

SLP2 and Prohibitins : novel key CHCHD10 partners in related diseases

Genin E.C* (1), Bannwarth S* (1), Ropert B (1), Mauri-Crouzet A (1), Lespinasse F (1), Augé G (1), Fragaki K (1), Cochaud C (1), Lacas-Gervais S (2), Paquis-Flucklinger V (1)

(1) IRCAN, Inserm U1081, CNRS UMR7284, Université Côte d'Azur, CHU de Nice, Nice, France

(2) Université Côte d'Azur, Centre Commun de Microscopie Appliquée, Nice, France

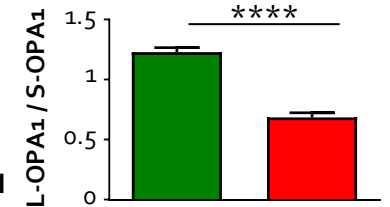
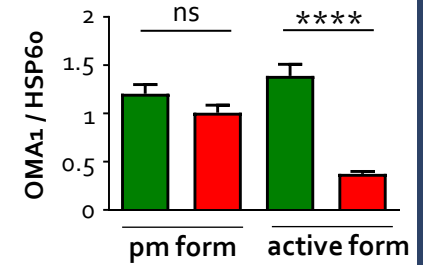
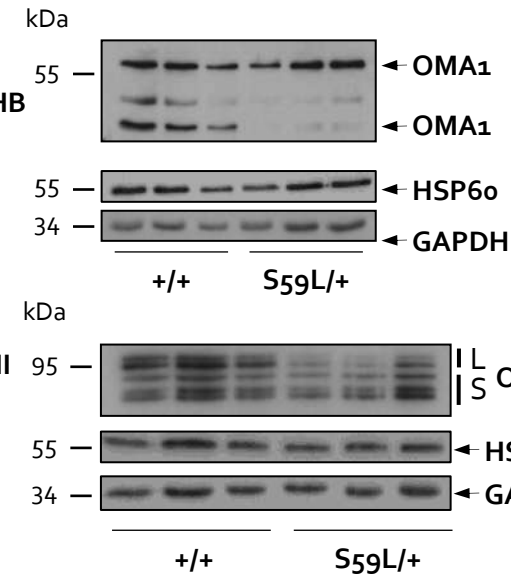
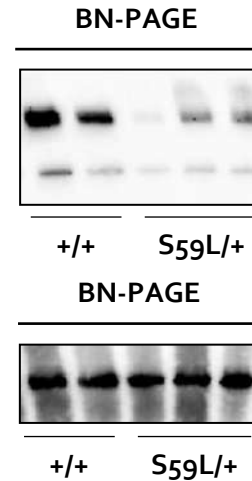
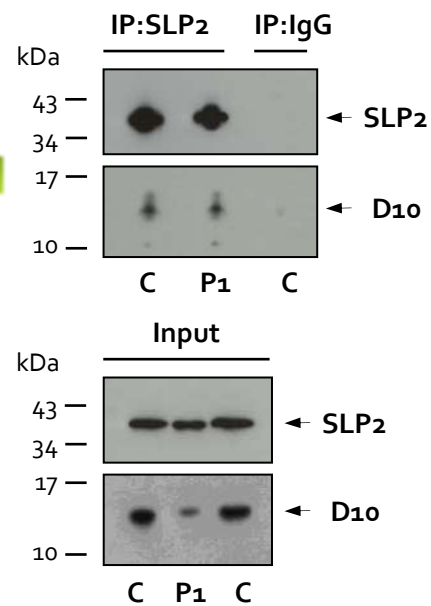
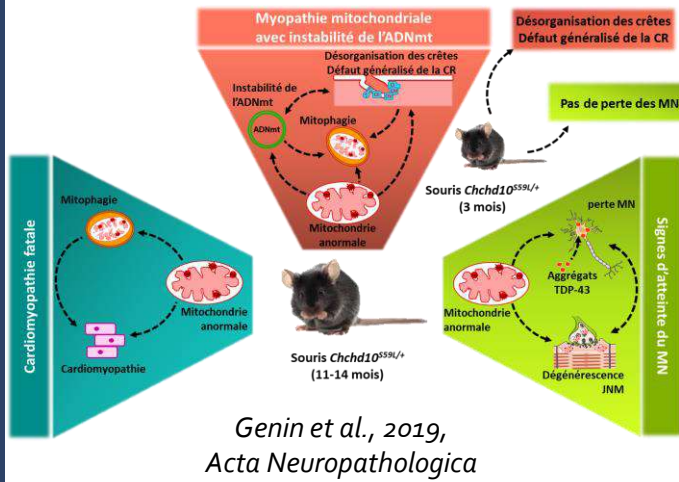
****co-1st authors***



