 2003 Aug;54(2):176–185.
8)
Camargos ST, Dornas LO, Momeni P, et al. Familial Parkinsonism and early onset Parkinson's disease in a Brazilian movement disorders clinic: phenotypic characterization and frequency of SNCA, PRKN, PINK1, and LRRK2 mutations. Mov Disord. 2009 Apr 15;24(5):662–666.

9)
Macedo MG, Verbaan D, Fang Y, et al. Genotypic and phenotypic characteristics of Dutch patients with early onset Parkinson's disease. Mov Disord. 2009 Jan 30;24(2):196–203.
10)
Hertz JM, Ostergaard K, Juncker I, et al. Low frequency of Parkin, Tyrosine Hydroxylase, and GTP Cyclohydrolase I gene mutations in a Danish population of early-onset Parkinson's Disease. Eur J Neurol. 2006 Apr;13(4):385–390.
11)
Chung EJ, Ki CS, Lee WY, Kim IS, Kim JY. Clinical features and gene analysis in Korean patients with early-onset Parkinson disease. Arch Neurol. 2006 Aug;63(8):1170–1174.
12)
Bras J, Guerreiro R, Ribeiro M, et al. Analysis of Parkinson disease patients from Portugal for mutations in SNCA, PRKN, PINK1 and LRRK2. BMC Neurol. 2008;8:1.
13)
Vinish M, Prabhakar S, Khullar M, Verma I, Anand A. Genetic screening reveals high frequency of PARK2 mutations and reduced Parkin expression conferring risk for Parkinsonism in North West India. J Neurol Neurosurg Psychiatry. 2009 Sep 3;
14)
Kunath T, Natalwala A, Chan C, Chen Y, Stecher B, Taylor M, Khan S, Muqit MMK. Are PARKIN patients ideal candidates for dopaminergic cell replacement therapies? Eur J Neurosci. 2018 Dec 26. doi: 10.1111/ejn.14314. [Epub ahead of print] PubMed PMID: 30586214.

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