

SUPPLEMENTARY INFORMATION

Different Niemann-Pick C1 Genotypes Generate Protein Phenotypes that Vary in their Intracellular Processing, Trafficking and Localization

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SUPPLEMENTARY FIGURES

Captions for supplementary figures:

ESM 1. Cellular localization of the ER-located NPC1 mutants

COS-1 cells were transfected with NPC1-Flag constructs harboring one of the following mutations: V378A, R404Q, H510P, Q775P, I1061T, M1142T, N1156S, G1162V and R1186H. The mutants were analyzed by confocal microscopy. All NPC1 mutants were localized to the ER as assessed by the co-localization with the ER chaperone calnexin, while no co-localization was observed with the Golgi protein marker GM130 and the lysosomal marker Lamp2.

ESM 2. Cellular localization of NPC1 mutants exhibiting delayed trafficking

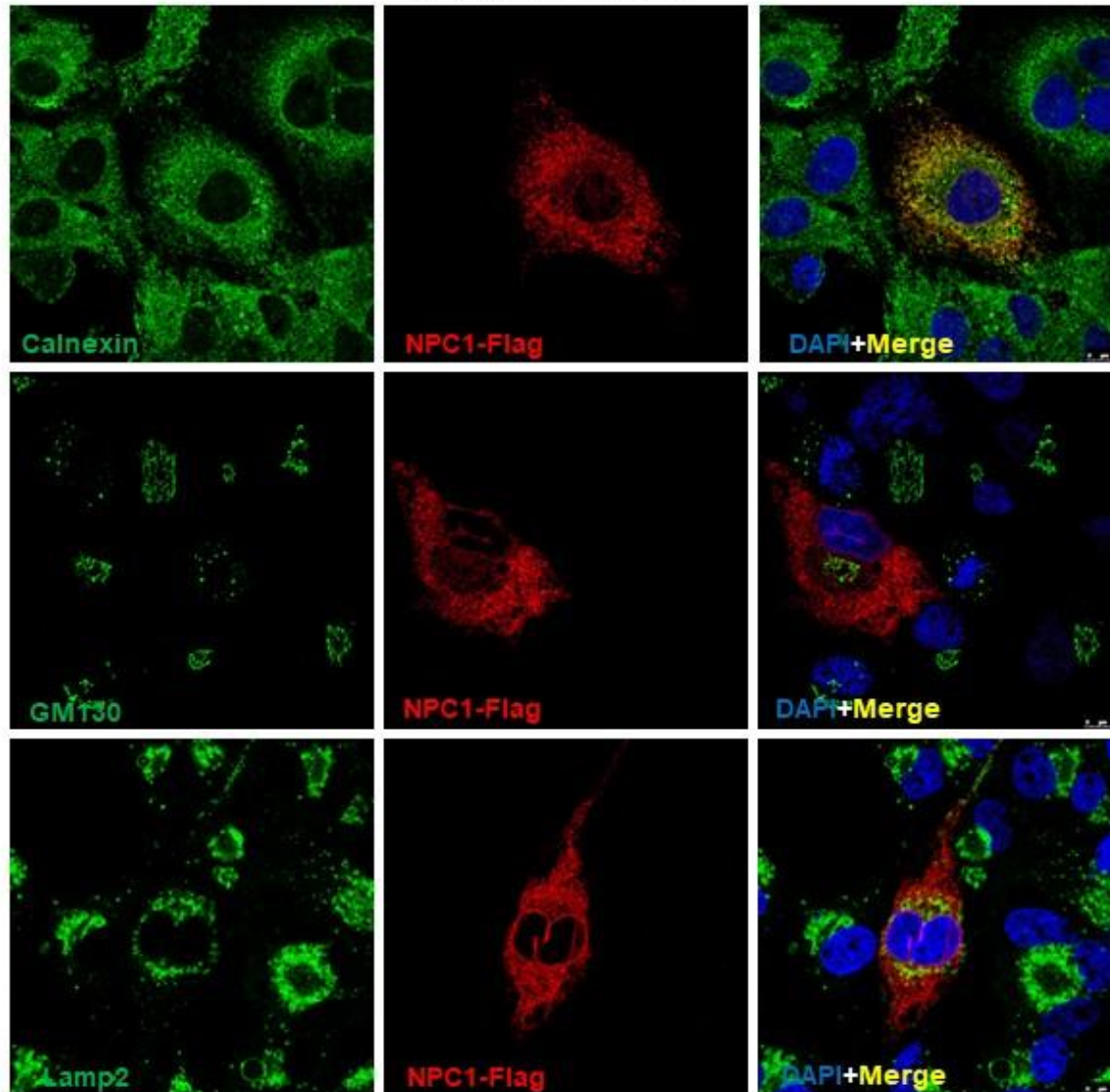
COS-1 cells were transfected with NPC1-Flag constructs harboring one of the following mutations: M631R, G1162A, and C1168Y. The mutants were analyzed by confocal microscopy. Substantial co-localization of all NPC1 mutants with calnexin and a partial co-localization with GM130 as well as with the lysosomal protein marker Lamp2 was clearly detectable.

ESM 3. Cellular localization of NPC1 mutants trafficking similar to wild type NPC1

COS-1 cells were transfected with NPC1-Flag constructs harboring one of the following mutations: D948Y, P1007A, and V950M. The mutants were analyzed by confocal microscopy. The intracellular localization of all NPC1 mutants showed a partial co-localization with calnexin in the ER and a strong co-localization with the lysosomal marker Lamp2.

