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Differential Utilization of Dietary Fatty Acids in Benign and Malignant Cells of the Prostate.

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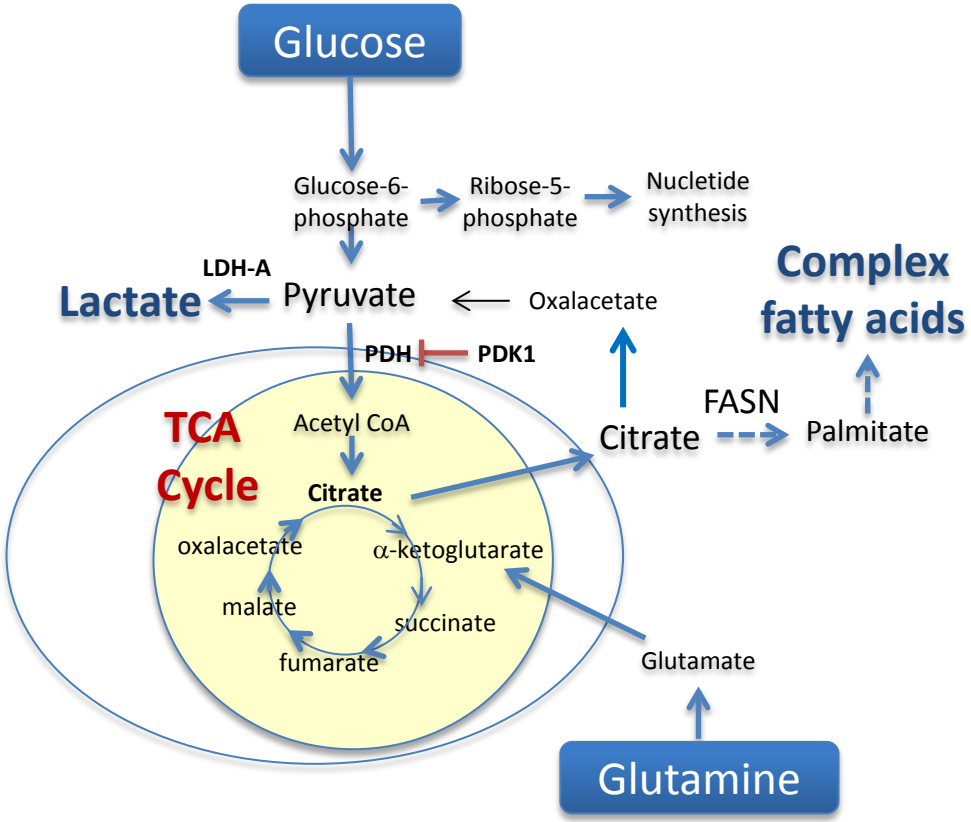
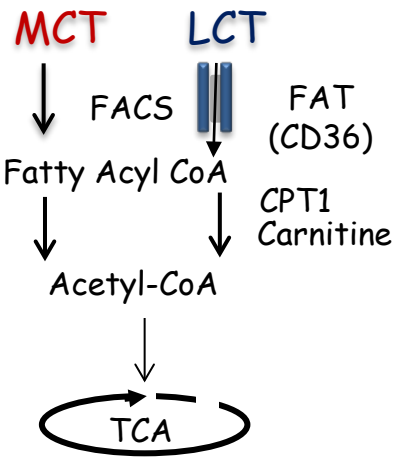
Metabolic reprogramming of cancer cells

- Tumor cells adapt to elevated energy demands via metabolic reprogramming (Warburg effect)
- Ketogenic diets
- Prostate cancer: highly active lipogenesis
- Fatty acids are used for energy storage, synthesis of cell membranes, and generation of cell signaling molecules.



