CLN3 Research Tools and Resources

Original References

Amoeba

1. **Dictyostelium discoideum**
   - Huber RJ, Myre MA, Cotman SL. Loss of CLN3 function in the social amoeba Dictyostelium discoideum causes pleiotropic effects that are rescued by human CLN3.

Yeast Models

1. **Schizosaccharomyces cerevisae**
   - Pearce DA, Sherman F. A yeast model for the study of Batten disease. Proc Natl Acad Sci U S A. 1998 Jun 9;95(12):6915-8.
2. **Schizosaccharomyces pombe**
   - Gachet Y, Codlin S, Hyams JS, et al. BTN1, the Schizosaccharomyces pombe homologue of the human Batten disease gene CLN3, regulates vacuole homeostasis. J Cell Sci. 2005 Dec 1;118(Pt 23):5525-36.

Roundworm

1. **Caenorhabditis elegans**
   - Voer G1, van der Bent P, Rodrigues AJ, et al. Deletion of the Caenorhabditis elegans homo- logues of the CLN3 gene, involved in human juvenile neuronal ceroid lipofuscinosis, causes a mild progeric phenotype. J Inherit Metab Dis. 2005;28(6):1065-80.

Fruitfly

1. **Drosophila melanogaster - Genetic gain-of-function system**
   - Tuxworth RI, Chen H, Vivancos V, et al. The Batten disease gene CLN3 is required for the re- sponse to oxidative stress. Hum Mol Genet. 2011. May 15;20(10):2037-2047.

Zebrafish

1. **Danio rerio - Morphant**
   - Wager K, Zdebik AA, Fu S, et al. Neurodegeneration and Epilepsy in a Zebrafish model of CLN3 Disease (Batten Disease). PLoS One. 2016; 11(6).

Mouse Models

1. **Mus musculus - Deletion of exons 2-6 and most of exon 1 on 129/Sv inbred and 129Sv3 Black Swiss outbred lines**
   - Mitchison HM, Bernard DJ, Greene ND, et al. Targeted disruption of the CLN3 gene provides a mouse model for Batten disease. Neurobiol Dis. 1999 Oct;6(5):321-34. Erratum in: Neurobiol Dis 2000 Apr;7(2):127. The Batten Mouse Model Consortium [corrected].

2. **Mus musculus - Cln3Δex7/8 knock-in mice bearing the common ~1 kb deletion on an out-bred 129Sv-CD1 background**
   - Cotman SL, Vrbanac V, Lebel LA, et al. Cln3(Deltaex7/8) knock-in mice with the common JNCL mutation exhibit progressive neurologic disease that begins before birth. Hum Mol Genet. 2002. Octo 15:11(22):2709-2721.
3. **Mus musculus - Cln3Δex7/8 knock-out Exons 7-8 replacement insertion on C57BL/6J-129Sv and C57BL/6J congenic**
   - M.L. Katz, H. Shibuya, P.C. Liu, et al. A mouse gene knockout model for juvenile ceroid-lipofuscinosis (Batten disease). J. Neurosci. Res., 57 (1999), pp. 551–556
4. **Mus musculus - Targeted replacement of most of exon1 and all of exons 2-8 of the CLN3 gene with β-galactosidase on SV129 and onto C57BL/6**
   - Eliason SL, Stein CS, Mao Q, et al. A knock-in reporter model of Batten disease. J Neurosci. 2007 Sep 12;27(37):9826-34.
5. **Mus musculus – $CLN3_{\Delta ex7/8}$ mice carrying the leucine variant of RPE65 on a C57BL/6J background**
   - Dannhausen, K., Moble, C., Langmann T. Immunomodulation with minocycline rescues retinal degeneration in juvenile neuronal ceroid lipofuscinosis mice highly susceptible to light damage. Dis ModelMech. 2018. Sep 5;11(9).
6. **Mus musculus – TgCRND8/Cln3Δex7/8 mice homozygous for Cln3Δex7/8 with the hAPP transgene**
   - Centa JL, Jodelka FM, Hinrich AJ, et al. Therapeutic efficacy of antisense oligonucleotides in mouse models of CLN3 Batten disease. Nat Med. 2020. Sep;26(9):1444-51.

Porcine Model

1. **$CLN3^{\Delta ex7-8/\Delta ex7-8}$ porcine model of CLN3-Batten**
   - Johnson TB, Sturdevant, DA, White KA, et al. Characterization of a novel porcine model of CLN3-Batten disease. Mol Genet Metab, 2019;126:S81.

