

Summary The mutation of a mysterious protein causes a devastating childhood dementia. The explanation may be inside the cell, in lysosome behaviour...

CLN3 disease: Juvenile Dementia

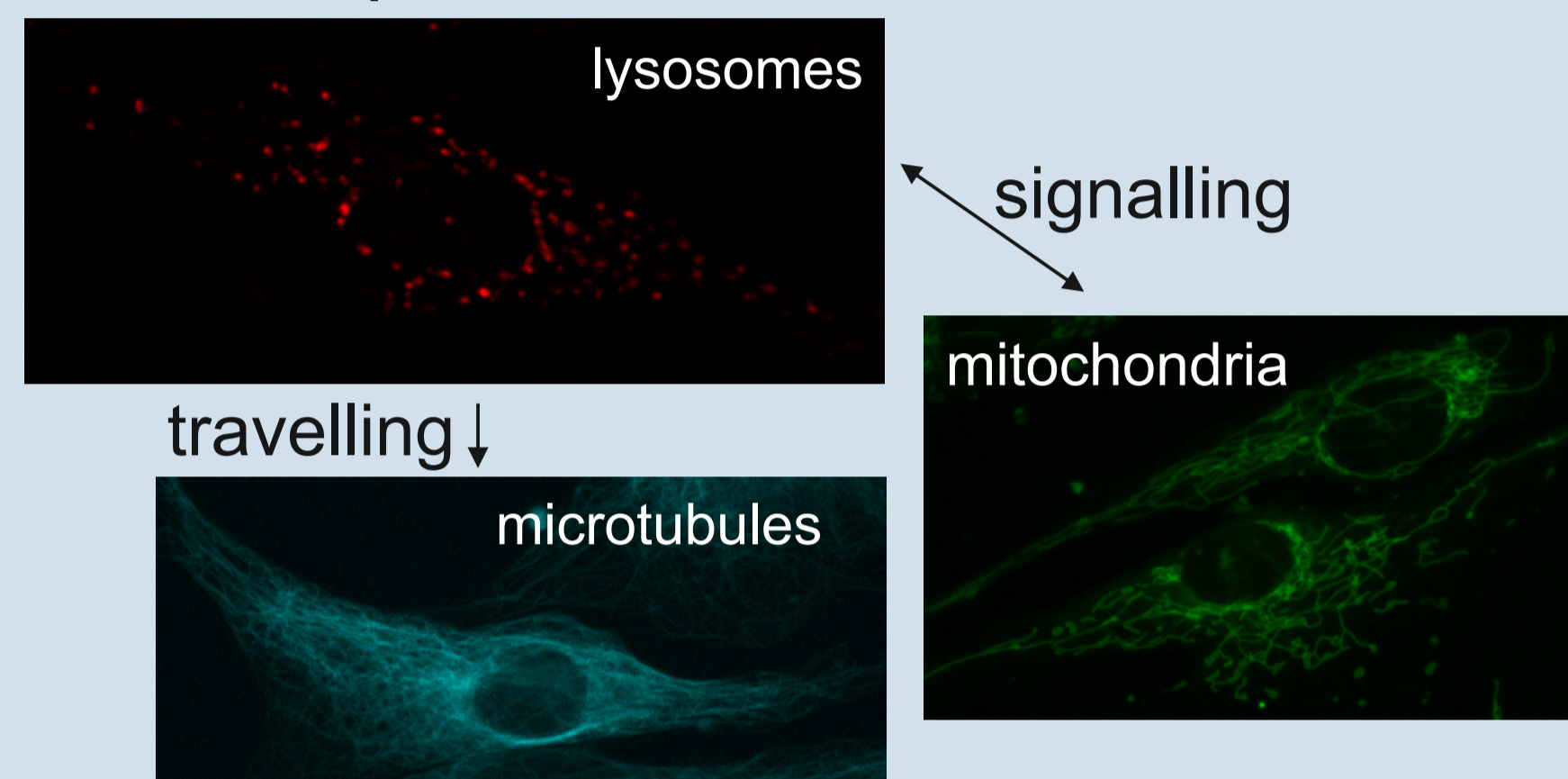
Emily Coode (LHCS)



Inside the cell

The cell contains more than just a nucleus.

