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ENABLING MICROSCALE RESEARCH

Inhibition of metabolic activity in acute myeloid leukemia

Real-time measurements of oxygen consumption rates in response to 2-deoxy-D-glucose treatment

The application note is based on the research and article by:

Christensen et al.

The application note is written by:

Petersen et al., Unisense

Introduction

Acute myeloid leukemia (AML) is a fast-growing cancer characterized by poorly differentiated, abnormal white blood cells. These abnormal blood cells crowd healthy blood cells causing fatigue, increased bleeding tendency, and reduced immune defense. AML is the most common type of leukemia, and it is notoriously difficult to treat due to resistance, heterogeneity and rapid progress.

"The Unisense system has been beneficial to our research by enabling measurements in demanding experimental setups and supporting the generation of high-quality data. We have also had positive experiences with their technical support, which has been both responsive and knowledgeable."

Associate Prof. Lotte Bonde Bertelsen,
MR Research Centre, Aarhus University

Abnormal blood cells in AML have altered metabolism due to the Warburg Effect, leading to elevated glucose uptake through glycolysis - even in the presence of oxygen. This metabolic phenotype makes AML a promising candidate for treatment strategies targeting glycolytic metabolic. Among the compounds investigated, 2-deoxy-D-glucose (2-DG) has attracted significant interest. 2-DG is a glucose analog taken up by glucose transporters, which are often overexpressed in cancer. Once inside the cell, 2-DG is phosphorylated by hexokinase into a metabolite that cannot be further processed, resulting in inhibited glycolytic flux, reduced ATP production, and eventually cell death.

Christensen et al. investigated 2-DG-induced metabolic shifts in cancer cells as a proof-of-concept for targeting glycolysis in leukemia. They employed biochemical assays, hyperpolarized nuclear magnetic resonance spectroscopy, and real-time measurements of cellular respiration.

Laboratory Setup

Christensen et al. assessed the effect of 2-DG on basal glycolysis, glycolytic capacity, and oxygen consumption rate using the Unisense MicroRespiration System. Cells were pre-treated with either 0, 2 or 5 mM 2-DG and subsequently resuspended in glucose and sodium pyruvate-free media. Cells were then transferred to closed Unisense MicroRespiration chambers and allowed to stabilize for 15 minutes at 37 °C before initiation of oxygen measurements (Figure 1).

Figure 1: MicroRespiration setup showing the sample chambers submerged in a water bath.

The cells were sequentially exposed to 50 mM glucose, 5 µM oligomycin, 100 mM 2-DG, and 4 µM antimycin A with 20-minute intervals between each addition. Glucose was expected to stimulate oxygen consumption, whereas oligomycin, 2-DG, and antimycin were anticipated to inhibit it. This setup enabled the researchers to monitor real-time metabolic activity during the sequential addition of metabolic inhibitors and stimulants (Figure 2).

Results and conclusion

The oxygen consumption rate was significantly reduced in cells pre-treated with 2-DG compared to untreated controls. Furthermore, glucose only stimulated oxygen consumption in untreated cells. No stimulation was observed in cells pre-treated with 2 or 5 mM 2-DG, likely due to competitive inhibition.

Subsequent addition of 2-DG further decreased oxygen consumption – most notably in cells already exposed to 2-DG. Basal glycolysis and the glycolytic capacity, measured after oligomycin-induced inhibition of oxidative phosphorylation, were also significantly diminished.

In summary, 2-DG profoundly inhibited metabolic activity and cell proliferation, underscoring its potential to enhance chemosensitivity in AML treatment.

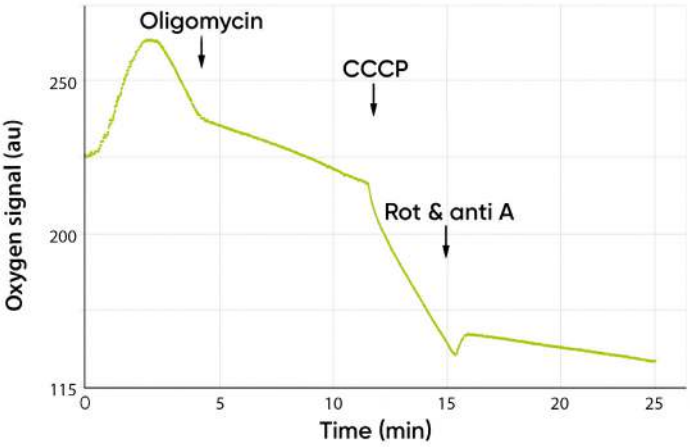

Figure 2: Oxygen consumption rate of kidney cell-line upon addition of metabolic inhibitors.

You can read more in the article by Christensen et al. "The effect of 2-Deoxy-D-glucose on glycolytic metabolism in acute myeloblastic leukemic ML-1 cells", Scientific Reports, 2025 (15:17685)

Suggested products

- O_2 Microsensor
- O_2 MicroOptode
- MicroRespiration System
- Opto UniAmp, Multichannel UniAmp
- SensorTrace Rate

Related publications

Ravera et al. "808-nm Photobiomodulation Affects the Viability of a Head and Neck Squamous Carcinoma Cellular Model Acting on Energy Metabolism and Oxidative Stress Production." Biomedicines 2021, 9, 1717.

Villa et al. "The Human Fetal and Adult Stem Cell Secretome Can Exert Cardioprotective Paracrine Effects against Cardiotoxicity and Oxidative Stress from Cancer Treatment." Cancers 2021, 13, 3729.

Bertelsen, Lotte Bonde, et al. "Renal Energy Metabolism Following Acute Dichloroacetate and 2, 4-Dinitrophenol Administration: Assessing the Cumulative Action with Hyperpolarized [1-13C] Pyruvate MRI." Tomography 4.3 (2018): 105.

Bianchi et al. "Curcumin induces a fatal energetic impairment in tumor cells in vitro and in vivo by inhibiting ATP-synthase activity." Carcinogenesis 2018, Vol 39, No. 9, 1141-1150.

Ravera et al. "Concentration-dependent metabolic effects of metformin in healthy and Fanconi anemia lymphoblast cells." J Cell Physiol. 2018; 233: 1736–1751.

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