

IPSSC +
CMBO

STUDENTS' CONFERENCE

Jožef Stefan International Postgraduate School
and Young Researchers' Day CMBO

19 and 20 April

Die hard - use a detergent!

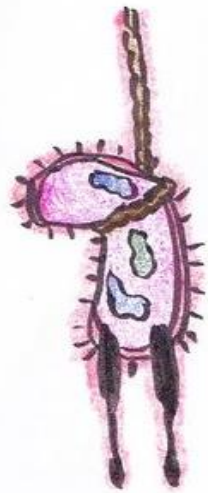
Lysosomal membrane permeabilization
- a cellular suicide strategy

Nežka Kavčič,
Jožef Stefan Institute

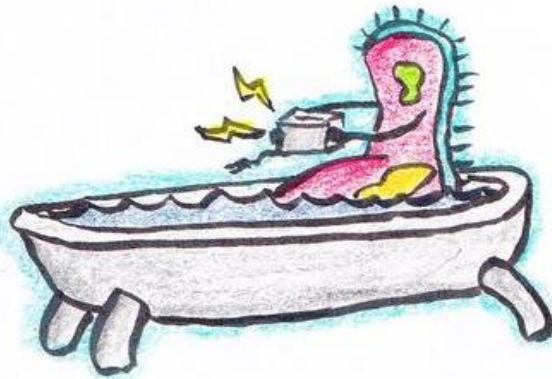
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What is a cell?

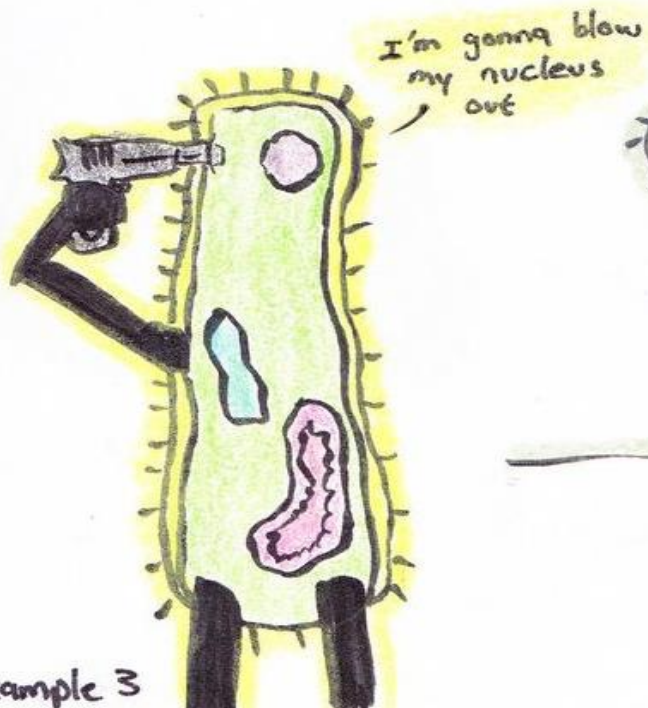
- the basic structural, functional and biological unit of all known organisms
- constantly works to stay alive
- and like any living thing it dies



Example 1



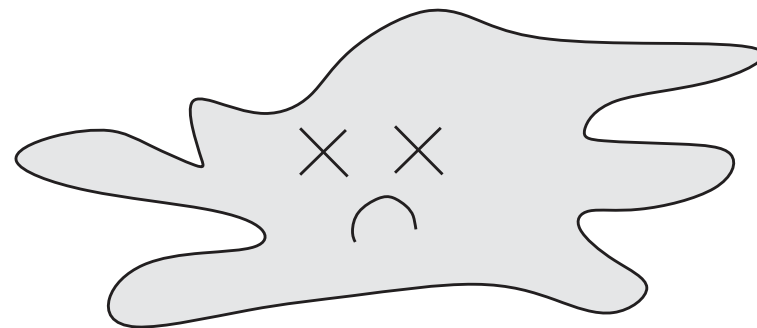
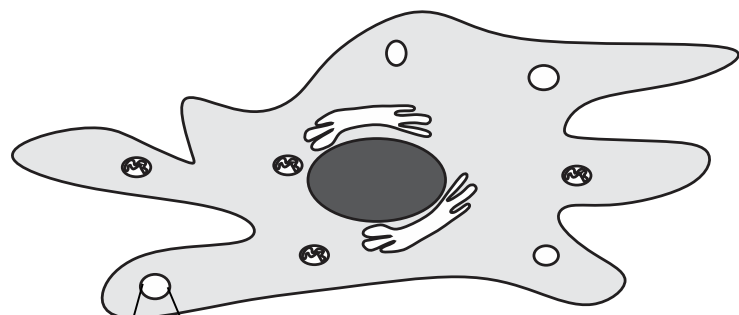
Example 2