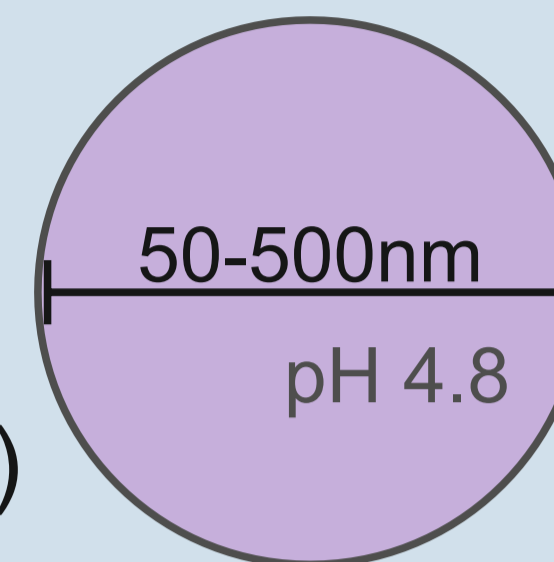
For example...



'Organelles' have a range of functions and interact with each other in the cell.

Lysosomes

Small vesicles 50-500nm
Acidic pH 4.8 (cytoplasm ~7.3)



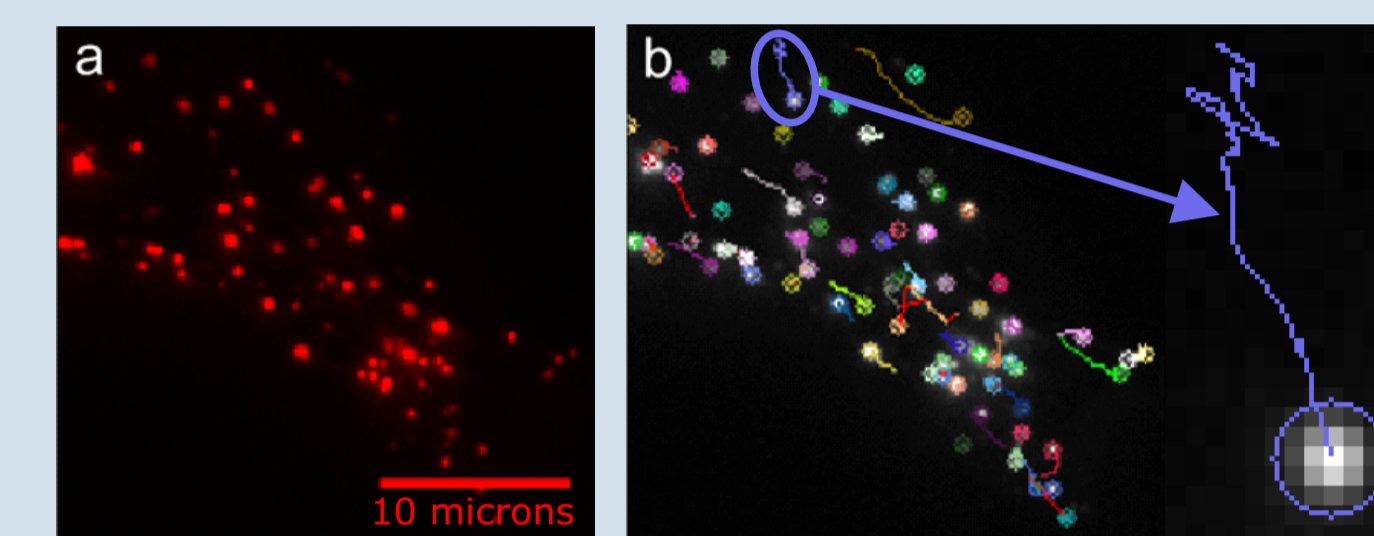
Contain enzymes to digest cell waste
Transport material in and out of the cell
Release and take up calcium for signalling

Distribution is important for some functions
Movement along microtubulue network
Meeting other organelles, they can interact

Methods

Tracking lysosomes:

(a) Lysosomes on fluorescence microscope
(b) Recording with Particle Tracker¹

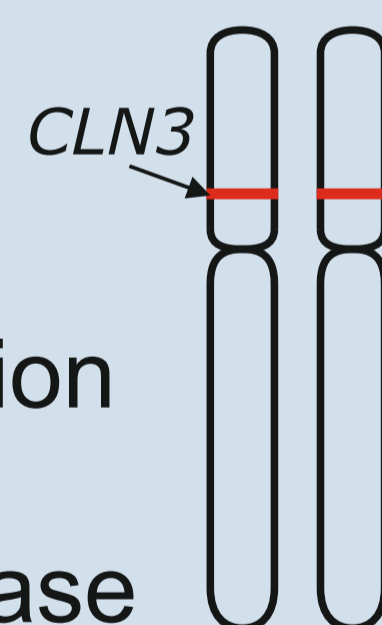


Other analysis; counting, measuring etc...

CLN3: a gene, a protein and a disease

Gene

Chromosome 16
Mutation: rare mutation inherited from both parents causes disease



In the cell

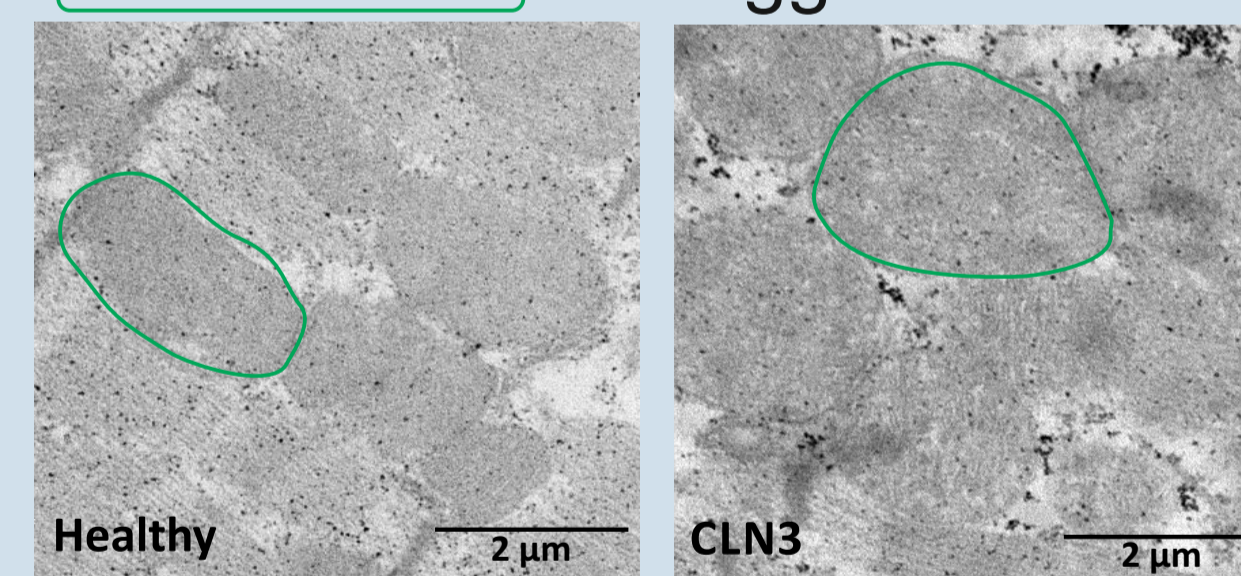
Cell waste accumulates
Disrupts normal functions
Affects eyes, brain & heart.

Disease

Symptoms tragically similar to Parkinson's, in childhood
Rare disease, 3-4 children diagnosed a year (*BFDA.org*)