Long chain vs medium chain triglycerides

- Long chain triglycerides (LCTs, C16-22) found in fish or fish oil
  - Reduced PCa incidence
  - Decreased immune responses



- Medium chain triglycerides (MCTs, C8-12):
  - Water soluble
  - Directly taken up by the cells
  - Enter mitochondria without carnitine
  - minimally stored as fat depots into adipocytes

Aim of the study: Are there differences in the utilization of fatty acids as energy source under normal growth conditions and under glucose starvation between benign prostate and prostate cancer cells?

LCTs and MCTs used in this study

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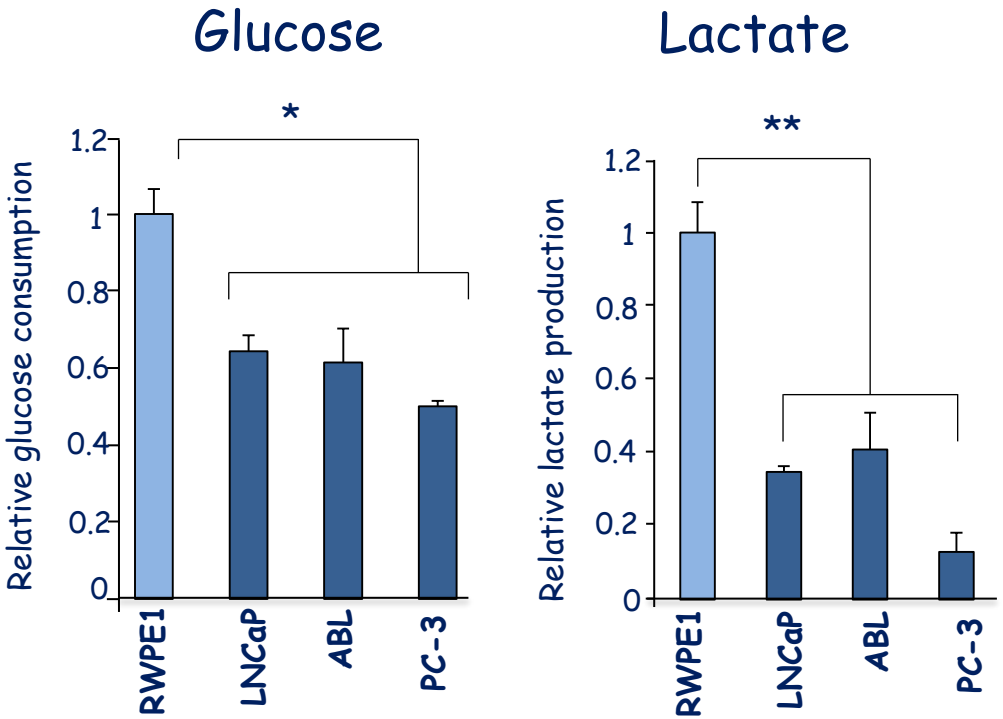
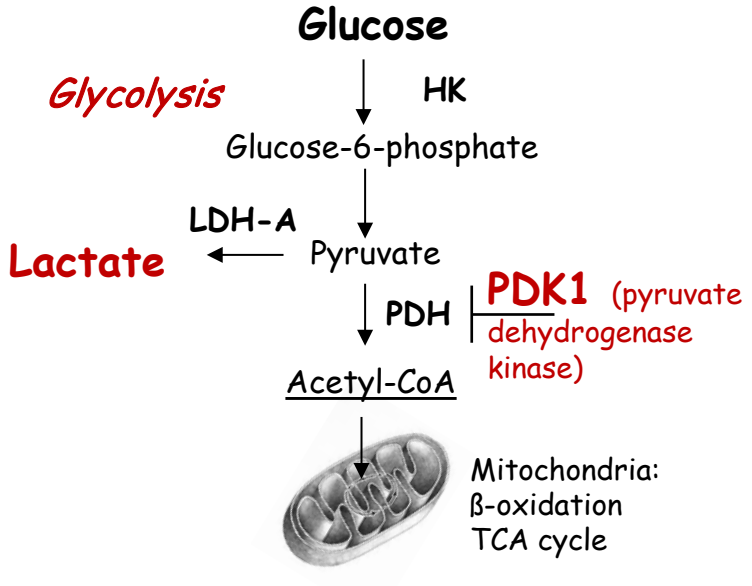
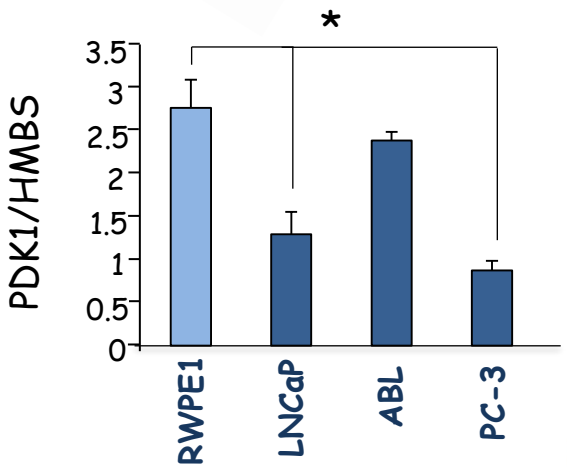
MCT	100%	Coconut oil Palm oil	lauric acid (C-10)
LCT	100%	Thistle oil Line seed oil	linoleic acid alpha-linolenic acid (C-22)
MCT/LCT	3:1	Coconut oil Palm oil Thistle oil Line seed oil	lauric acid (C-10) linoleic acid alpha-linolenic acid (C-22)