NPC1 mutants that are blocked in the endoplasmic reticulum

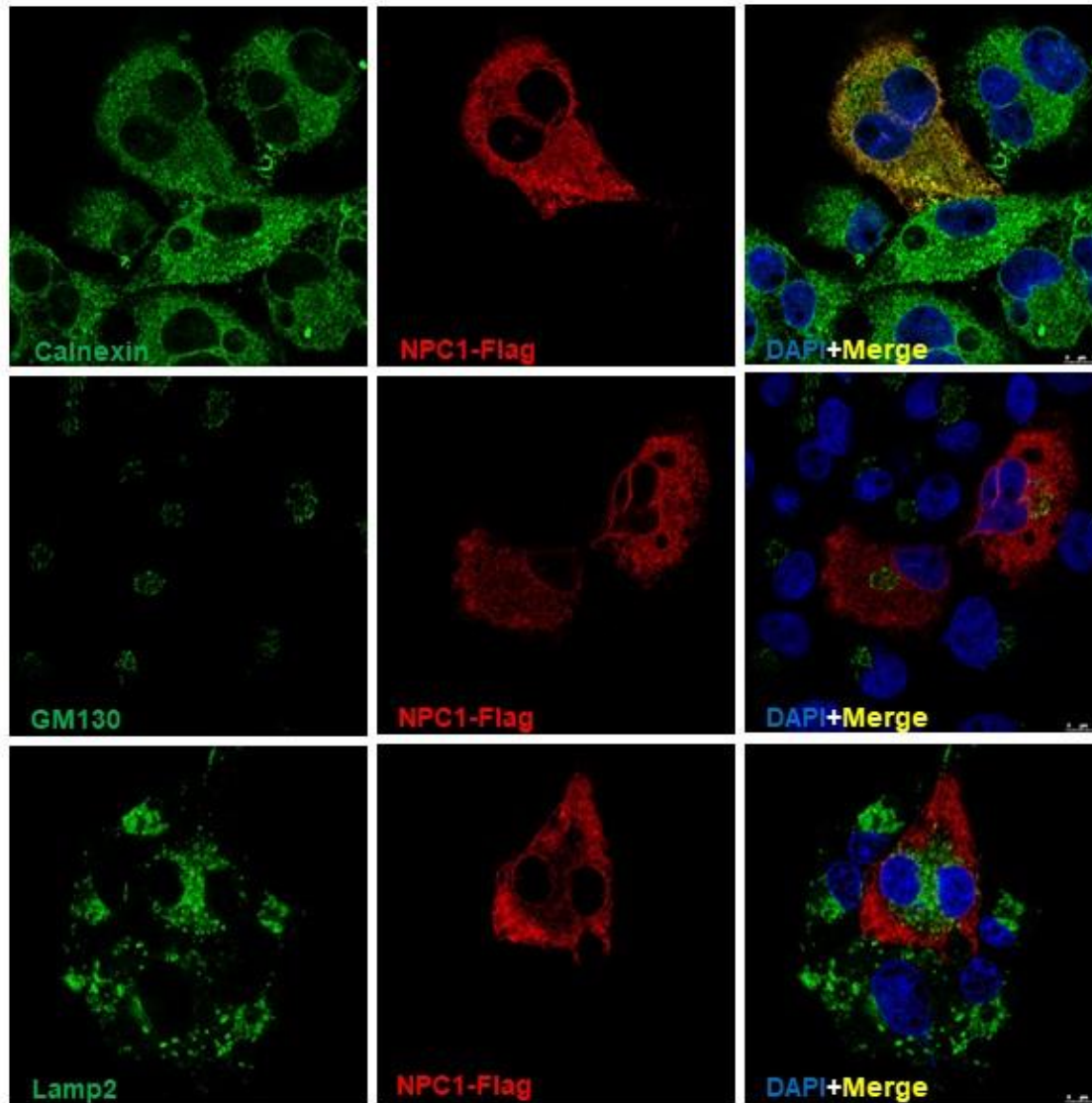
Mutation N1156S



ESM_1

NPC1 mutants that are blocked in the endoplasmic reticulum

