

The efficiency of modulated electro-hyperthermia may correlate with the tumor metabolic profiles

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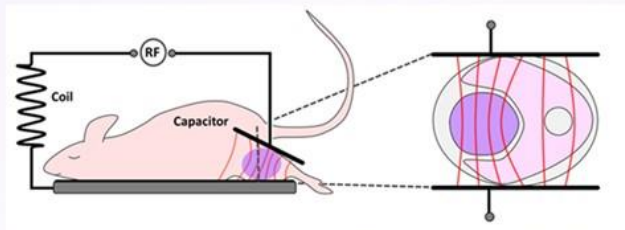
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The efficiency of modulated electro-hyperthermia may correlate with the tumor metabolic profiles

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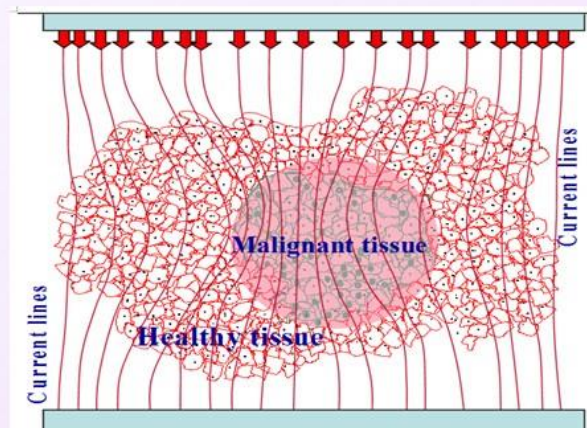
Modulated electro-hyperthermia (mEHT) – the method



- Loco-regional
- Non invasive
- Complementary therapy

Using 13.56 MHz radiofrequency it generates hyperthermia (~42°C) => Apoptotic cell death

The conductivity of **electric field** has an **affinity** to increased ion concentration tissue. **Malignant tissues**, due to their elevated glycolysis, results more ion particles (**Warburg effect**). So the treatment target these tissues and acts there.



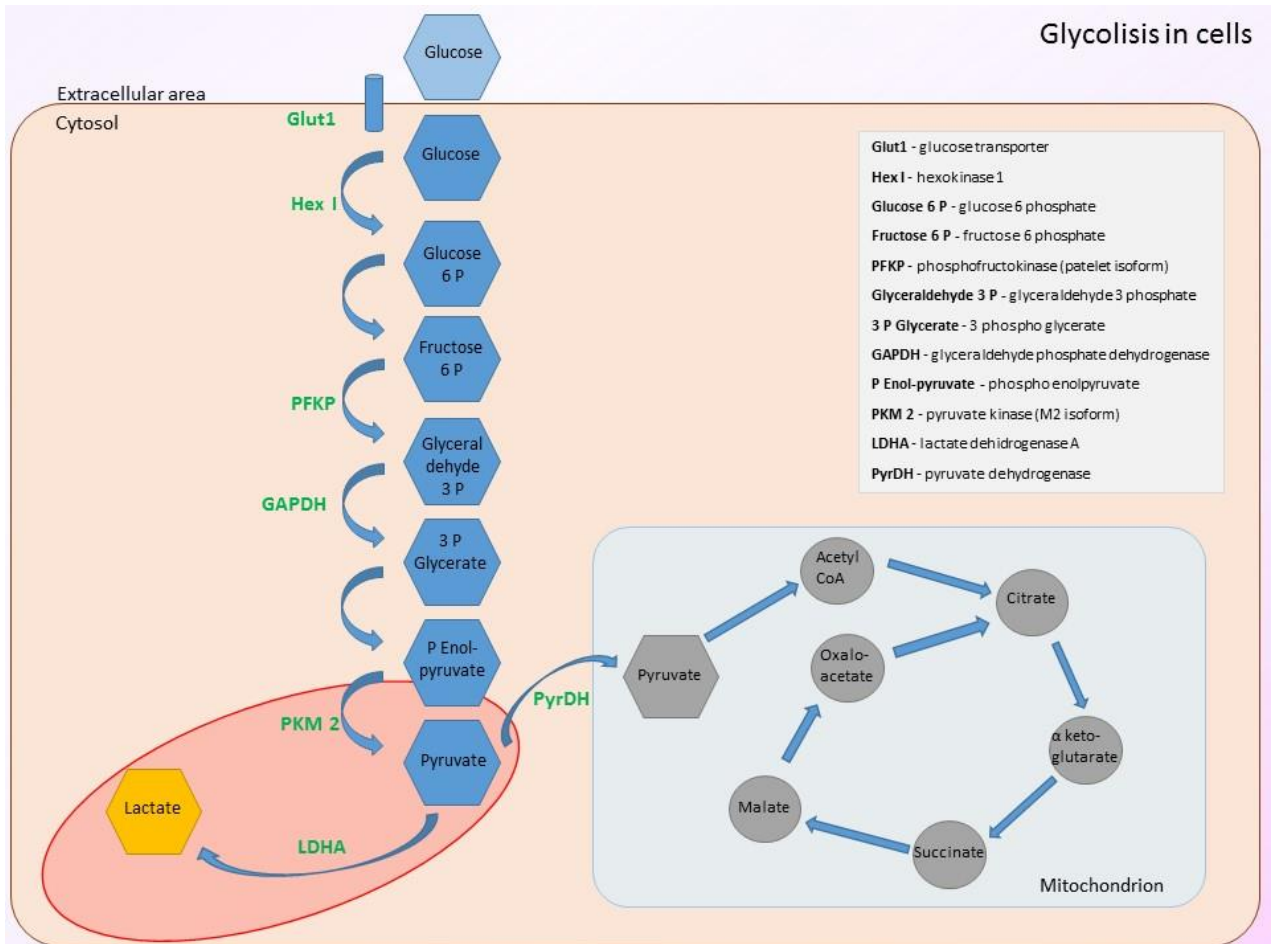
mEHT and Warburg effect (elevated glycolysis)