Glycoytic activity of benign vs prostate cancer cells



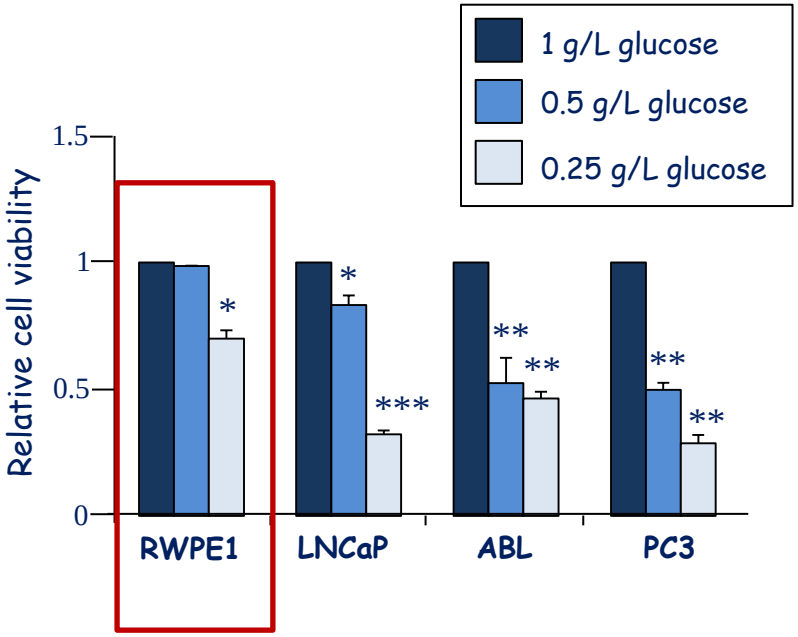




BE RWPE1 cells have a higher glycolytic activity than PCa cells.

Dueregger et al (2015) PLoS ONE 10(8): e0135704.

