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WEBINAR
CANCER BIOLOGY: FROM BASIC TO TRANSLATIONAL RESEARCH
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25th SEP 2020

cbma centre of molecular and environmental biology

3-bromopyruvate boosts the effect of chemotherapy in acute myeloid leukaemia by reducing cell antioxidant defence

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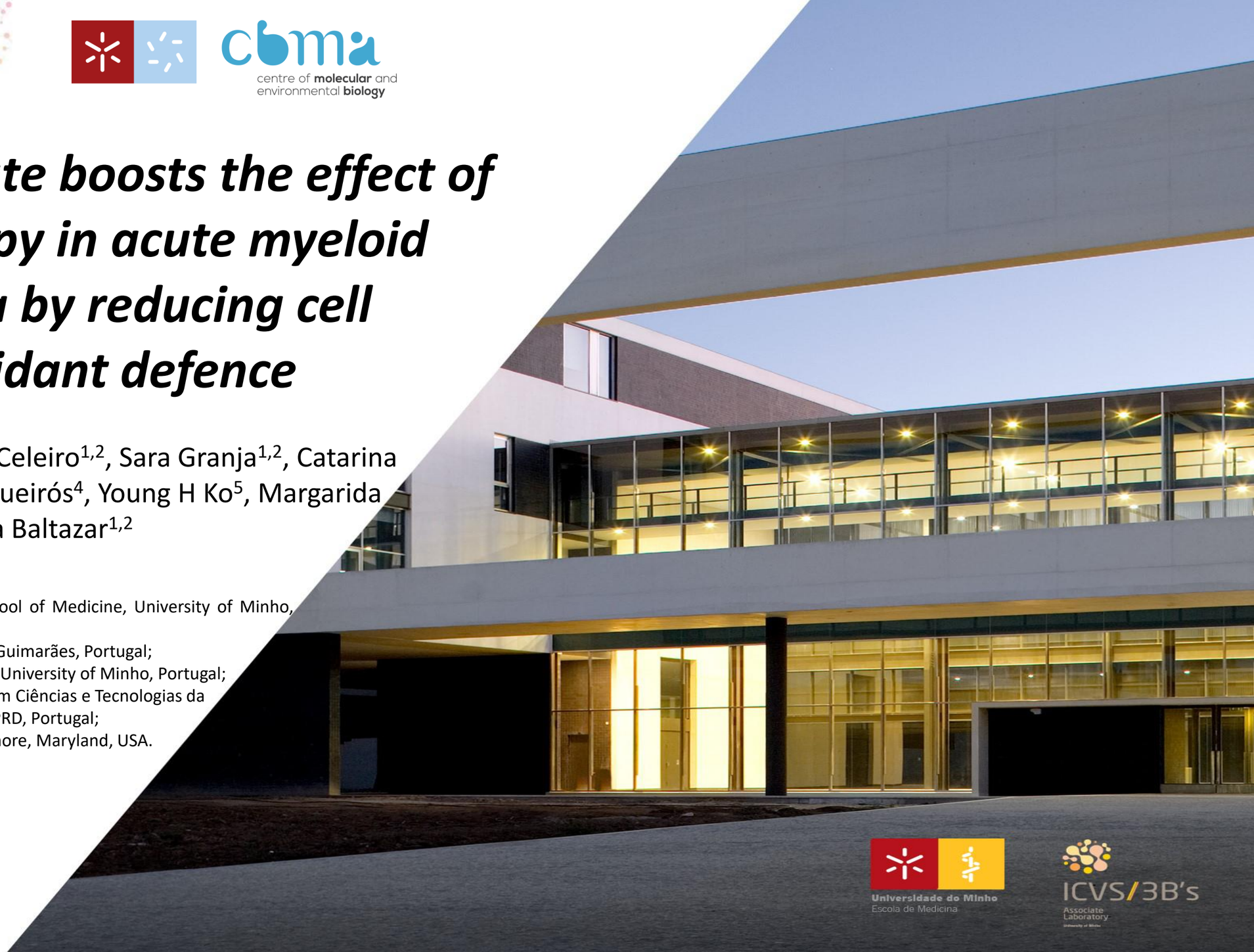

