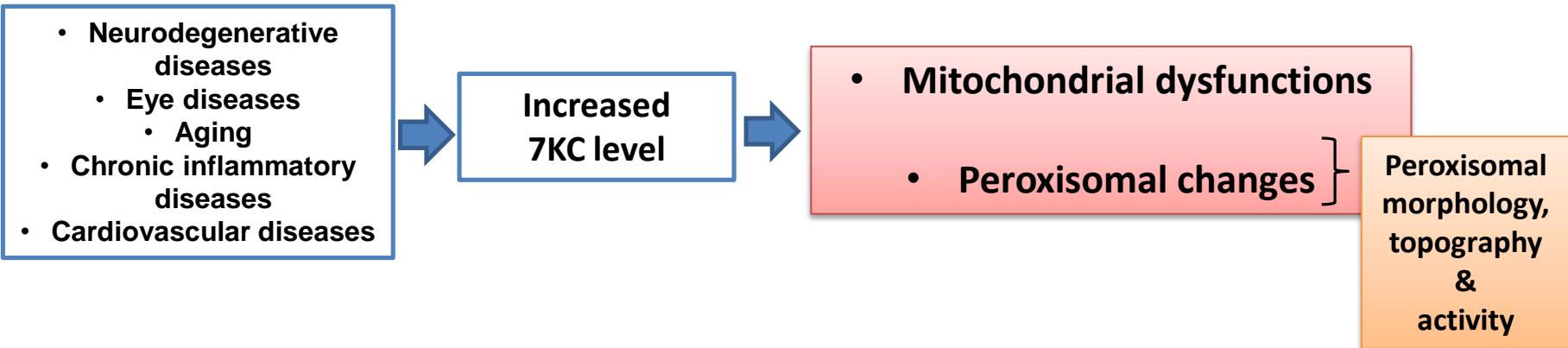


Alteration of peroxisomal functions by 7-ketocholesterol: potential involvement in age related diseases and aging

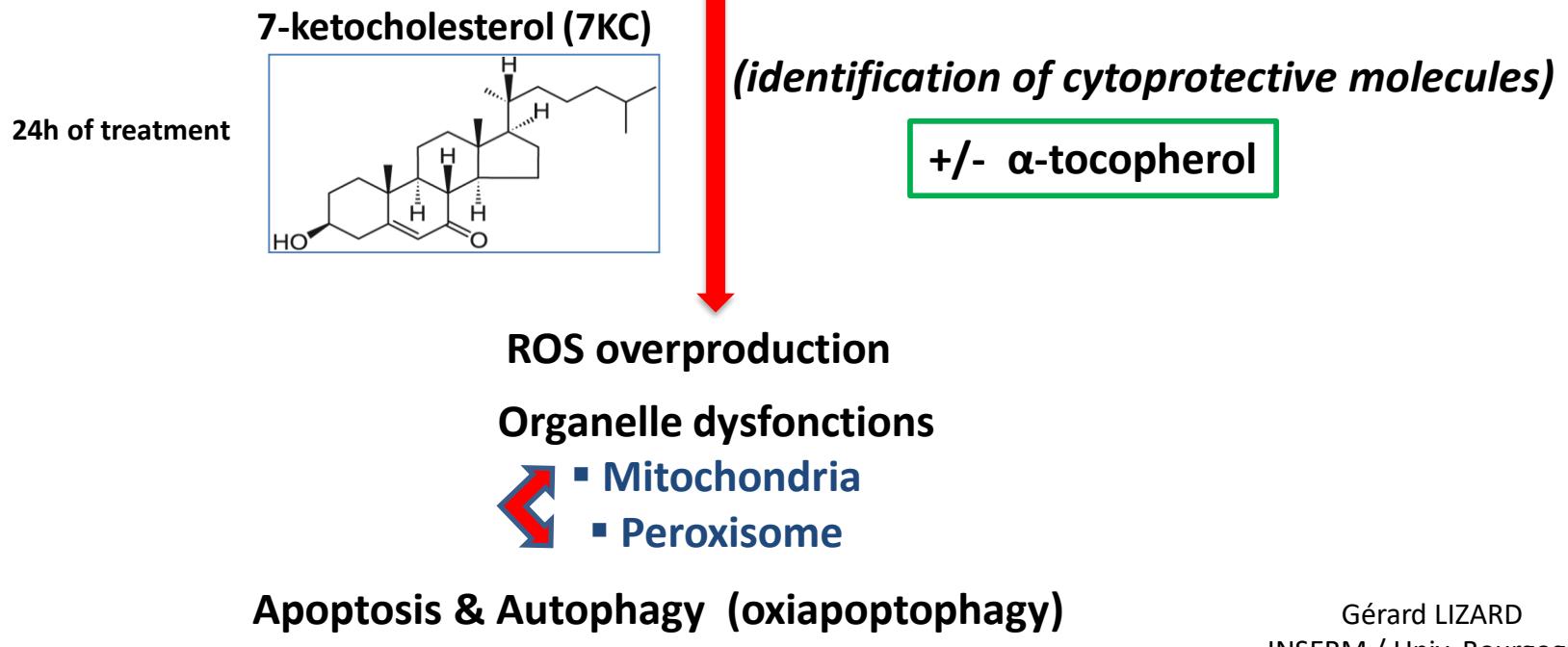
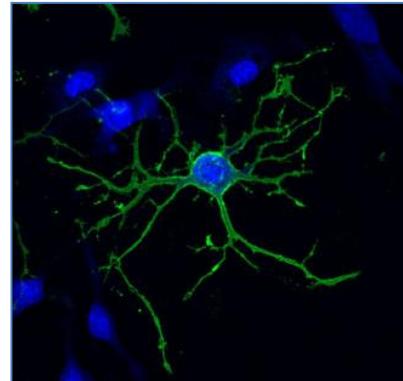