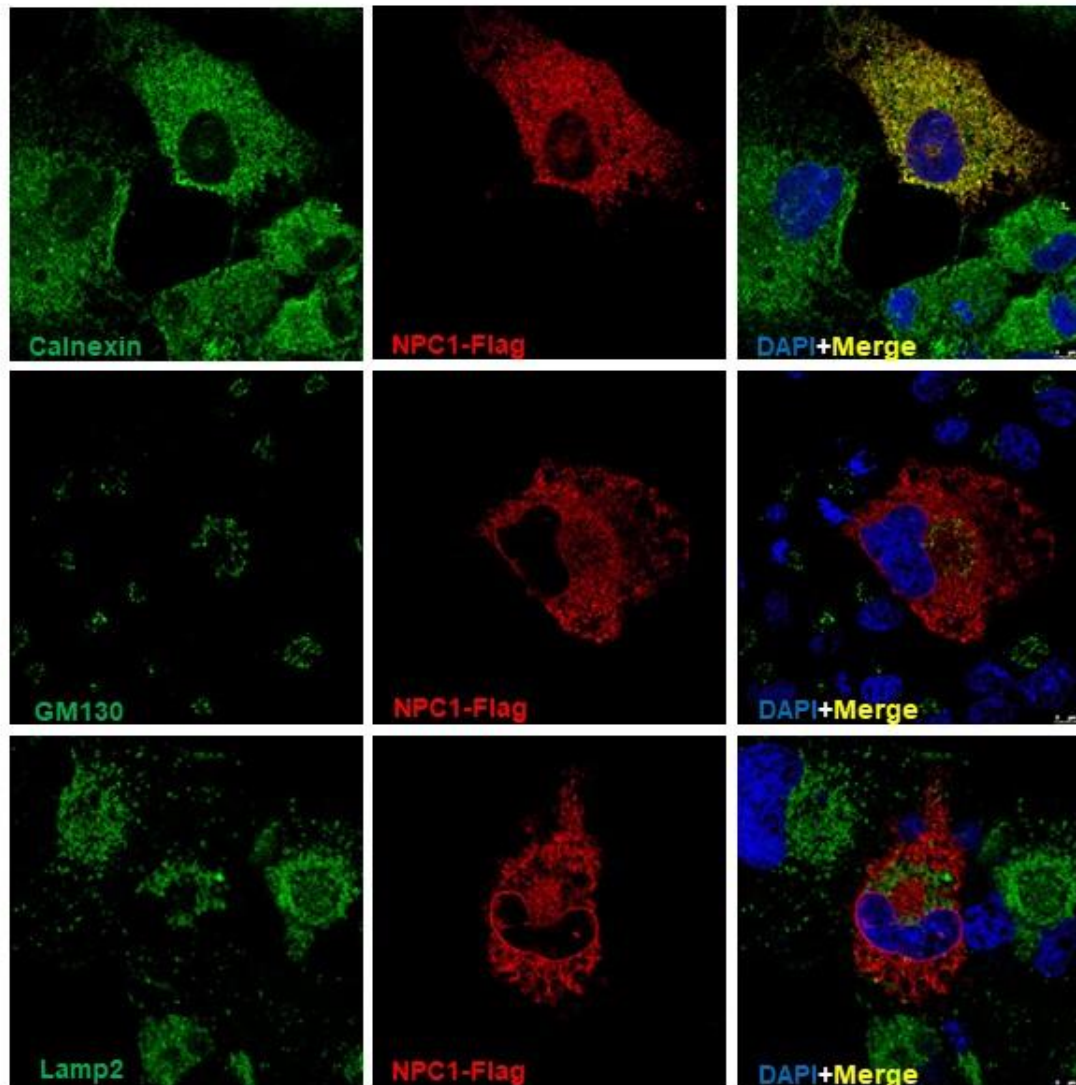
Mutation H510P



ESM_1

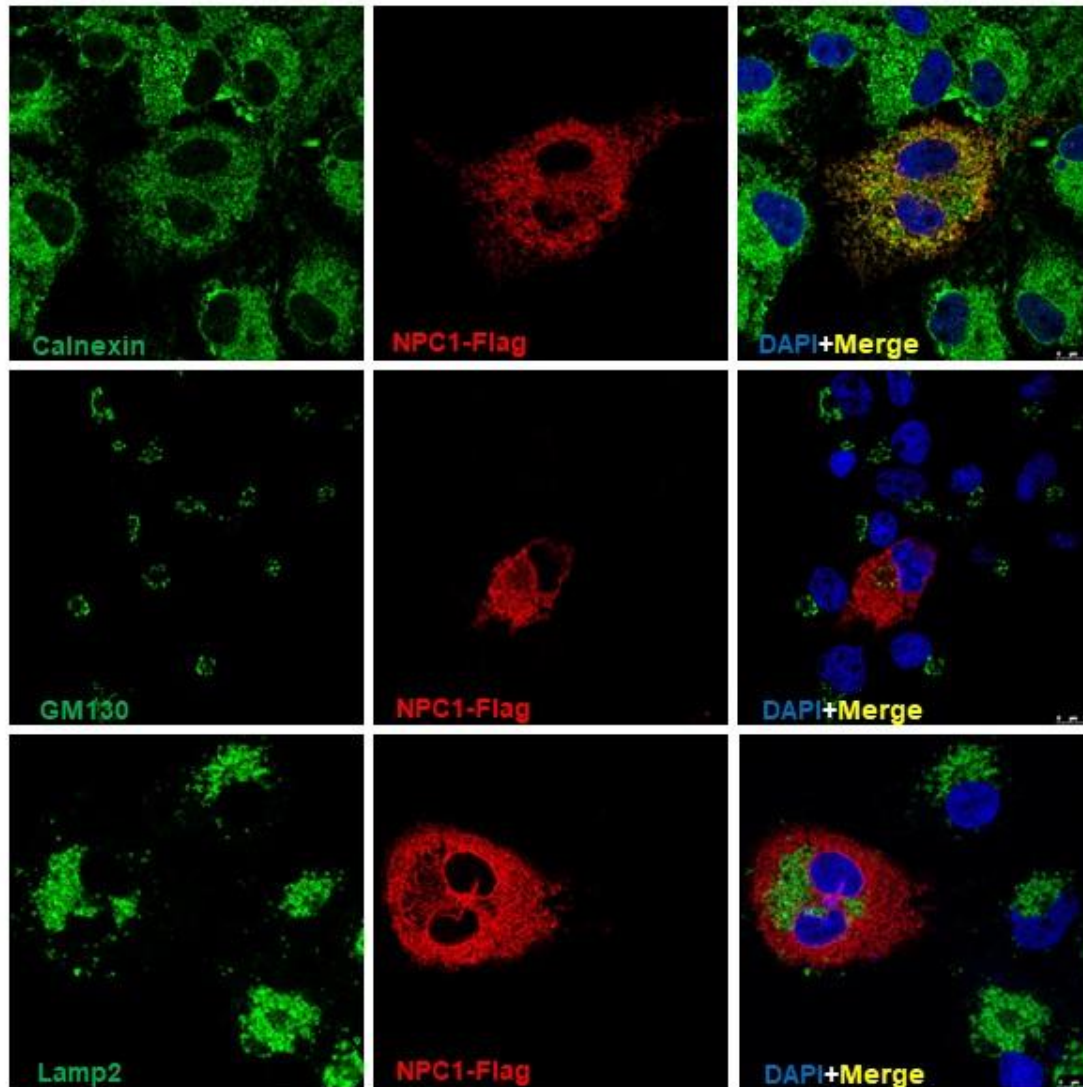
NPC1 mutants that are blocked in the endoplasmic reticulum