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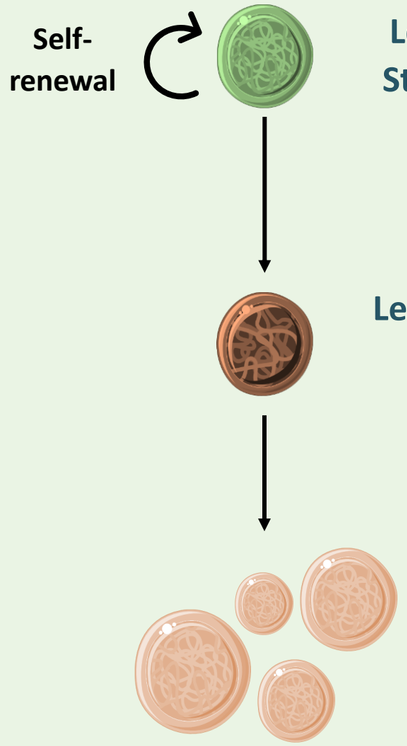
Instituto de Investigação em Ciências da Vida e Saúde

Universidade do Minho
Escola de Medicina

ICVS/3B's
Associate Laboratory

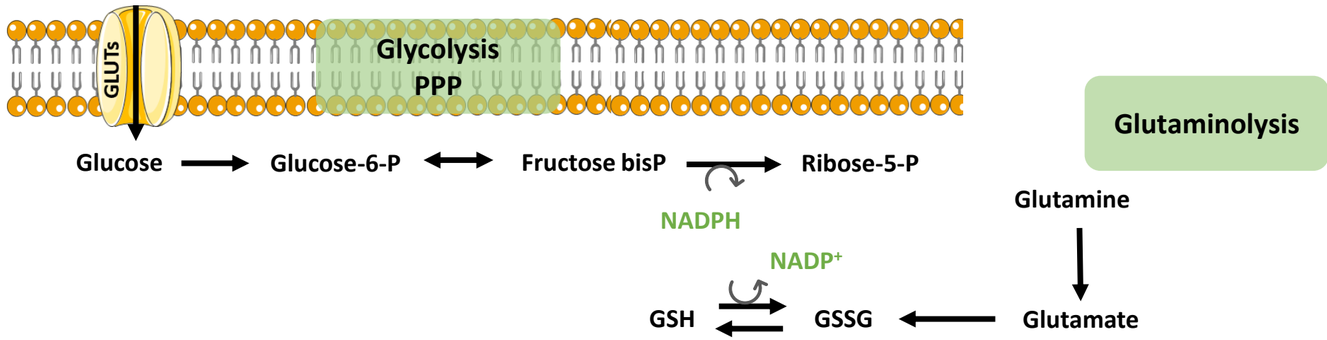
Acute Myeloid Leukemia (AML)



AML is most common type of leukemia in adults

1 in 4 adults survive longer than 5 year

Metabolism involved in chemoresistance



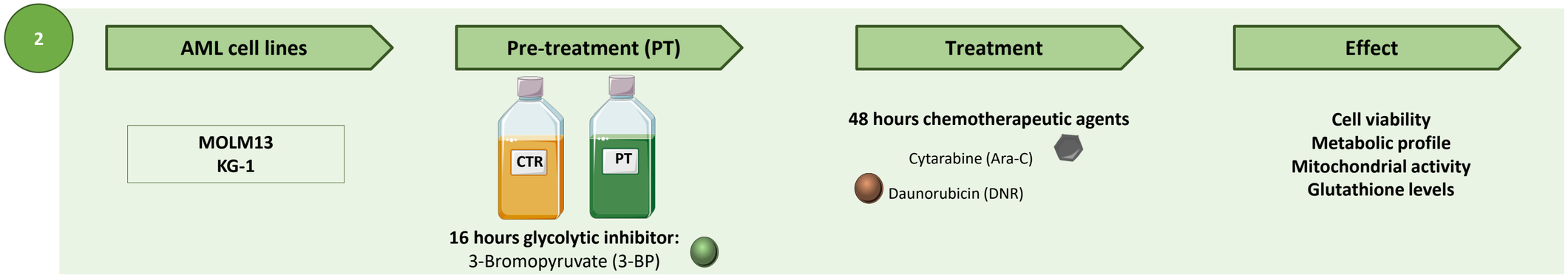
Resistance to chemotherapy is associated with altered glucose metabolism in acute myeloid leukemia

KUI SONG[1,2*], MIN LI[3*], XIAOJUN XU[2,4], LI XUAN[4], GUINIAN HUANG[4] and QIFA LIU[4]

Metabolic underpinnings of leukemia pathology and treatment

Travis Nemkov | Angelo D'Alessandro | Julie A. Reisz

AIM: Explore the metabolic inhibition as a therapeutic approach in AML in combination with classical chemotherapy regimens



