

## Inhibiting nucleotide catabolism, including in oncology

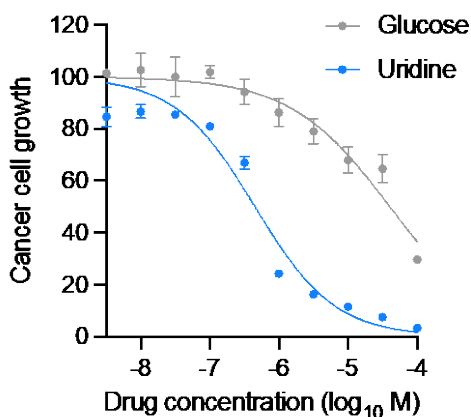
Glucose is vital for life, serving both as a source of energy and carbon building block for growth. When glucose is limiting, alternative nutrients must be harnessed by cells to survive (“metabolic flexibility”). Recent work reported that cancers and organisms can use nucleotides and nucleic acids as fuels, enabling them to survive glucose scarcity, such as in the tumor microenvironment. Nucleotides, RNA and DNA are abundant in our diet, and it was recently shown that genetically blocking their catabolism impairs cancers growth (*Nature Metabolism* 2023, *Nature* 2023).

Inhibiting nucleotide catabolism with small molecules has a high therapeutic relevance in the fields of oncology, immune modulation and metabolic syndrome.

### TECHNOLOGY OVERVIEW

This innovation describes a novel set of small molecular inhibitors of nucleotide catabolism, characterized by their ability to prevent cancer cell growth when nucleotides are used as a source of energy. The activity of these inhibitors is conserved in several cancer lineages.

Inhibitor activity in the metabolic pathways of glucose and uridine catabolism



### APPLICATIONS

The selected inhibitors are suitable for use in:

- **Oncology:** Blocking nucleotide catabolism decreases tumor burden or may be used in combination with other therapies (chemotherapy, immunotherapy).
- **Immunity and autoimmunity:** Nucleotide promotes immune cell survival and activity in glucose-limited conditions.
- **Metabolic modulators:** Nucleotide-rich diet leads to fatty liver, obesity and diabetes.

### COMPETITIVE ADVANTAGES

- New treatment for refractory cancers.
- First inhibitors to a novel metabolic pathway highly active in cancer and immune cells, with high specificity.
- Demonstrated drug activity in monocyte-derived macrophages, melanoma, leukemia, colon and pancreatic adenocarcinomas.
- For use alone, or in combination.

### STAGE OF DEVELOPMENT

Small molecule candidates have been identified and validated in melanoma, chronic myeloid leukemia, colon and pancreatic adenocarcinomas cancer cell lines based on their ability to prevent growth on nucleotides, but not on glucose. Project currently in preclinical stage Technology Readiness Level (TLR3): 3.

### INTELLECTUAL PROPERTY

Provisional Patent application EP23165620.8.

Priority date: 30 March 2023.

Applicant: University of Lausanne.

Inventor: JOURDAIN Alexis

### KEY PUBLICATIONS:

Salvage of ribose from uridine or RNA supports glycolysis in nutrient-limited conditions, *Nature Metabolism* 2023 May;5(5):765-776.

Uridine-derived ribose fuels glucose-restricted pancreatic cancer. *Nature* (2023), 618, 151–158.

### OPPORTUNITY

PACTT is looking for development partners and offers to grant exclusive or non-exclusive license.

### REFERENCE

IDF 26-22