Mutation R404Q



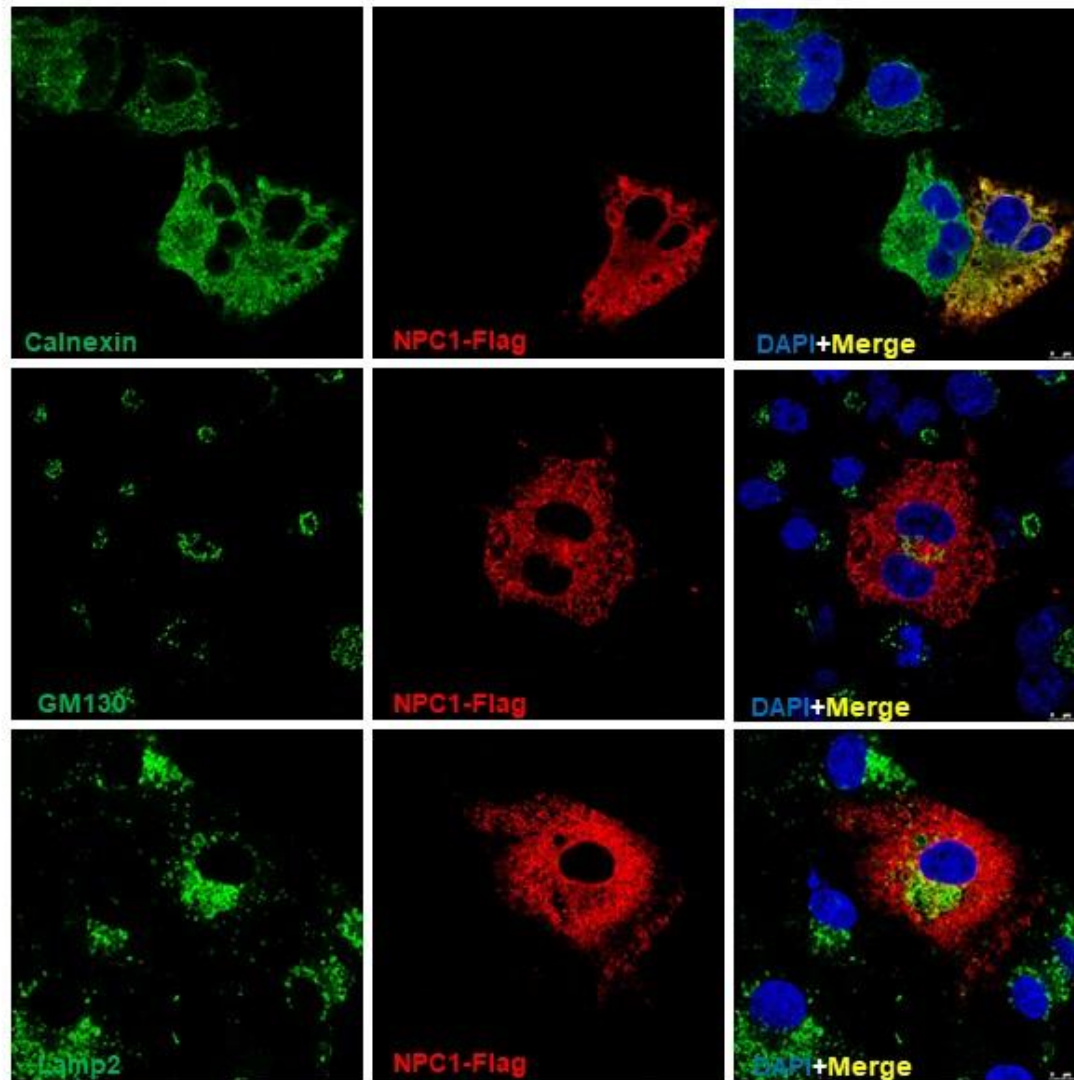
NPC1 mutants that are blocked in the endoplasmic reticulum

Mutation V378A



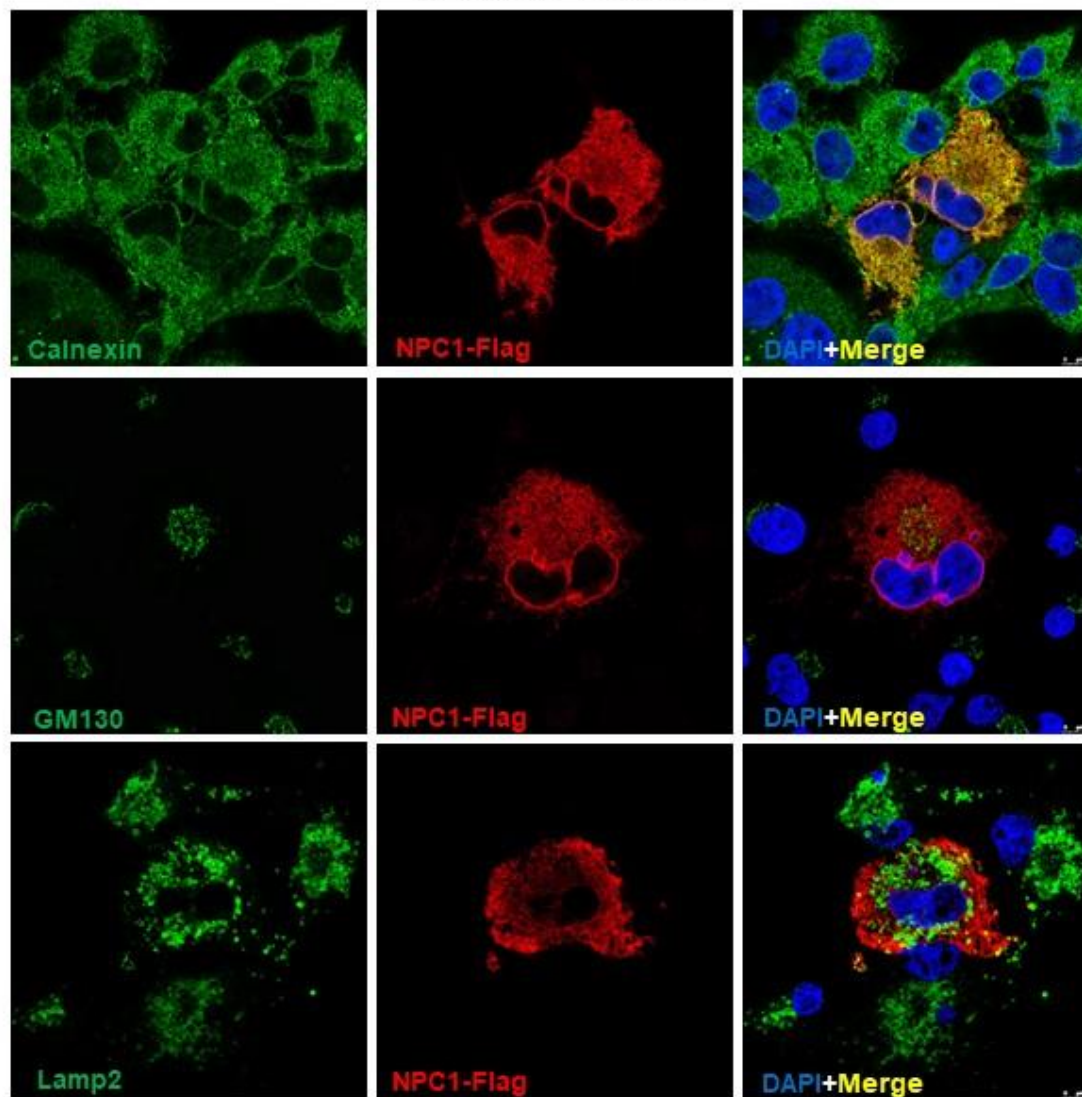
NPC1 mutants that are blocked in the endoplasmic reticulum