3.1 5µM 3-BP sensitize AML cells to DNR and/or Ara-C

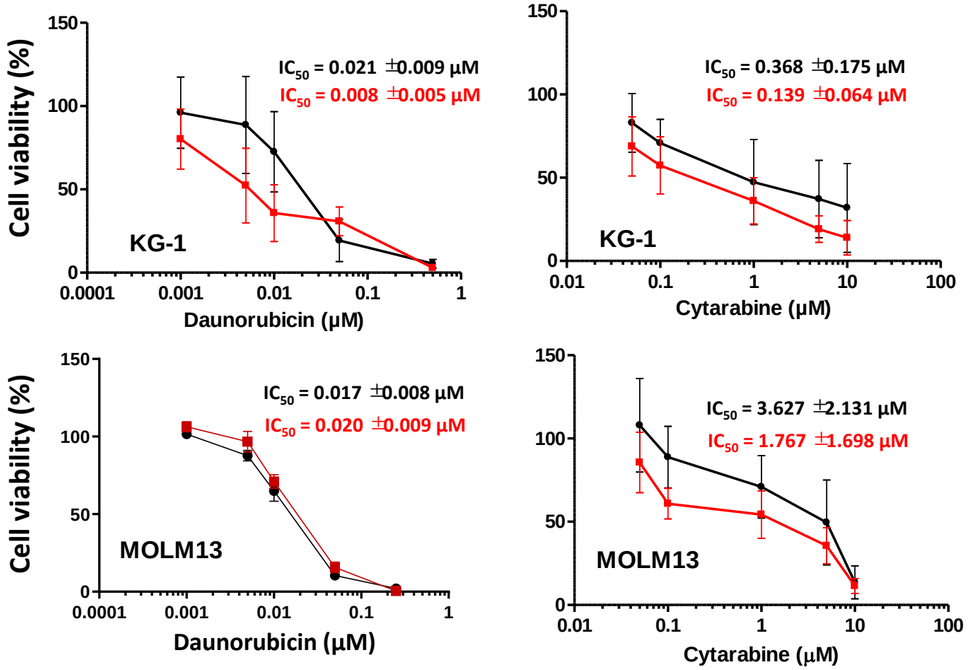


Figure 1. Effect of 3-BP pre-treatment on daunorubicin and cytarabine cytotoxicity in KG-1 and MOLM13 cells by trypan blue assay. Pre-treated with 5 µM 3-BP — Untreated