Aim of our work

- ✓ To precise the impact of 7KC on the peroxisome
And
- ✓ To determine the contribution of the peroxisome
in 7KC-induced cell death

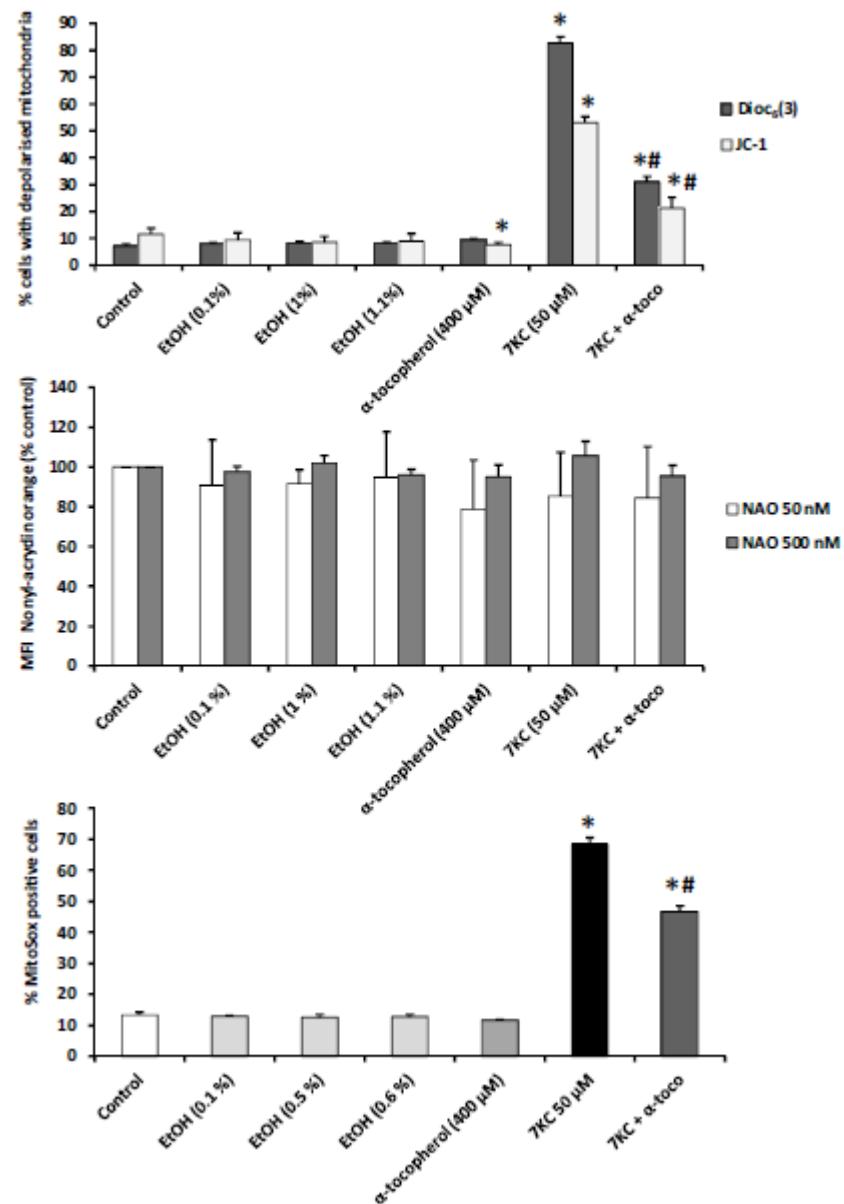
In vitro models used

Murine oligodendrocytes 158N
Murine microglial BV-2 cells & murine N2a cells

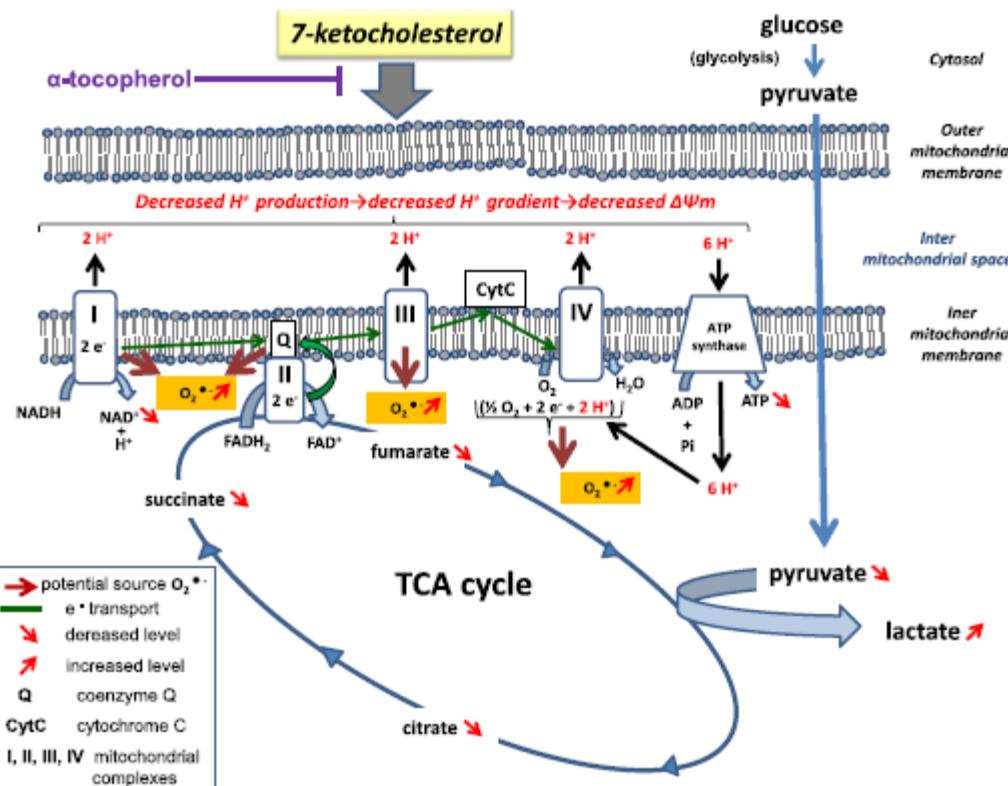


Impact of 7-ketocholesterol at the mitochondria level

