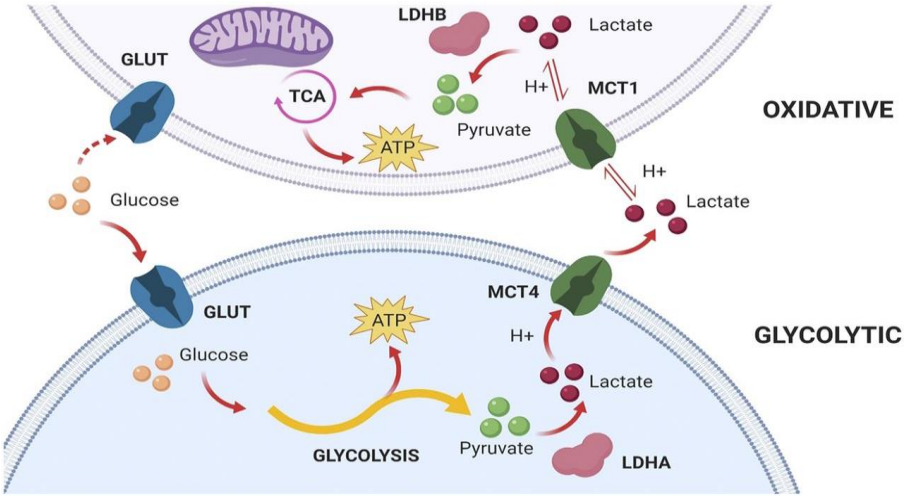
"Development of new PET radiotracers based on monocarboxylate transporter inhibitors for theranostic applications in oncology"

Due to their increased demand of glucose, a large variety of tumor cells show a dysregulated glucose metabolism, known as Warburg effect, responsible in many cases for the tumor aggressiveness. The Warburg effect is characterized by the presence of two subpopulation of cells that cooperate one another.

One develops a glycolytic metabolism thus increasing the uptake of glucose and producing as a byproduct lactate that is externalized from the cell into the extracellular environment. The other subpopulation develops an oxidative metabolism and uptakes the lactate from the extracellular environment to use it as the starting substrate for the Krebs cycle.

MCT1 e MCT4 are membrane proteins responsible for the transport of molecules consisting of monocarbon units (Lactic Acid, Pyruvic Acid, Ketone Bodies) and are widely expressed in different healthy tissues. However, their dysregulated expression allow the establishment of the Warburg effect. In fact, MCT1 is overexpressed by oxidative cells and is used to internalize lactate, while MCT4 is usually overexpressed by glycolytic cells and allows the externalization of lactate.



Recently, some molecules behaving as MCT's inhibitors have been identified, but the search for more effective inhibitors is still ongoing.

This project aims to modify the structure of a few of the already existing molecules and define new available scaffolds suitable for theranostic purposes exploiting radiolabeling techniques with specific radionuclide well known in the field of nuclear medicine such as Fluorine-18, and metal ions such as Copper-61/64/67 or Gallium-68.

References

1. Molecular Metabolism 2020, 33, 48-66.
2. Cell Reports 2018, 25, 3047–3058.