3.2 5µM 3-BP do not induce cell death or loss in viability of AML cells

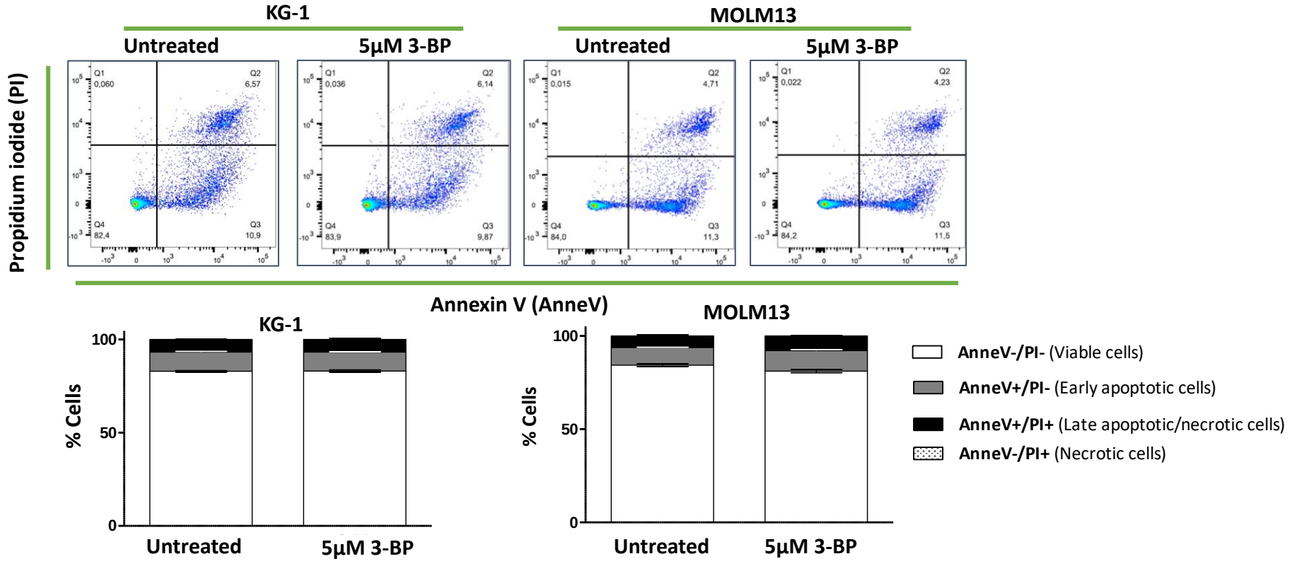


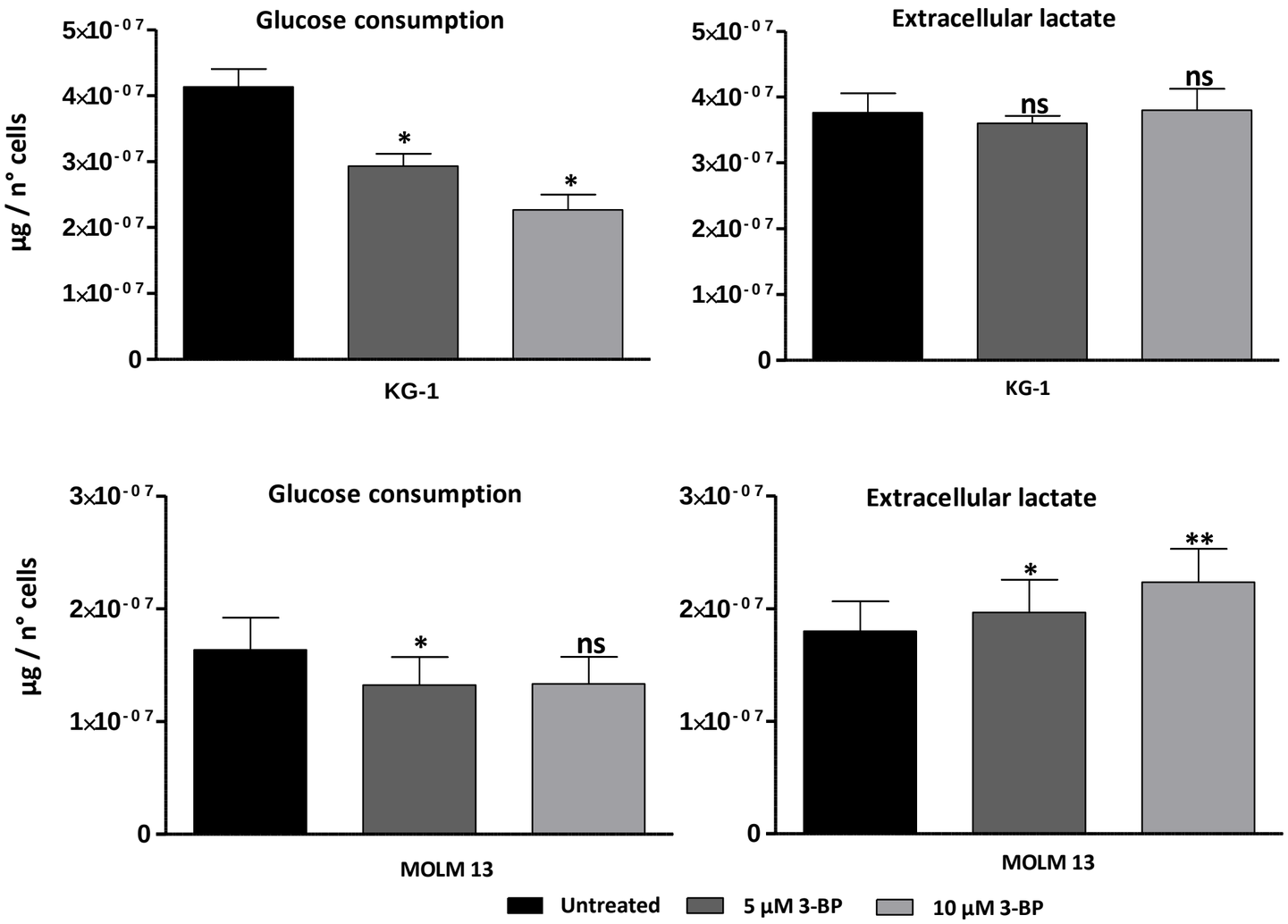
Figure 2. Characterization of apoptotic effect of 5 µM of 3-BP in AML cell lines by flow cytometry.