Mutation I1061T



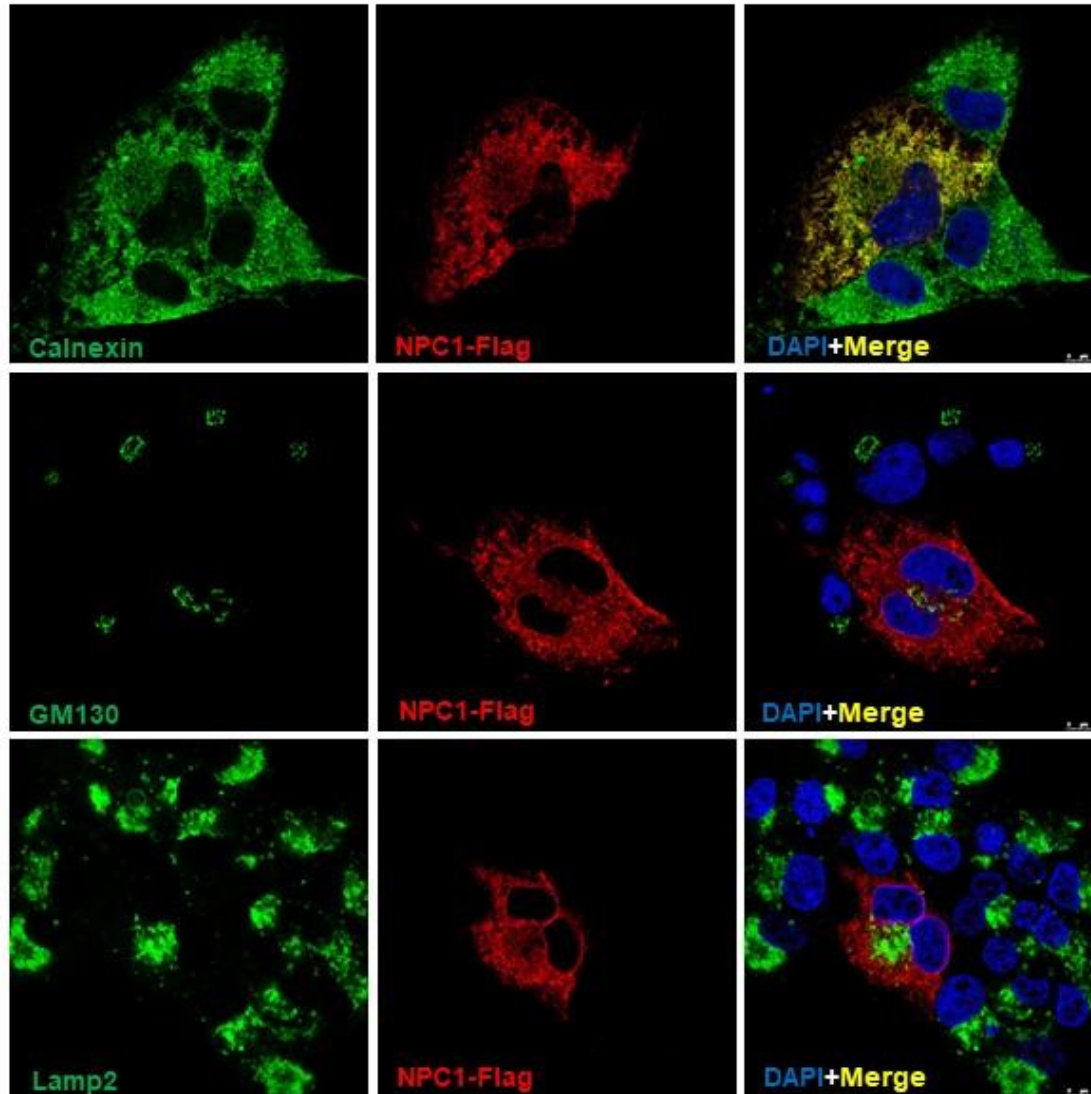
NPC1 mutants that are blocked in the endoplasmic reticulum