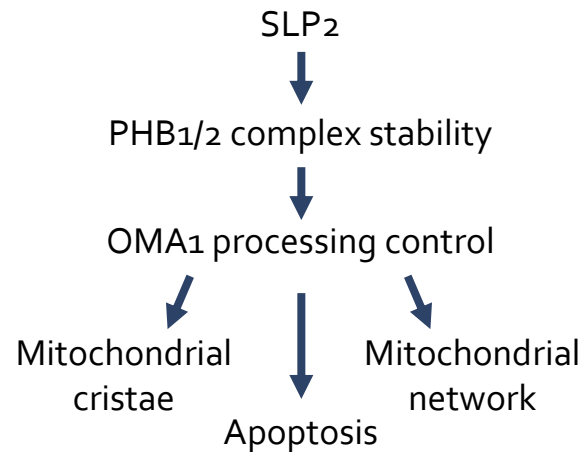
CHCHD10 physically interacts with Stomatin-Like Protein 2 (SLP2)

Instability of the PHB complex in the hearts of S59L/+ mice => OMA1-OPA1 cascade activation

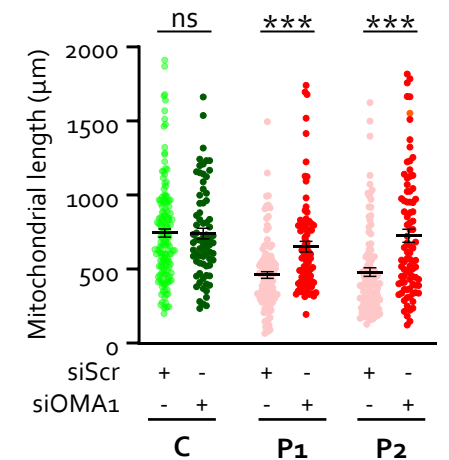
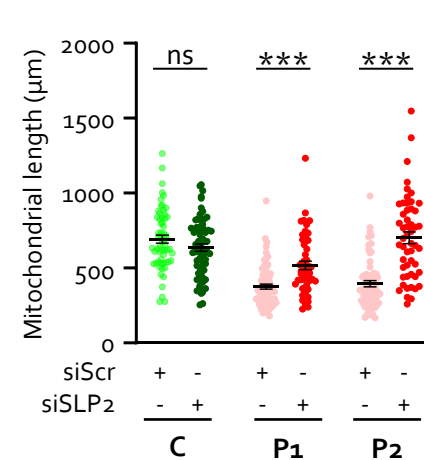
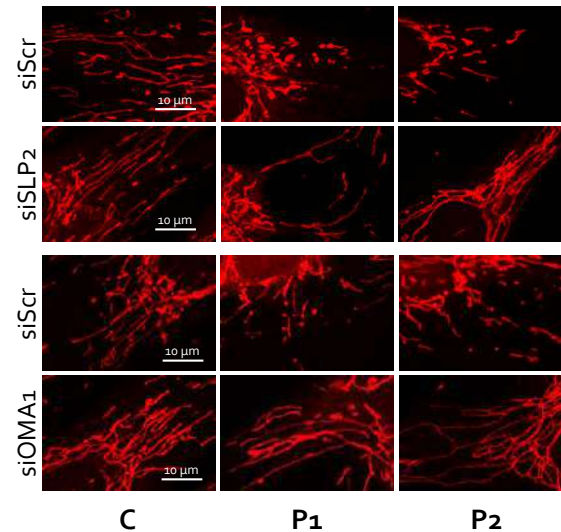
Chchd10^{S59L/+} mice