V. Leoni et al / Journal of Steroid Biochemistry & Molecular Biology 169 (2017) 96–110



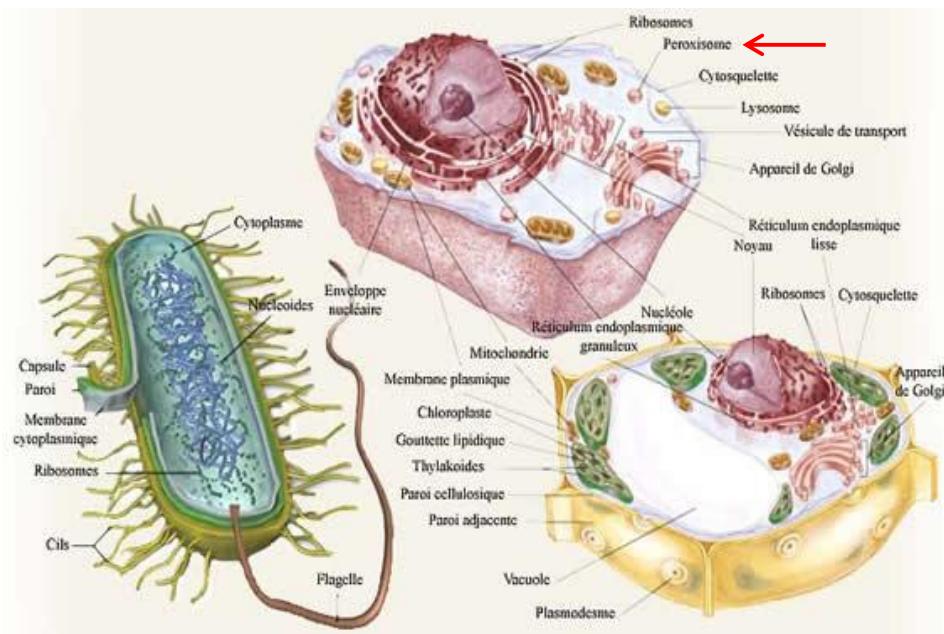
V. Leoni et al / Journal of Steroid Biochemistry & Molecular Biology 169 (2017) 96–110



Peroxisome

- Cell organelle: often round (diameter: 0.1-1 µm)

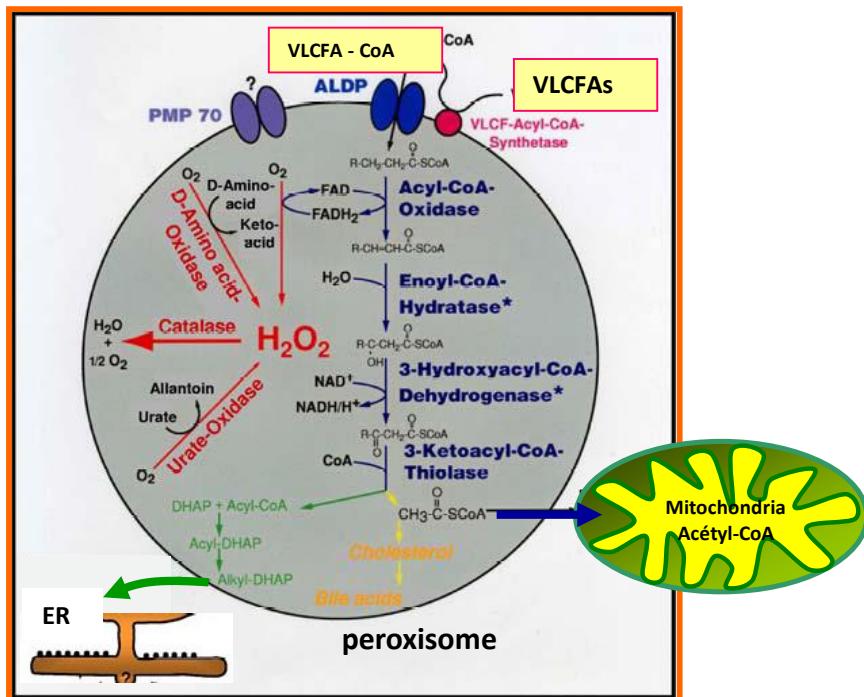
High polymorphism (size, shape, number: depending on environmental conditions)



- One membrane (lipid bilayer)
 - No DNA, protein import from the endoplasmic reticulum
 - Present in all animal and vegetal cells (eukaryotic cells), excepted in erythrocytes
 - Contain oxidative enzymes : catalase, urate oxidase ...
- Biochemical definition (1960)
- one oxidase producing H_2O_2
 - one catalase degrading H_2O_2

Peroxisomal activity: major roles in lipid metabolism and RedOx homeostasis

Peroxisomal metabolism includes :