Elevated charged metabolite level existed in solid malignant tumors

- Lactic acid, other charged ions => acidic environment
- Better conductivity -> concentrate the electric field -> selectivity of tumor treatment
- The question arises: Can the glycolysis proprietors of tumor influence the treatment efficacy?

Objective

- To quantify the tumor destruction rate (TDR) on different cell lines after mEHT treatment
- To make a glycolysis profile for the cell lines
- To respond to the question if the tumor destruction rate is influenced by the glycolytic pathway activity

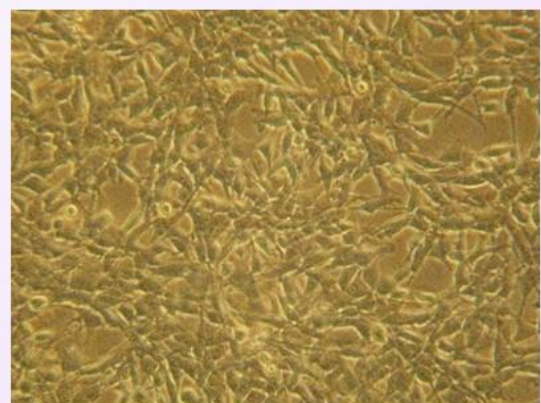


Used cell lines

- HT29 - human colorectal carcinoma
- HepG2 - human hepatocellular carcinoma
- C26 - mouse colorectal carcinoma
- C38 - mouse colorectal carcinoma

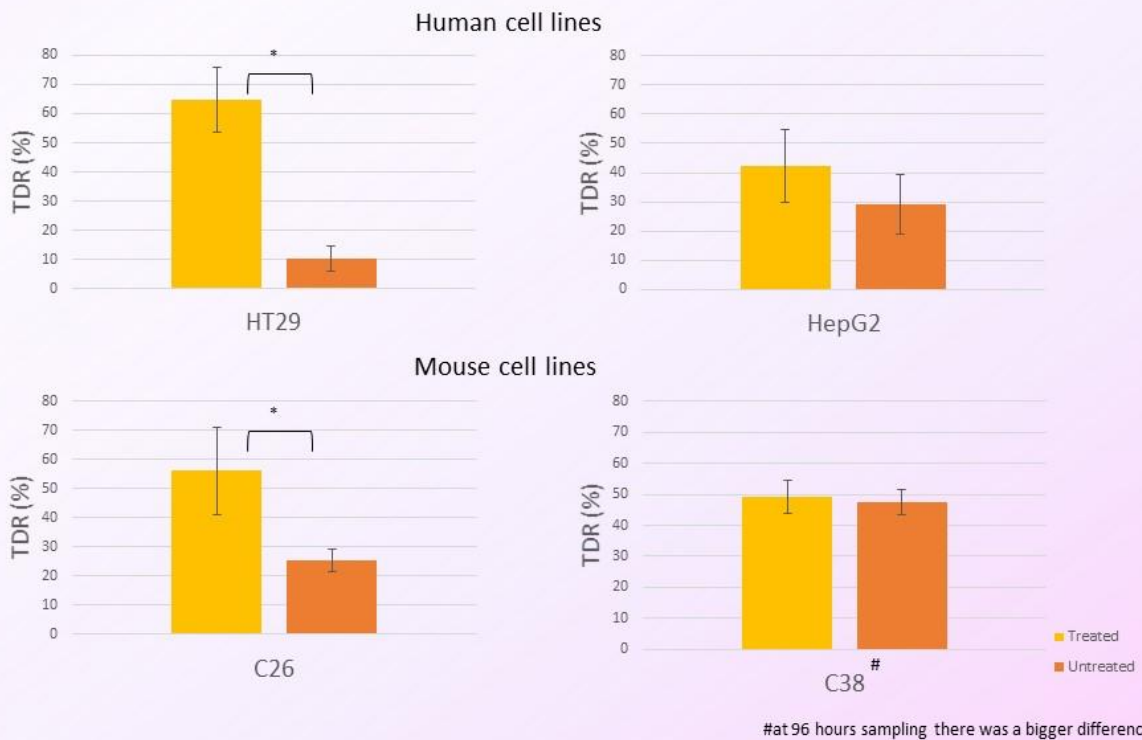
Cell glycolysis profiling:

- Intracytoplasmatic metabolits
- pH and buffer capacity measurements
- In situ glycolytic enzyme production

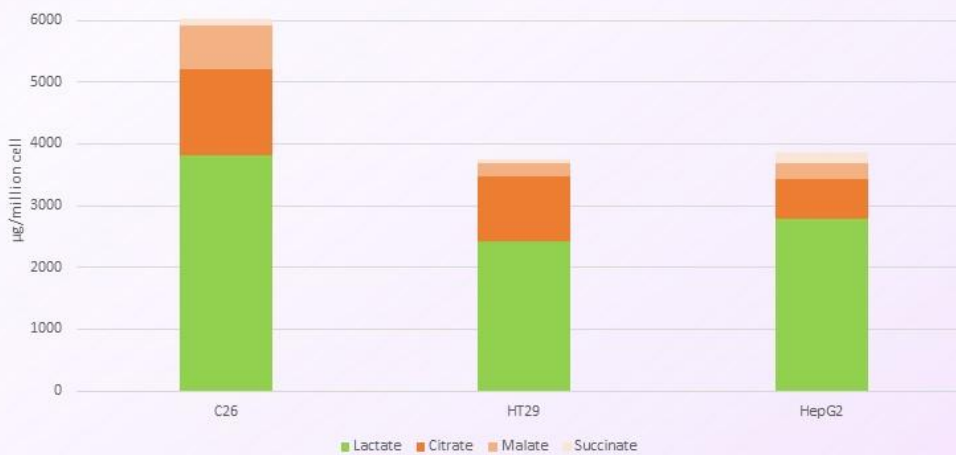


mEHT induced tumor destruction rate (TDR)