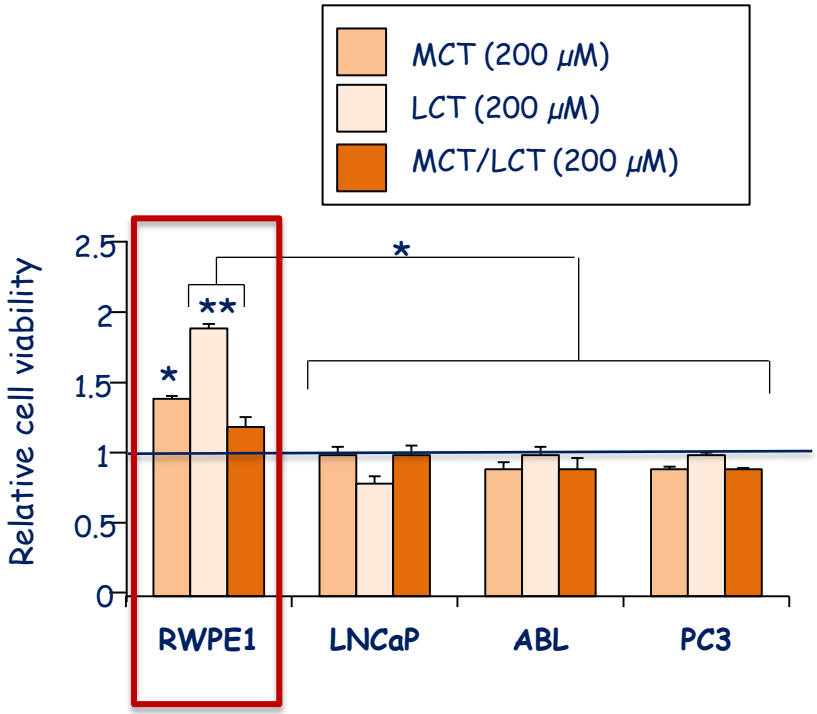
Cell viability under reduced glucose conditions

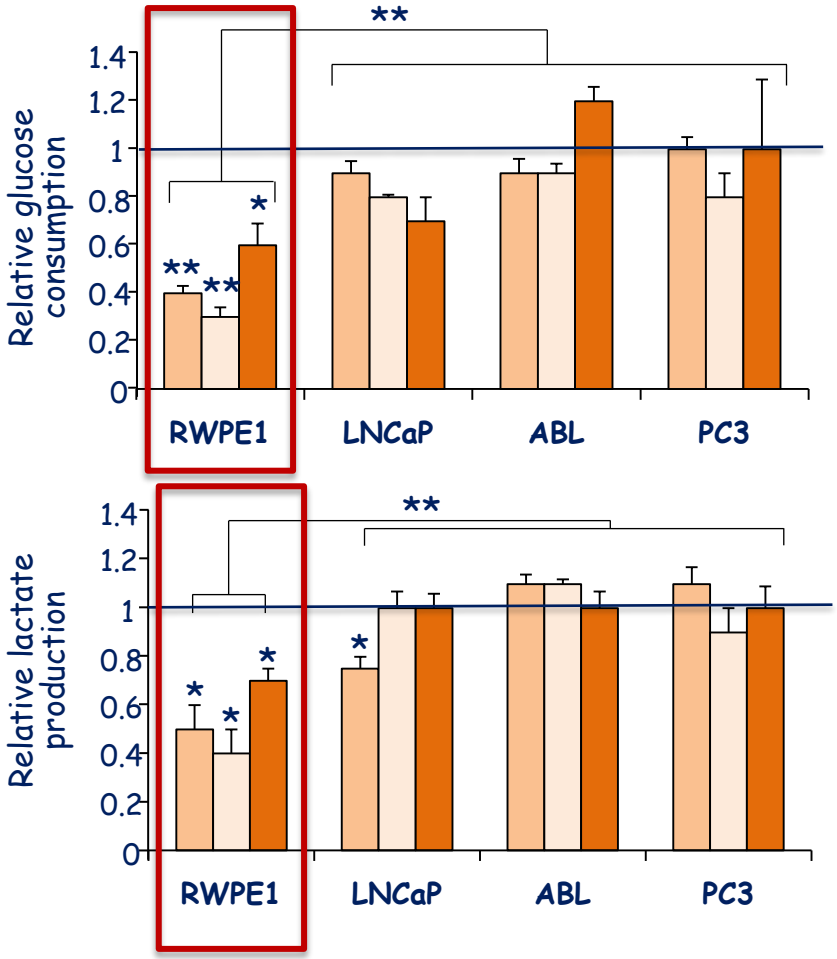


Despite their high glycolytic phenotype, BE RWPE1 cells are less dependent on glucose, which is mainly metabolized via glycolysis.