Mutation M1142T



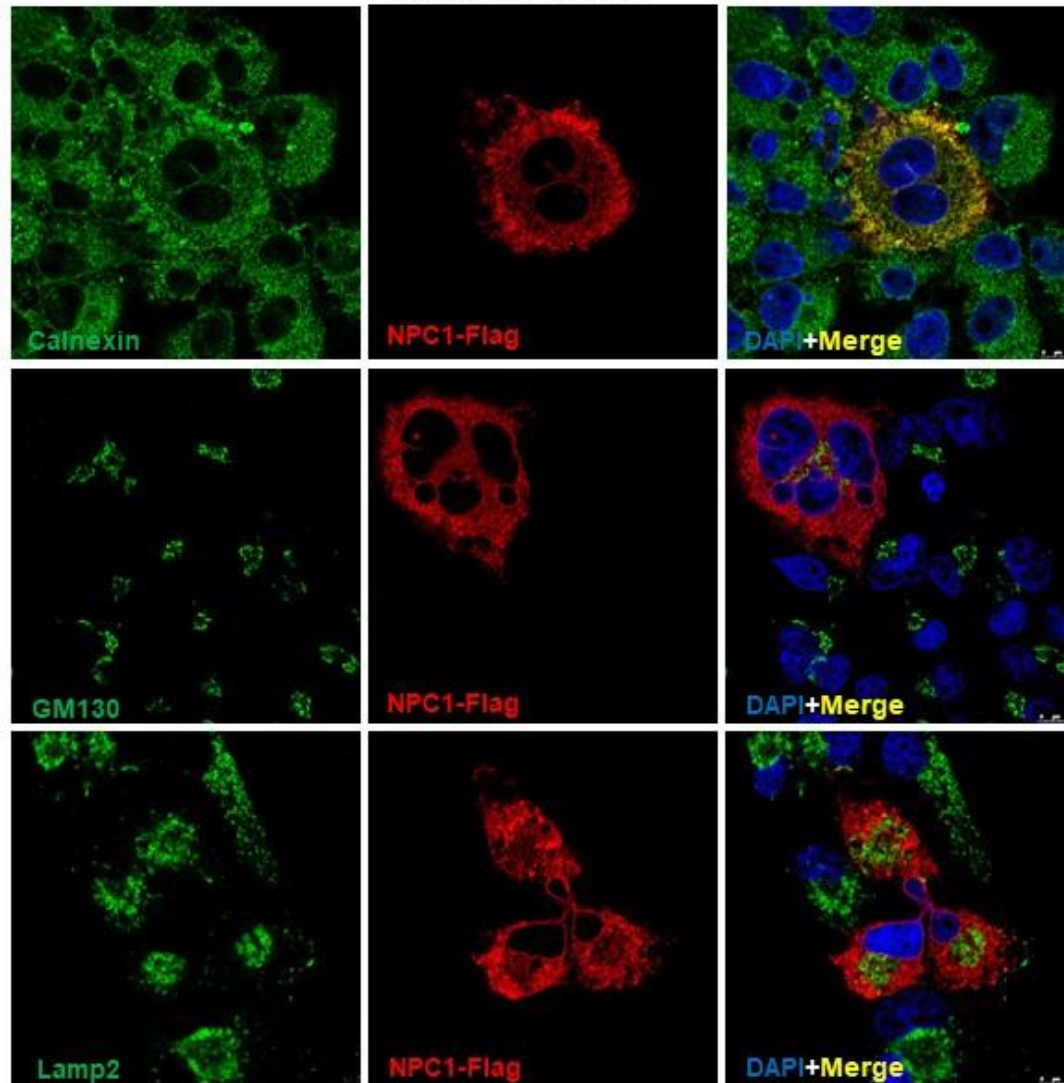
NPC1 mutants that are blocked in the endoplasmic reticulum

Mutation G1162V



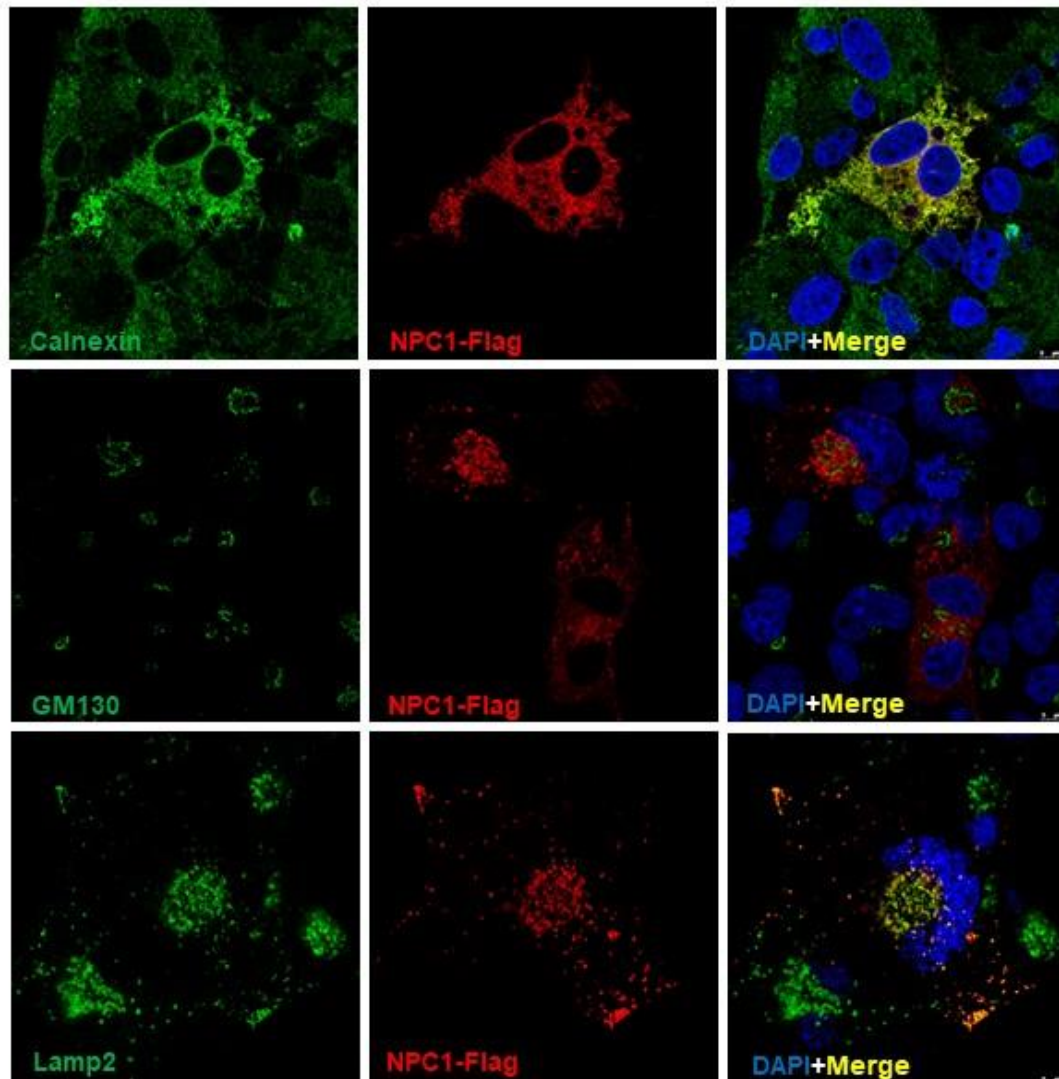
NPC1 mutants that are blocked in the endoplasmic reticulum