- Single shot, 30 minutes long mEHT treatment. Samples after 24 hours

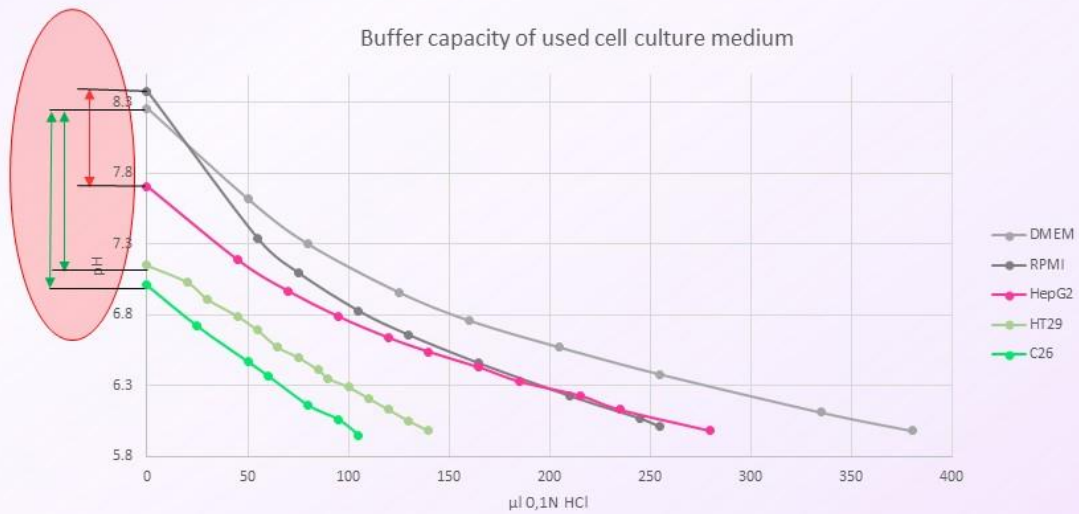


Intracytoplasmic glycolysis metabolites



The intracytoplasmic level of lactate and some of Krebs cycle products are the same in the HepG2 and HT29 cell lines. The C26 has an elevated metabolite production

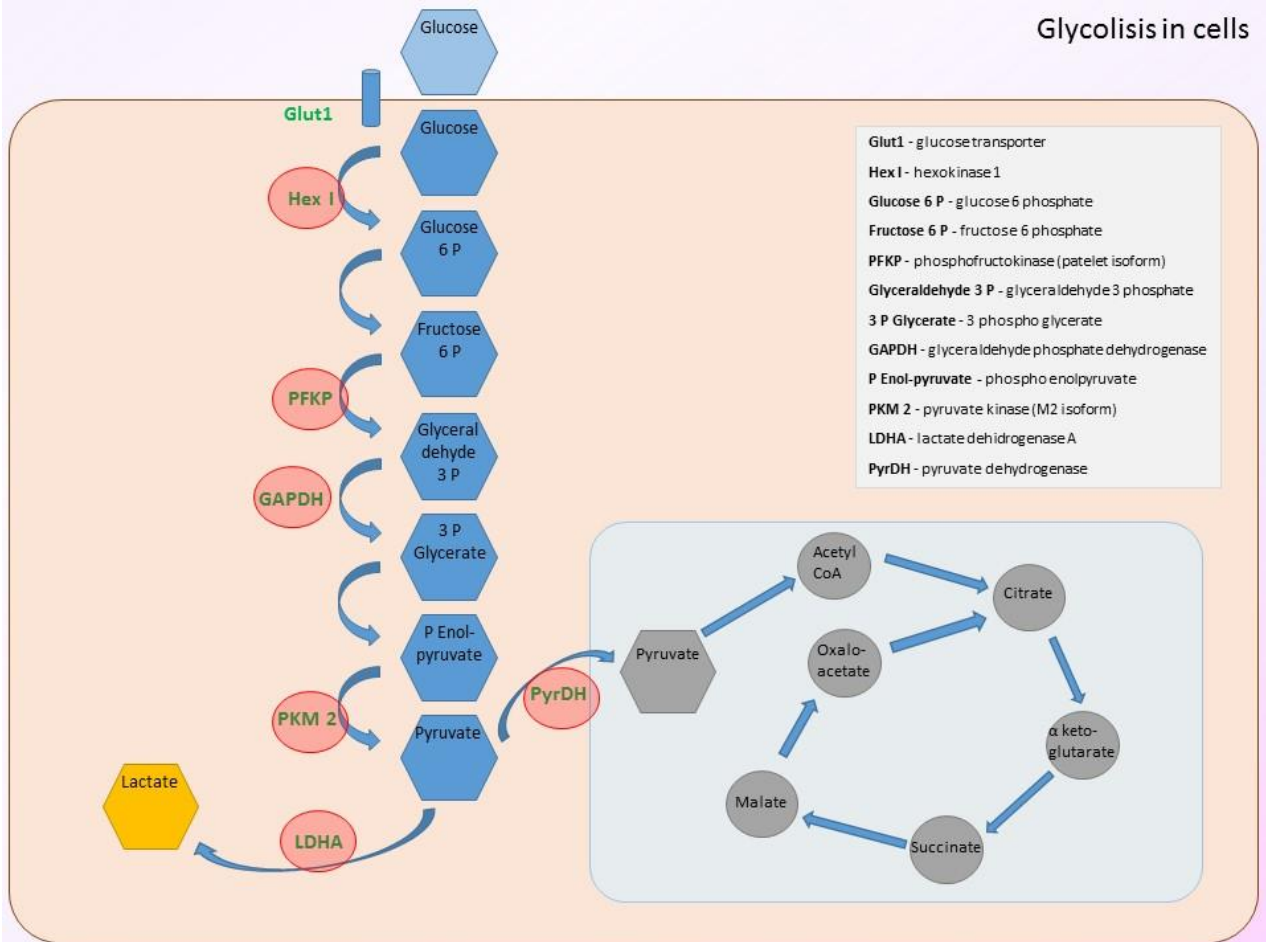
Extracellular acidification rate (ECAR)