Molecular pathway

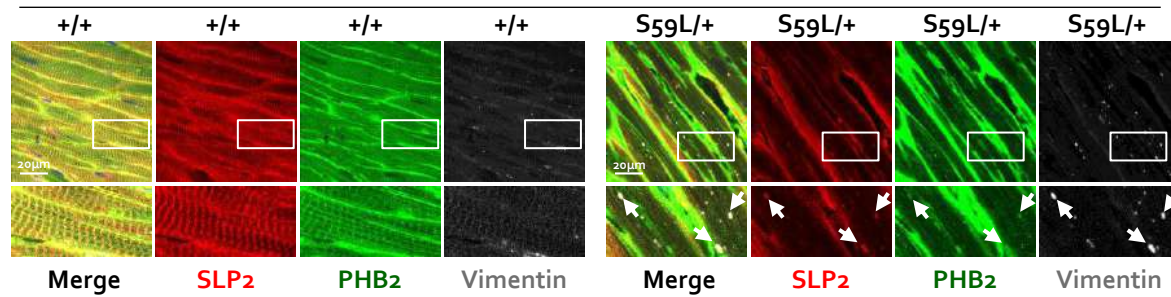


Depletion of SLP2 or OMA1 compensates mitochondrial network fragmentation in patient fibroblasts



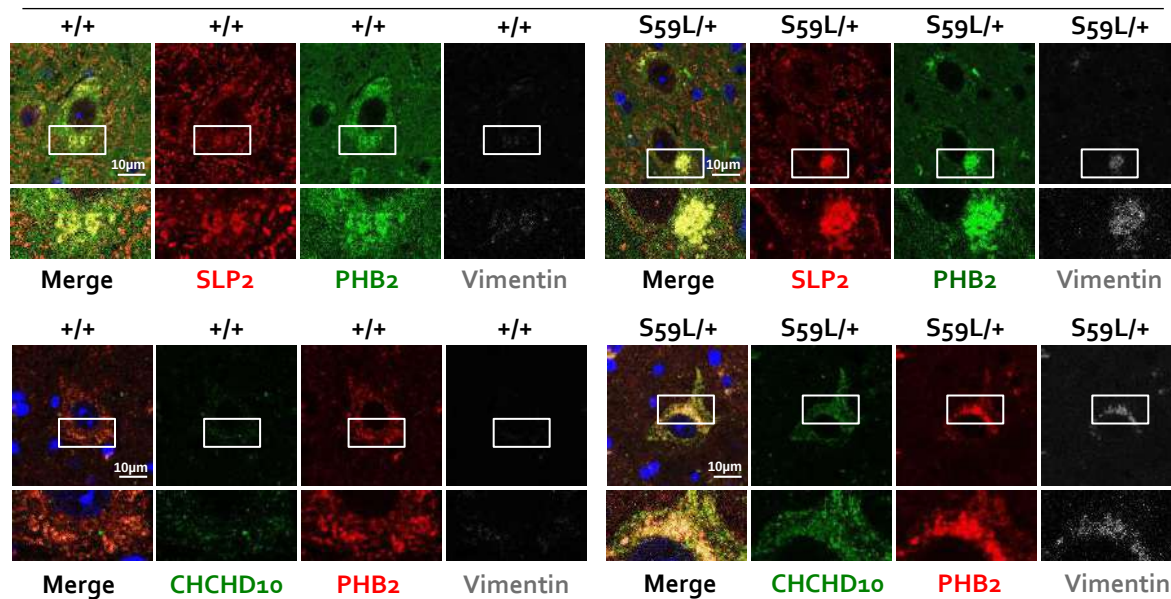
SLP2/PHBs form large aggregates in the hearts of S59L/+ mice