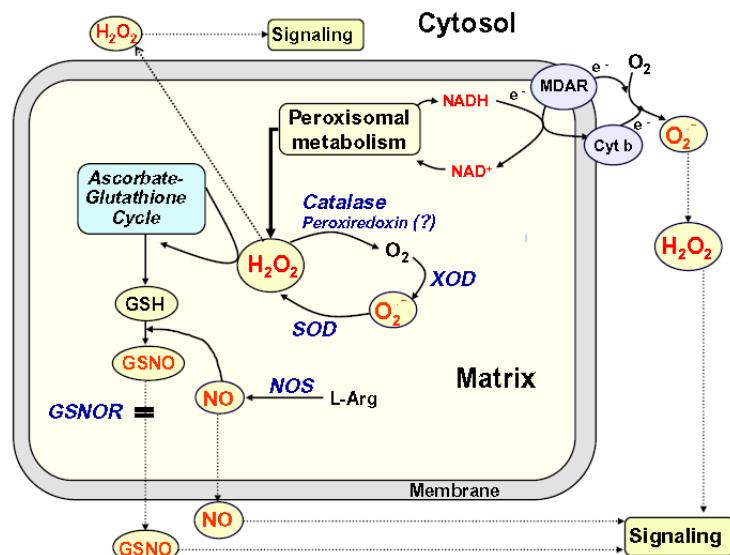


- Lipid metabolism

- * peroxisomal β-oxidation
(fatty acid degradation ≥ C22)

- Oxidative metabolism

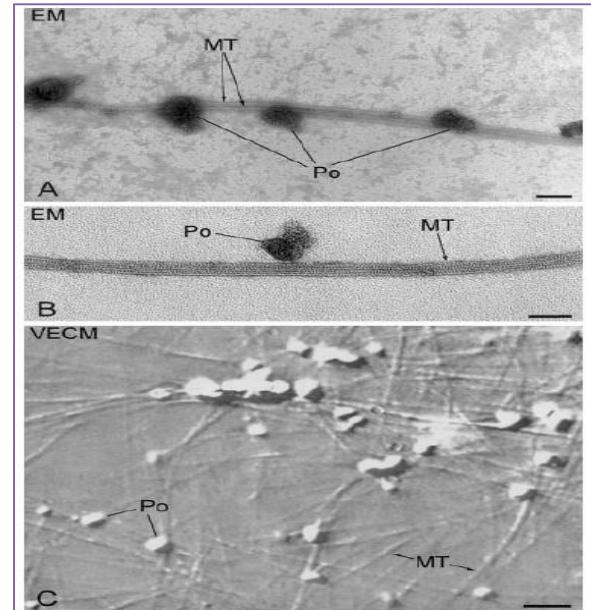
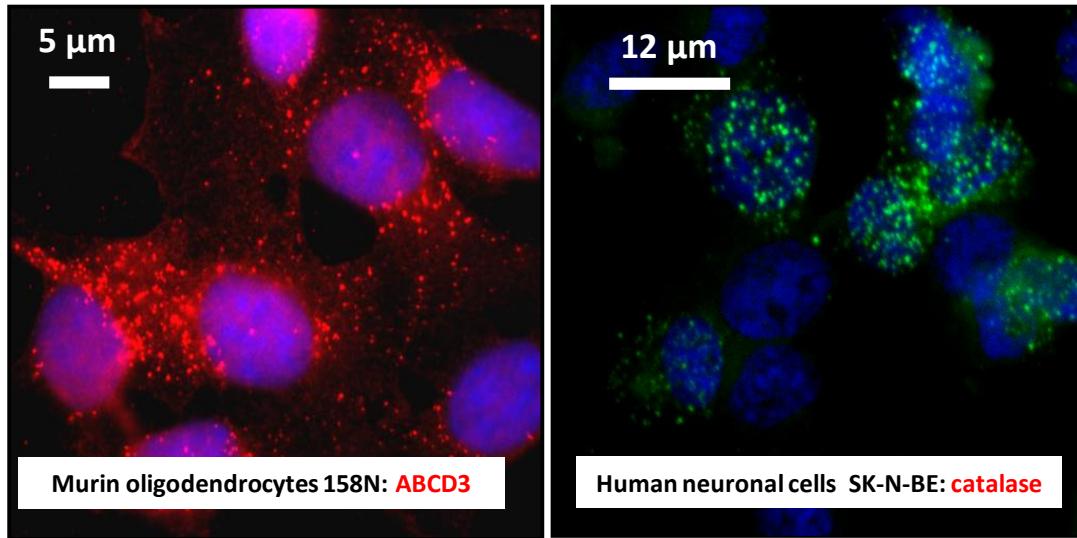
- * catalase (H₂O₂ degradation);
Involvement in NO, GSNO, H₂O₂ et O₂[•] production
(oxidative stress)