Mutation Q775P



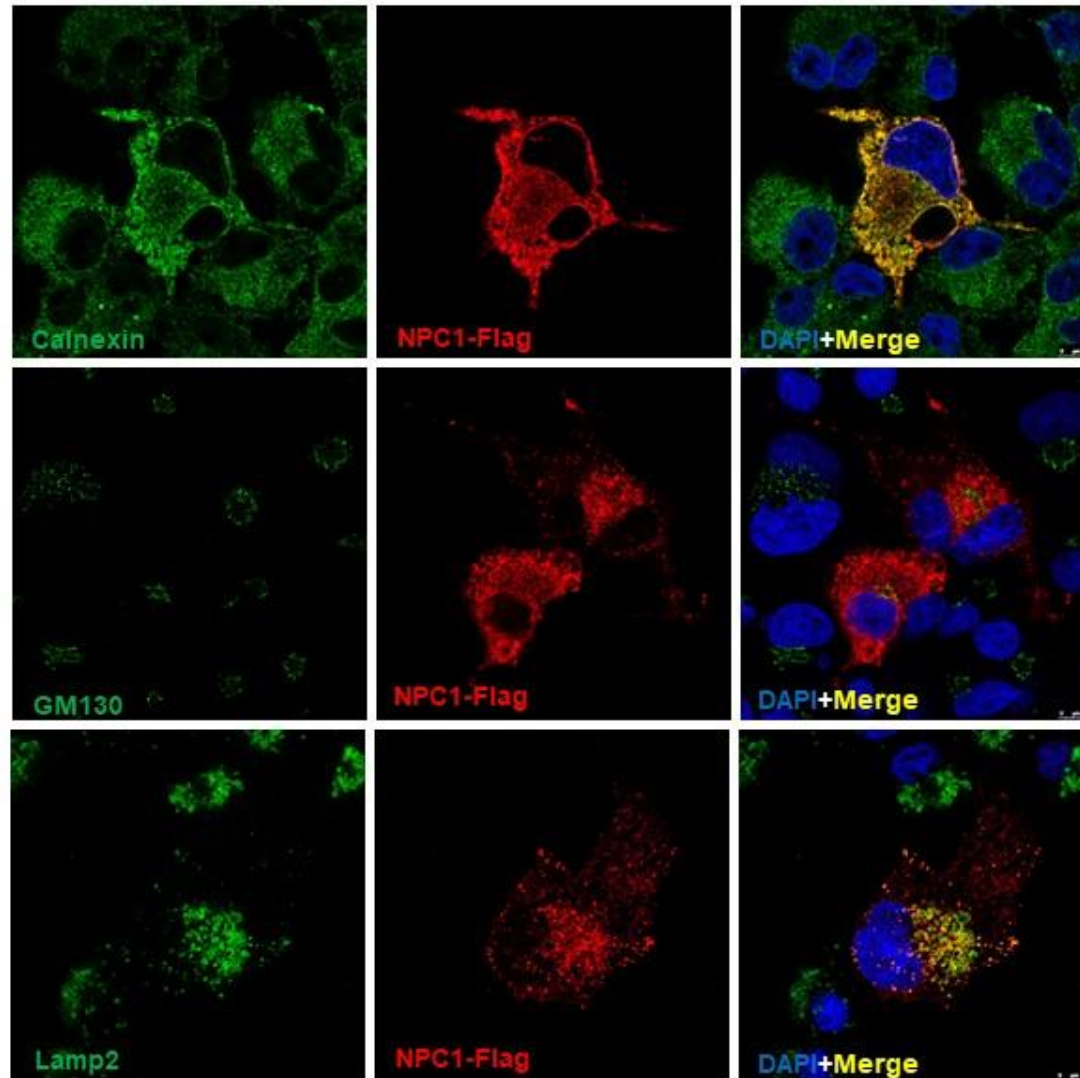
NPC1 mutants that are partially trafficked along the secretory pathway