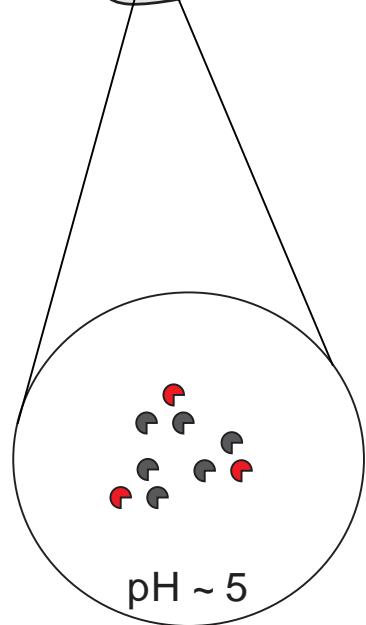
Example 3



Example 4

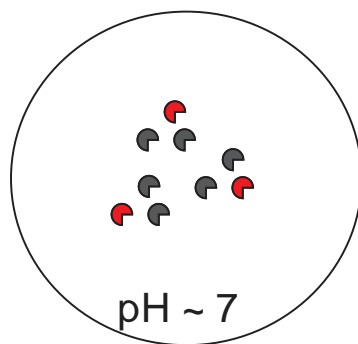


Cell death in a few hours

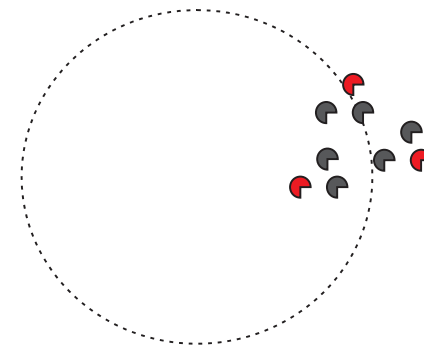


Lysosome

+ LLOMe
→



Accumulation of LLOMe
Polymerization



Membrane permeabilization



Acknowledgement

- Boris Turk (mentor)
- Barbara Sobotič
- Miha Butinar
- other co-workers from B1 department

Cathepsin C is critical for the release of other cathepsins from lysosomes in LLOMe-triggered apoptosis



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*Study programme: Nanosciences and Nanotechnologies

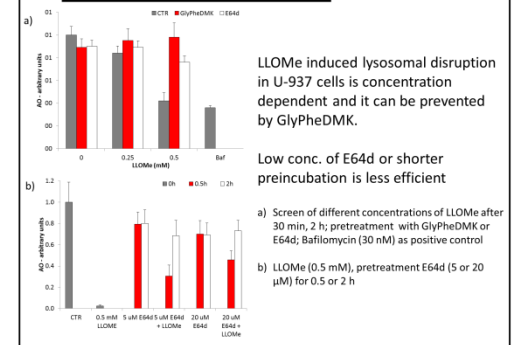
#Mentor



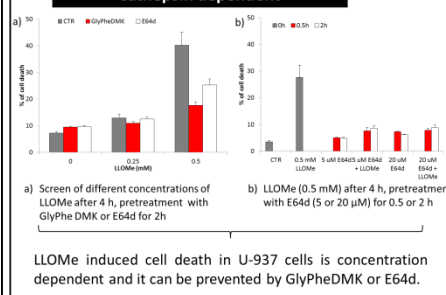
BACKGROUND

Lysosomotropic detergents remain captured in acidic vesicles and can induce lysosomal membrane permeabilization (LMP). LMP is a point-of-no-return, followed by cell death, usually mediated by cathepsins. L-Leu-Leu-methyl ester (LLOMe) is a synthetic lysosomotropic detergent, which showed extremely good results in preventing the graft-versus-host disease in vivo by successfully eliminating immune cells of the donor. The mechanism of compound action is dependent on the transferase activity of cathepsin C, which leads to the formation of LeuLeu oligomers that in turn act as detergent, leading to lysosomal leakage, release of cathepsins into the cytosol and triggering of apoptotic cell death. However, the exact mechanism of action and interconnection between different cathepsins were never clarified.

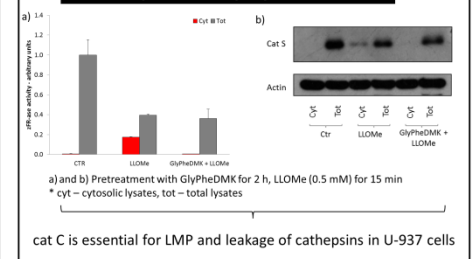
LLOMe affects lysosomal integrity



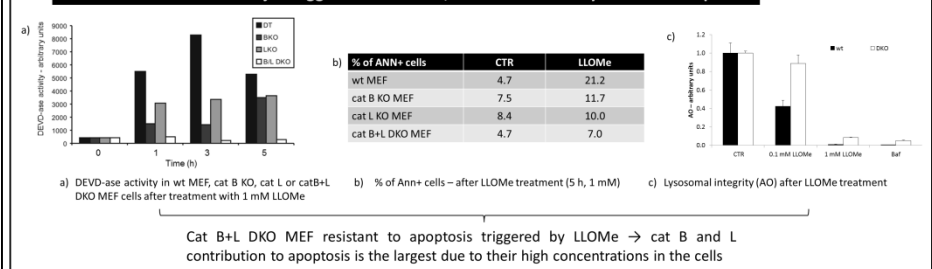
LLOMe induced cell death is cysteine cathepsin dependent



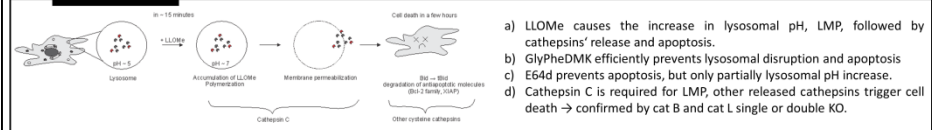
LLOMe induced leakage of cathepsins can be prevented by GlyPheDMK



cat B and cat L are the major triggers of cell death, but do not affect lysosomal disruption



CONCLUSIONS



Poster number: 60