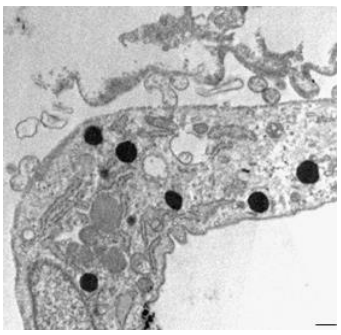
Pantothenate rescues iron accumulation in Pantothenate Kinase-associated neurodegeneration depending on the type of mutation

Mónica Álvarez-Córdoba, Aida Fernández Khoury, Marina Villanueva-Paz, Carmen Gómez-Navarro, Irene Villalón-García, Juan M. Suárez-Rivero, Suleva Povea-Cabello, Mario de la Mata, David Cotán, Marta Talaverón-Rey, Antonio J. Pérez-Pulido, Joaquín J. Salas, Eva Mª Pérez-Villegas, Antonio Díaz-Quintana, José A. Armengol and José A. Sánchez-Alcázar.

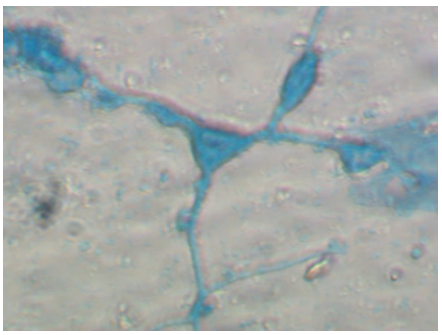
Molecular Neurobiology, 2018 in press

Highlights

- Mutant PANK2 fibroblasts derived from patients show accumulation of iron and lipofuscin (age pigment). Furthermore, mutant fibroblasts show a characteristic senescent morphology.
- Paradoxically, impaired mitochondrial iron metabolism in patient cells induces cytosolic iron deficiency and a vicious cycle with increased iron uptake which is accumulated in lipofuscin granules.
- Pantothenate can correct pathological alterations depending on the type of mutation in mutant fibroblasts.
- Expression levels of mutant PANK2 can be restored by pantothenate in particular mutations.
- For the first time, iron accumulation is demonstrated in induced neurons obtained by direct reprograming of mutant fibroblasts.
- The positive effect of pantothenate is also confirmed in induced neurons.
- Residual enzyme expression raises the possibility of treatment with pantothenate in selected mutations.
- The methodological strategy described in this manuscript can be also applied to other NBIA subtypes such as PLAN, BPAN or MPAN.



Electron microscopy image of a PANK2 mutant fibroblast with lipofuscin granules.



Iron accumulation in mutant PANK2 induced neurons revealed by Prussian blue staining.