Mutation C1168Y



NPC1 mutants that are partially trafficked along the secretory pathway

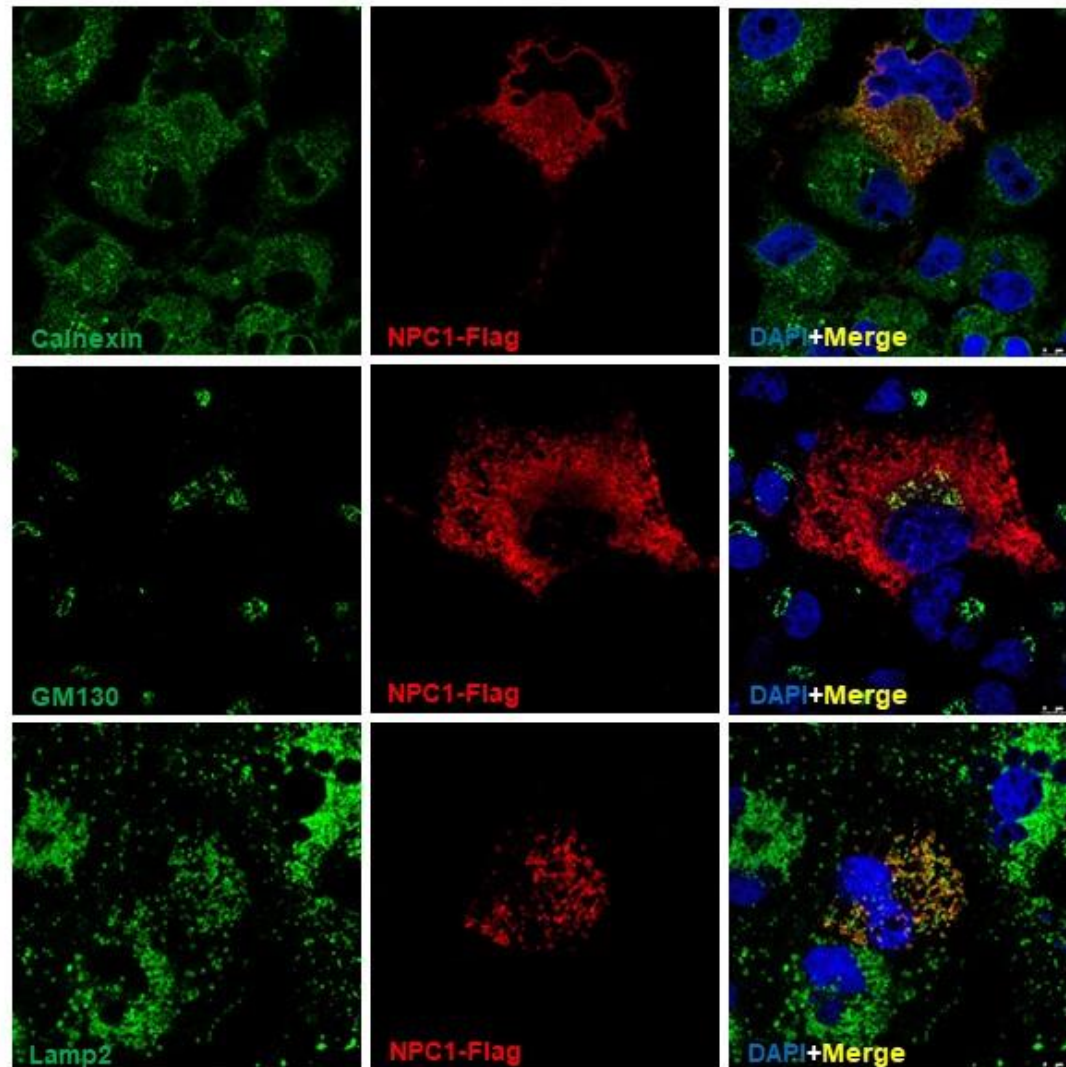
Mutation M631R



ESM_2

NPC1 mutants that are partially trafficked along the secretory pathway

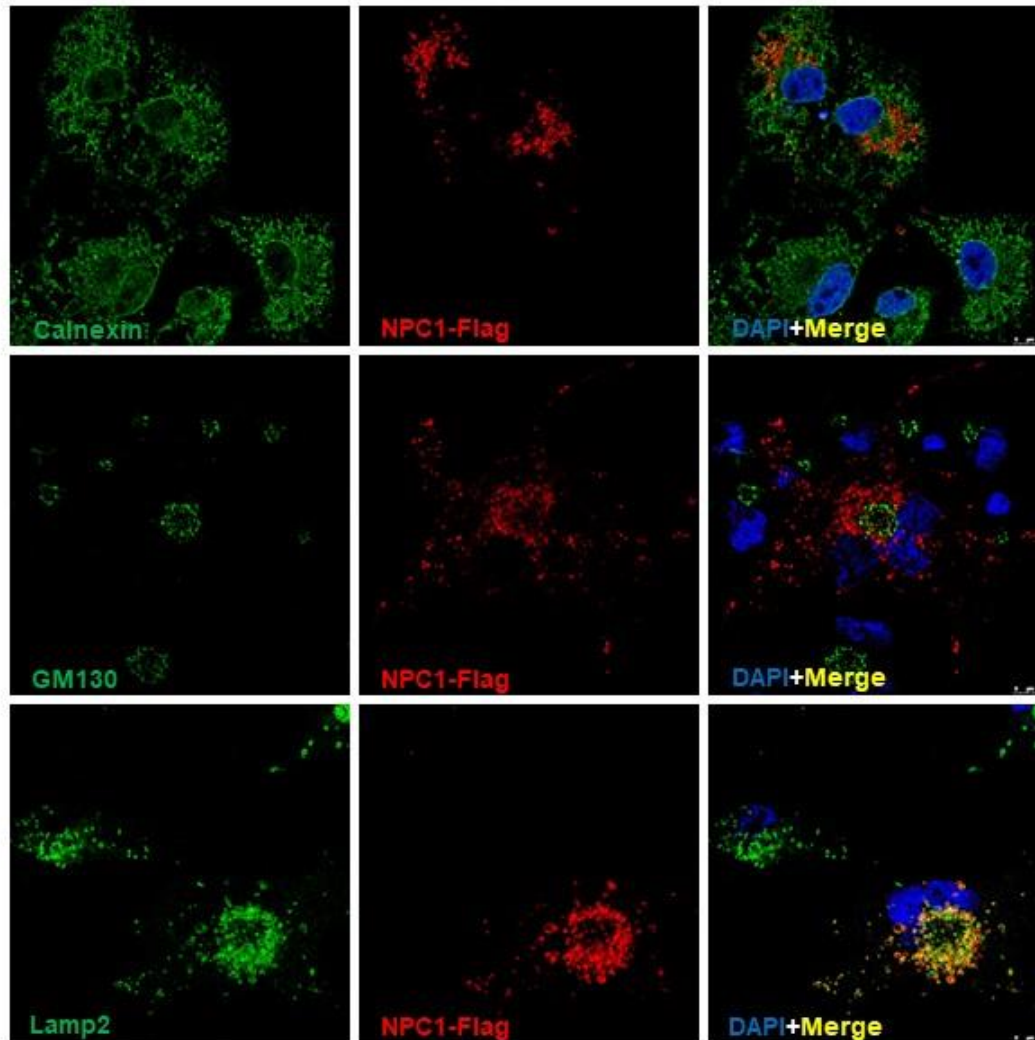
Mutation G1162A



ESM_3

NPC1 mutants that are trafficked in a fashion similar to wild type NPC1

Mutation D948Y



ESM_3

NPC1 mutants that are trafficked in a fashion similar to wild type NPC1

Mutation V950M