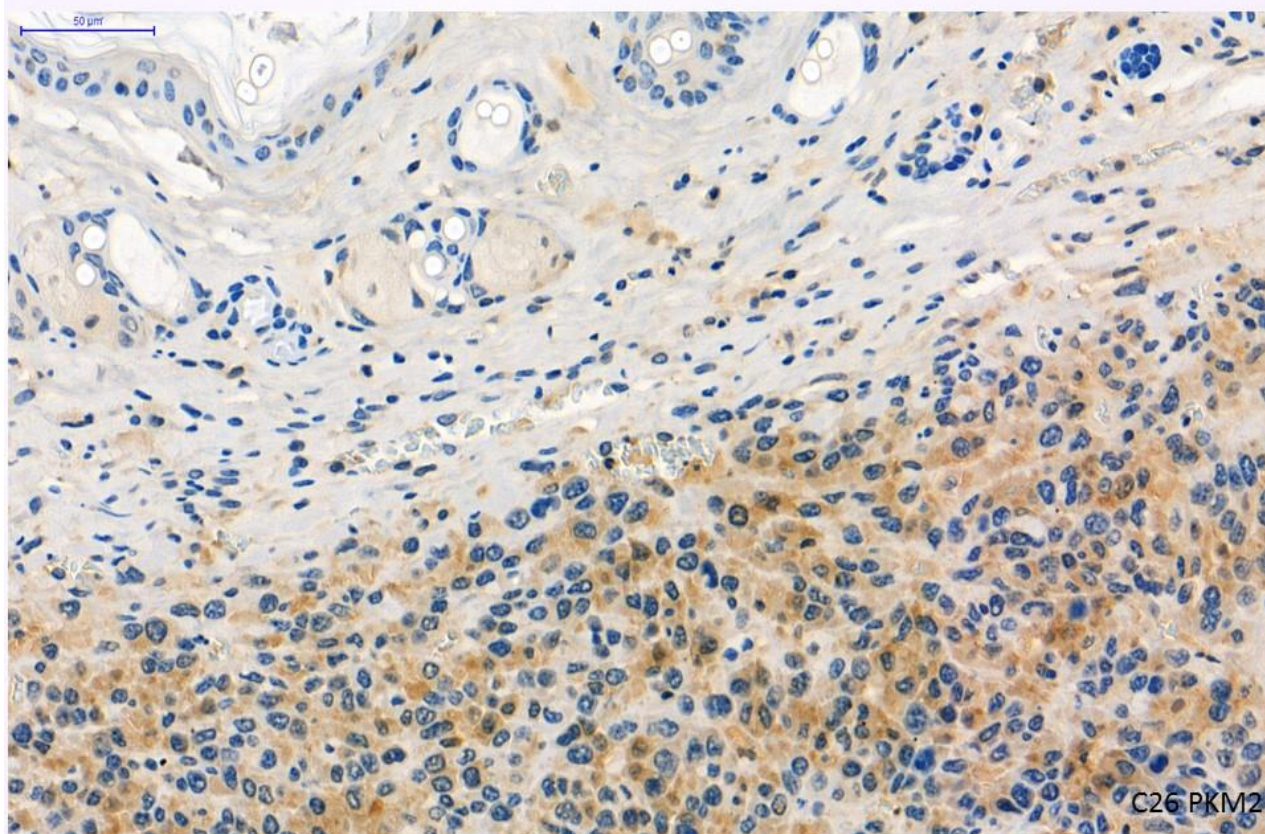
The culture mediums buffer capacity shows **the amount of acidic particles exported** by cells. The medium used by **HepG2** cell line was the **less acidic**, so the C26 and HT29 produced the most acidifying particles in the extracellular area.

- Cell culture media removed after the cell culture growth to confluent form (3 days)

Glycolysis in cells



Presence of glycolytic enzymes



Conclusion

- Warburg effect is present in the studied cell lines
- mEHT treatment efficiency varied among different tumor types based on TDE (*tumor destruction rate*)
- The intracytoplasmatic ion concentration may differ from the extracellular environment
- The extracellular lactate amount can be a precise indicator for treatment efficiency
- The elevated ion concentration supports the accumulation of electric field



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