Onset 4~8 years
Death ~early 20s

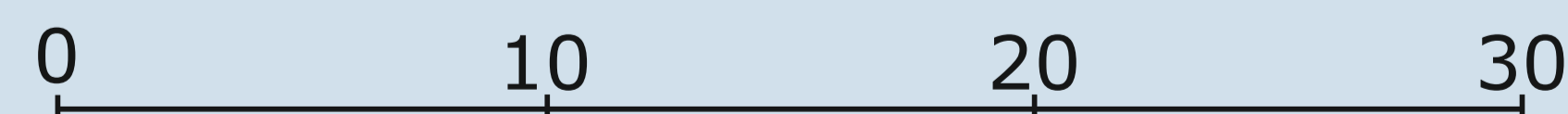
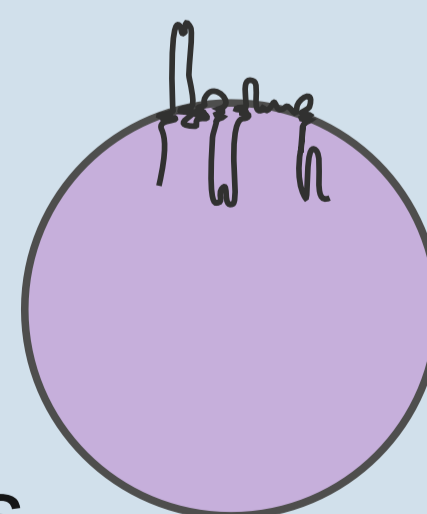
Heart cells, healthy & CLN3 mice
mitochondria are bigger in CLN3



Electron microscopy

Protein

Unknown function!
Transporter (?)
Found on lysosomes, crosses membrane
Mutation: shorter protein



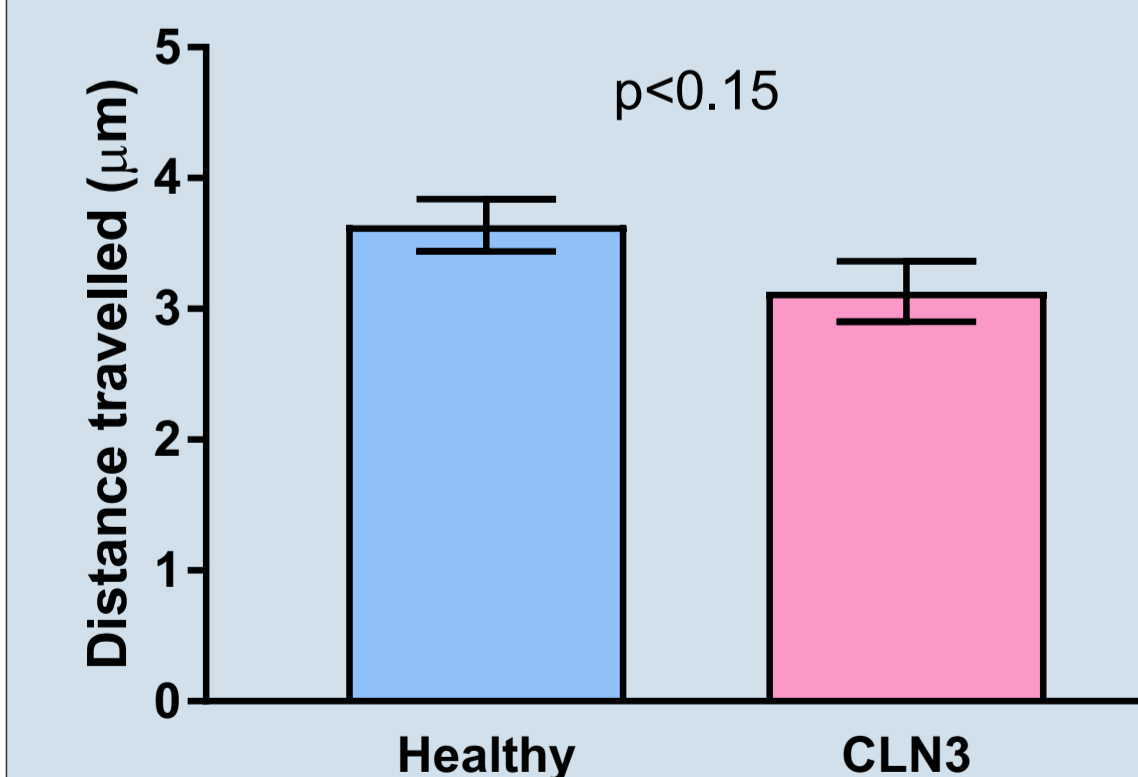
eyes decline of vision, blindness

brain seizures, mood changes, decline in cognition, speech, motor skills... etc

heart rhythm changes

Results

How do you study a channel of *unknown function*? Measuring changes to lysosome characteristics known to affect function.



Average distance of lysosomes that travel, in normal conditions; healthy cell compared to CLN3 patient cell.

Future work: investigating calcium signalling, mitochondria function and waste clearance...