Dueregger et al (2015) PLoS ONE 10(8): e0135704.

Use of fatty acids as energy source





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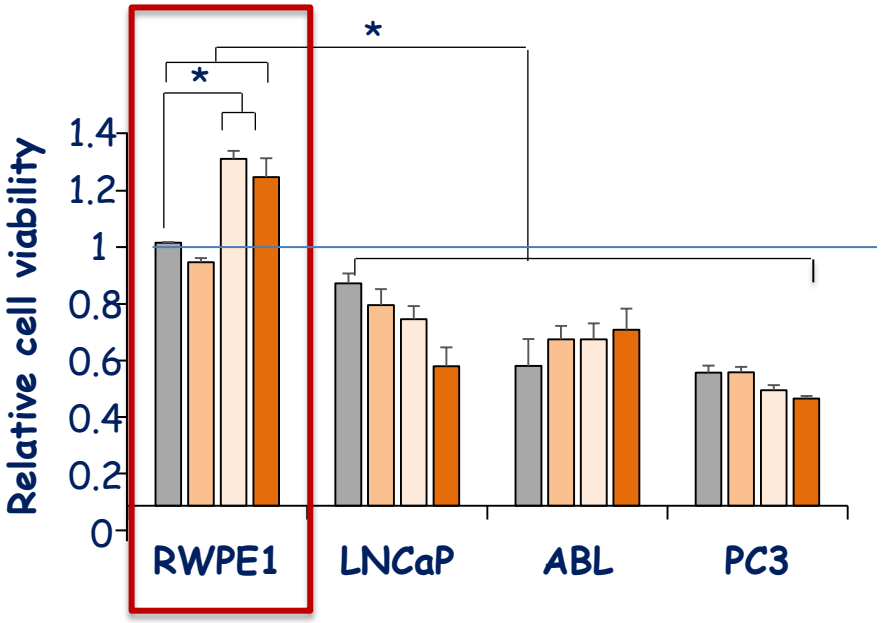
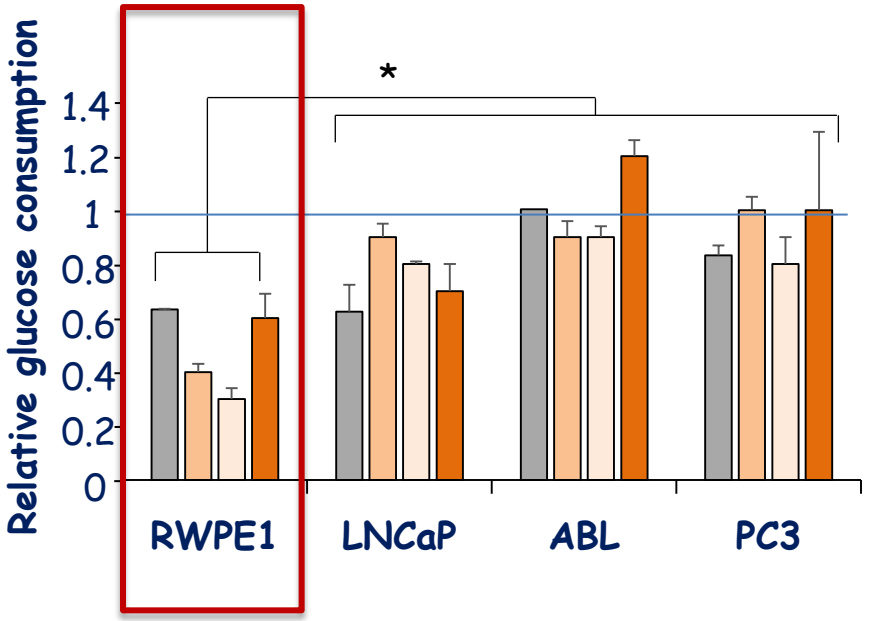
Effects of FAs under glucose starvation