Heart (end-stage)



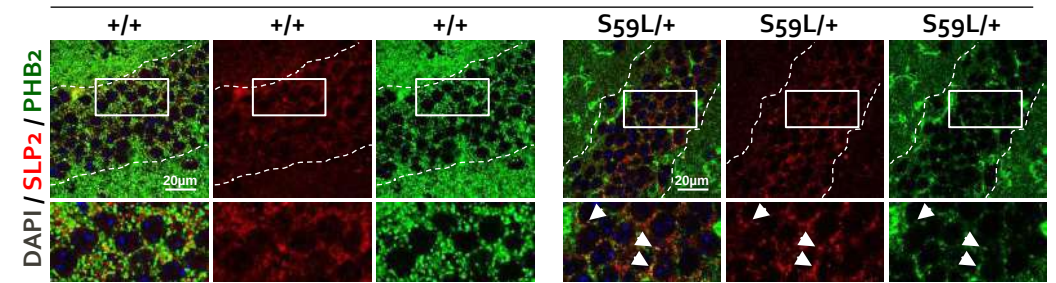
SLP2/PHBs form large aggregates with PHB complex destructuration in the spinal cord of S59L/+ mice

Spinal Cord (end-stage)

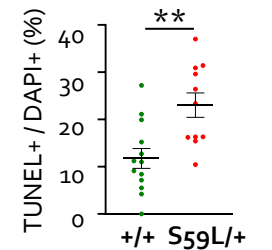
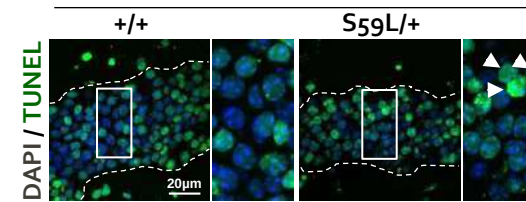


SLP2/PHBs form large aggregates with PHB complex destructuration in the hippocampus of S59L/+ mice

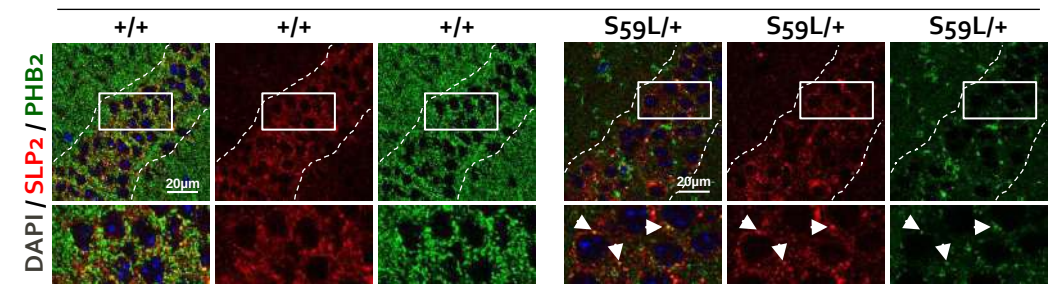
Hippocampus (DG) (end-stage)



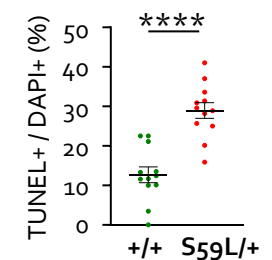
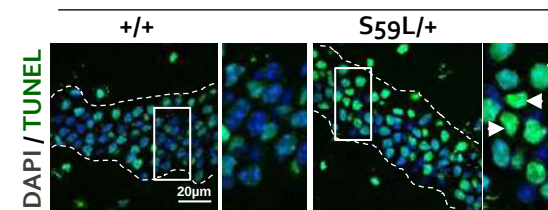
Hippocampus (DG) (end-stage)