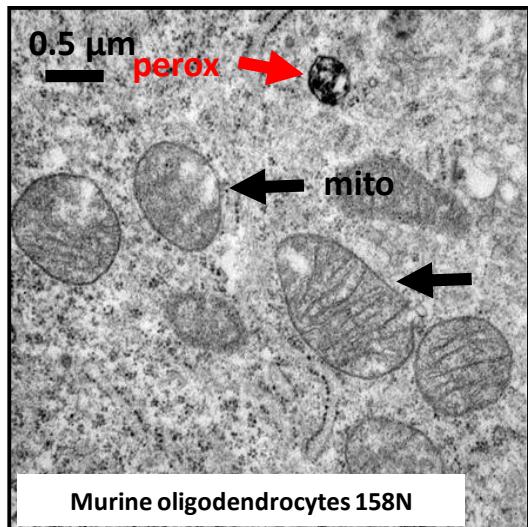
- Michael Schrader & H. Dariush Fahimi, *Histochem Cell Biol* 2008, 129 : 421–440
- Luis A. del Rio, *Arch Biochem Biophys* 2011, 506 : 1-11.

In situ characterization of peroxisome

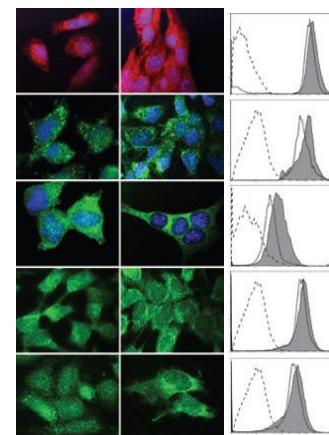
Confocal microscopy (ABCD3, catalase)



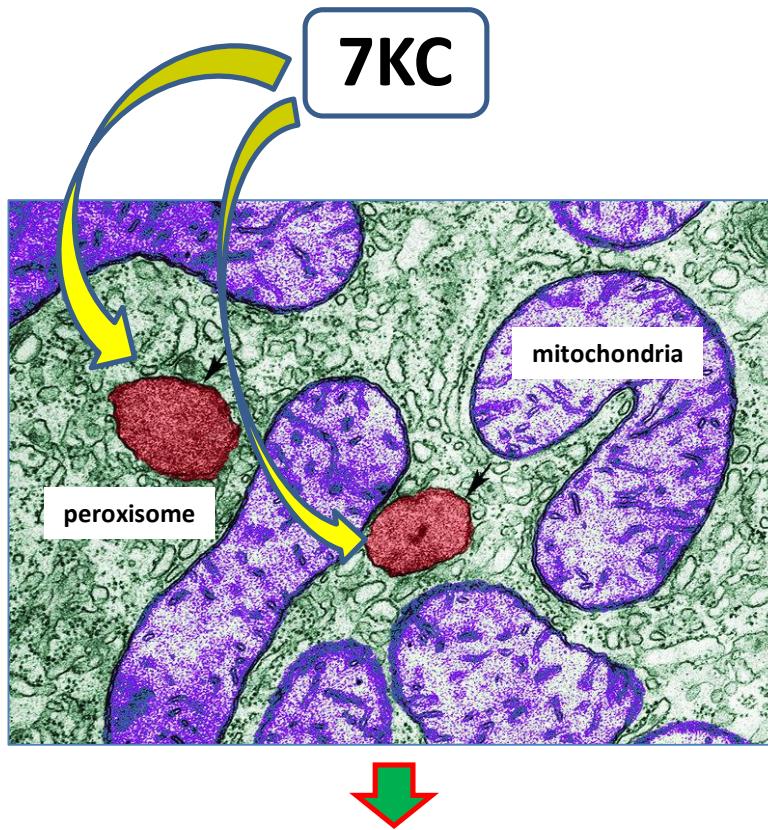
Microtubule / peroxisome interaction



- ABCD1
- ABCD3
- Catalase
- ACOX1
- L-PBE



Impact of 7-ketcholesterol on the peroxisome



- ✓ Morphological and topographical changes of peroxisomes
- ✓ Functionnal changes of peroxisomes
 - Oxidative stress: catalase activity, H_2O_2 production
 - Metabolic activity: modification of β -oxidation
- ✓ Cell reactivity: pexophagy