Mock control (0.5 g/L glucose)
MCT (200 µM)
LCT (200 µM)
MCT/ LCT (200 µM)





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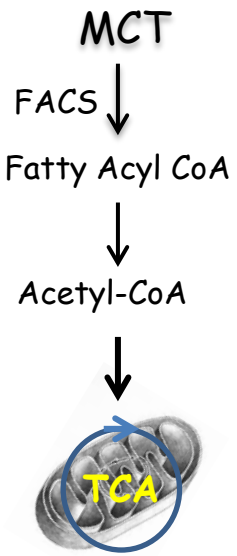
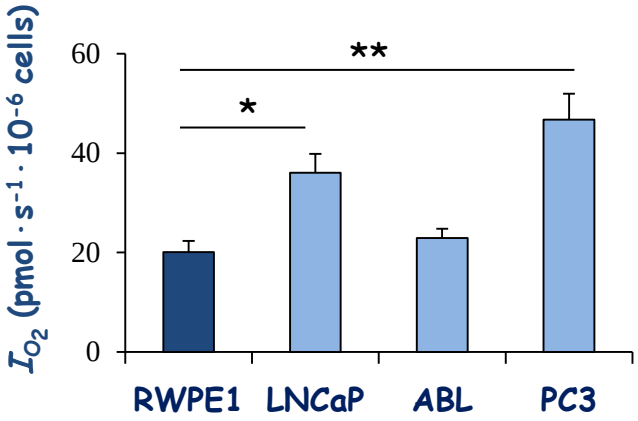
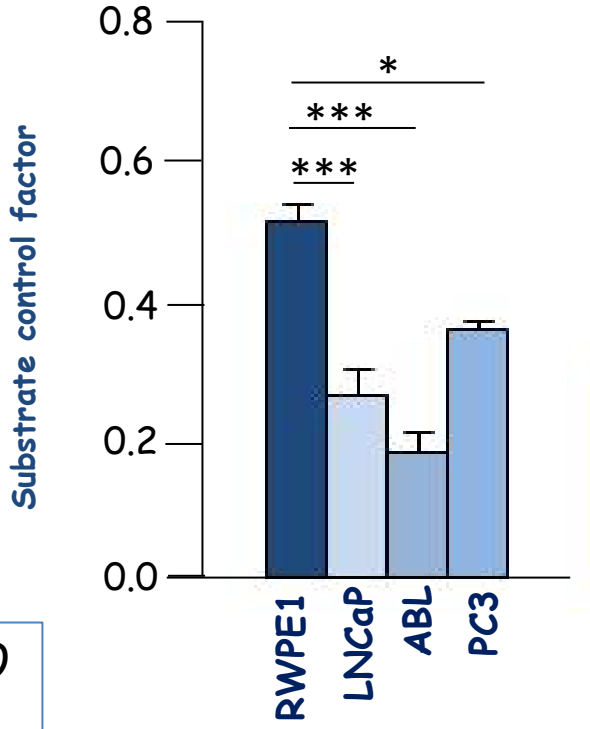
Mitochondrial Respiration