Animal Cell lines

1. **Hela CLN3 KO line**
   - Yasa S, Modica G, Sauvageau E, et al. CLN3 regulates endosomal function by modulating Rab7A-effector interactions. J Cell Sci. 2020. Mar 16;133(6).
2. **Mus musculus - Homozygous CbCln3Deltaex7/8 precursor cells**
   - Fossale E, Wolf P, Espinola JA, et al. Membrane trafficking and mitochondrial abnormalities precede subunit c deposition in a cerebellar cell model of juvenile neuronal ceroid lipofuscinosis. BMC Neurosci. 2004;5:57.
3. **Mus musculus - Mouse Brain Endothelial Cells**
   - Tecedor L, Stein CS, Schultz MS, et al. CLN3 Loss Disturbes Membrane Microdomain Properties and Protein Transport in Brain Endothelial Cells

Human

1. **CLN3 deficient**
   - **Homo sapien - Human CLN3 Knockout cell line 19 bp deletion**
     ✤https://www.horizondiscovery.com/human-cln3-knockout-cell-line-hzghc003369c002
   - **Homo sapien - Human CLN3 Knockout cell line 8 bp deletion**
     ✤https://www.horizondiscovery.com/human-cln3-knockout-cell-line-hzghc003369c010
   - **Panoply™ Human CLN3 Knockdown Stable Cell Line (CSC-DC003300)**
     ✤http://www.creative-biogene.com/Panoply-Human-CLN3-Knockdown-Stable-Cell-Line-CSC-DC003300-1256319-14.html

- **Homo sapien - Induced pluripotent stem cells**

  ✤Lojewski X, Staropoli JF, Biswas-Legrand S, et al. Human iPSC models of neuronal ceroid lipofuscinosis capture distinct effects of TPP1 and CLN3 mutations on the endocytic pathway. Hum Mol Genet. 2014. Apr 15;23(8):2005-22.

  ✤Paull D, Sevilla A, Zhou H, et al. Automated high-throughput derivation, characterization and differentiation of induced pluripotent stem cells. Nat. Methods. 2015. Sep;12(9): 885-92. https://nyscf.org/wp-content/uploads/2018/04/Available_BBDF_APRIL2018.pdf

  ✤Gomez-Giro G, Arias-Fuenzalida J, Jarazo J. Synapse alterations precede neuronal damage and storage pathology in a human cerebral organoid model of CLN3-juvenile neuronal ceroid lipofuscinosis. Acta Neuropathol Commun. 2019. Dec 30;7(1):222.

2. **CLN3 overexpression**

- **Homo sapien - Cancer cell lines**

  ◆Rylova SN, Amalfitano A, Persaud-Sawin DA, et al. The CLN3 gene is a novel molecu- lar target for cancer drug discovery. Cancer Res. 2002 Feb 1;62(3):801-8.

    - Glioblastoma (U-373G, T98g)
    - Neuroblastoma (IMR-32, SH-SY5Y, SK-N-MC)
    - Prostate (Du145, PC-3, LNCaP)
    - Ovarian (SK-OV-3, SW626, PA-1)
    - Breast (BT-20, BT-549, BT-474)

  ◆Zhu X, Huang Z, Chen Y, et al. Effect of CLN3 silencing by RNA interference on the proliferation and apoptosis of human colorectal cancer cells. Biomed Pharmacother. 2014 Apr;68(3):253-8.

    - Colon (SW1116, SW480, HCT 116)

- **Panoply™ Human CLN3 Knockdown Stable Cell Line(CSC-DC003300)**

  ✤http://www.creative-biogene.com/Panoply-Human-CLN3-Over-expressing-Stable-Cell-Line-CSC-SC003300-1237907-15.html

NCL Mutation and Patient Database http://www.ucl.ac.uk/ncl/mutation.shtml

"This database contains published mutations and sequence variations in genes that cause NCL together with unpublished data included with permission. It follows the mutation nomenclature recommendations of the Human Genome Variation Society. From mid-2012, there are now two sets of tables for each human NCL disease gene - the new Patient Database listing all published or reported patients and families, and the Mutation Database listing all published or reported mutations and many sequence variants as before, and now cross-referenced to the patient table. These are available to view via this web site and also to download as excel files for off-site use to aid local needs or interests (e.g. sorting according to occur- rence in particular countries)."