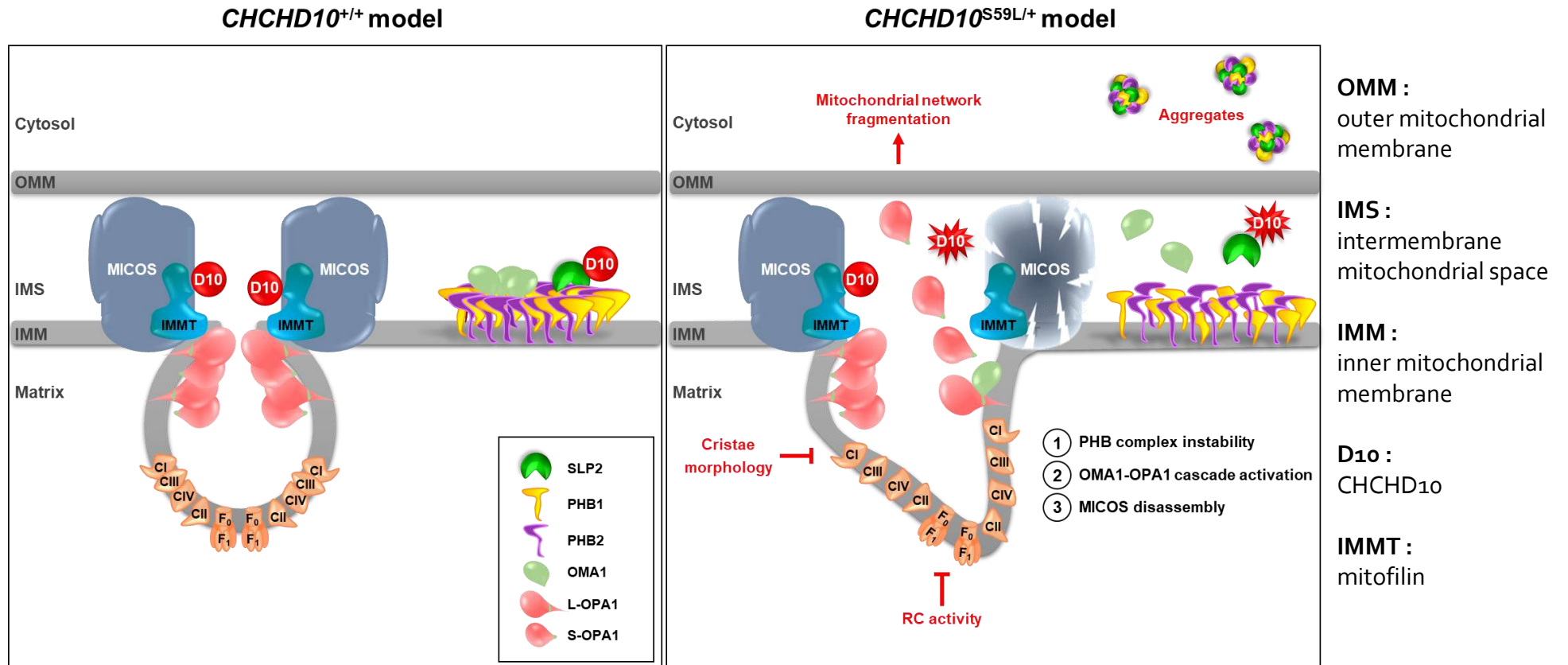
Hippocampus (CA) (end-stage)



Hippocampus (CA) (end-stage)



Model for the effects of wild type and mutant (*CHCHD10*^{S59L/+}) alleles in mitochondria



Genin et al. (submitted)

Next steps :

- determine which cell types of the hippocampus are affected
- determine if this molecular pathways may be implicated in diseases dependent on other ALS/FTD genes