Baseline respiration



OXPHOS capacity after addition of the MCT octanoylcarnitine

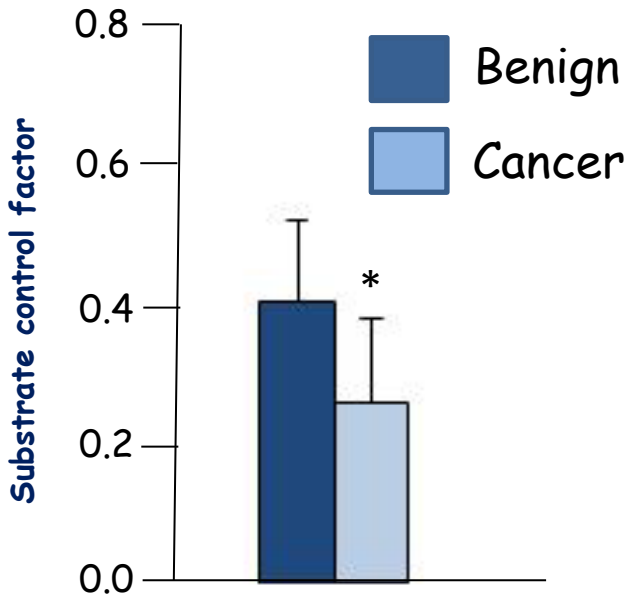


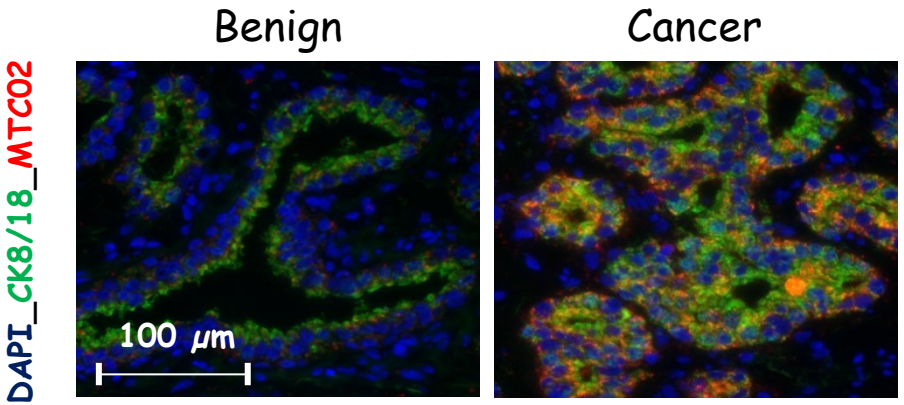
BE RWPE1 cells show a significantly higher FAO (fatty acid oxidation) capacity than PCa cells.

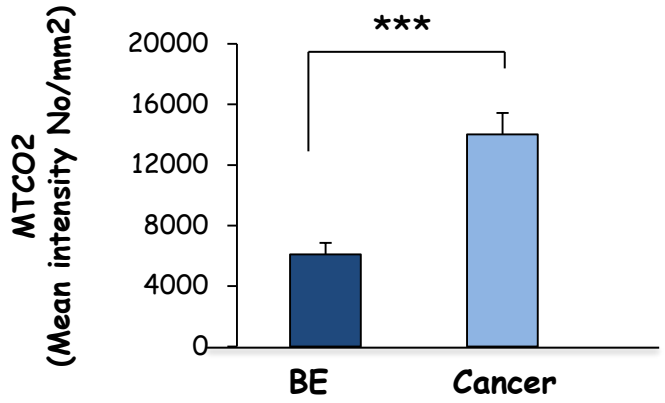
Dueregger et al (2015) PLoS ONE 10(8): e0135704.

FAO capacity in human prostate tissue

FAO capacity in paired BE and CA samples (n=6) after addition of the MCT octanoylcarnitine:







Significantly higher FAO capacity in benign vs cancer tissue.

Dueregger et al (2015) PLoS ONE 10(8): e0135704.

Summary

- Benign prostate cells have a higher glycolytic activity than PCa cells.
- Benign prostate cells have a high preference to utilize dietary FAS as energy source.
- Currently the effects of an MCT-enriched diet is tested in vivo using a PTEN KO mouse model.

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