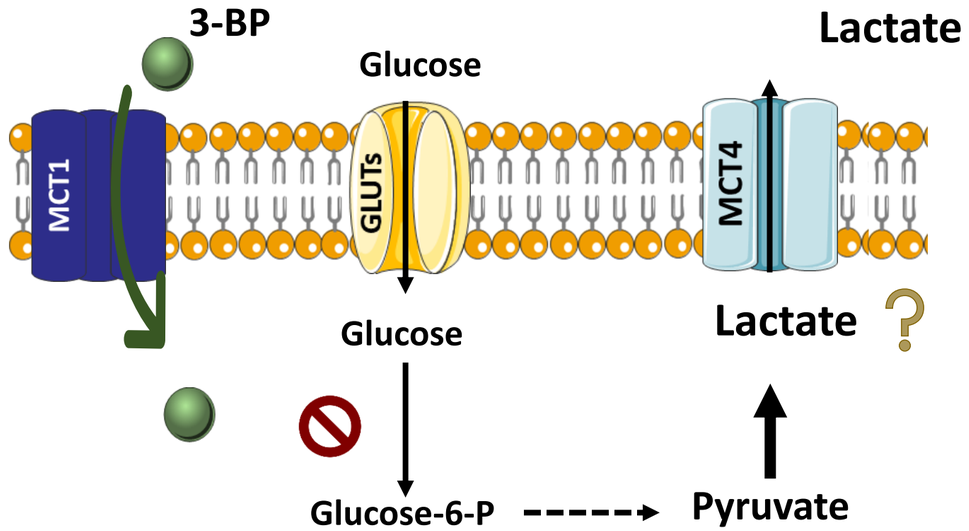
Table 1. Effect of 5 µM 3-BP on AML cell viability. MOLM13 and KG-1 cell viability was evaluated by MTS assay.

Cell line	KG-1			MOLM13		
3-BP (µM)	0	5	20	0	5	20
Cell viability (%)	100.00	109.86	38.96	100.00	146.26	70.70
± SD	4.94	8.43	22.06	7.20	23.93	14.38

3.3

5µM 3-BP decrease glucose consumption in AML cells



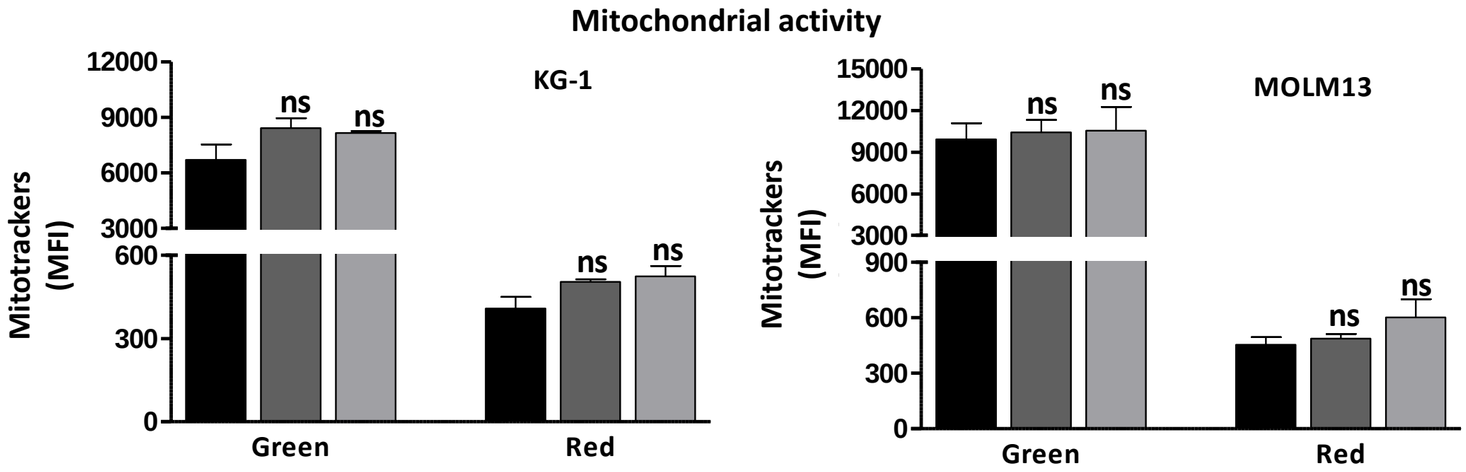


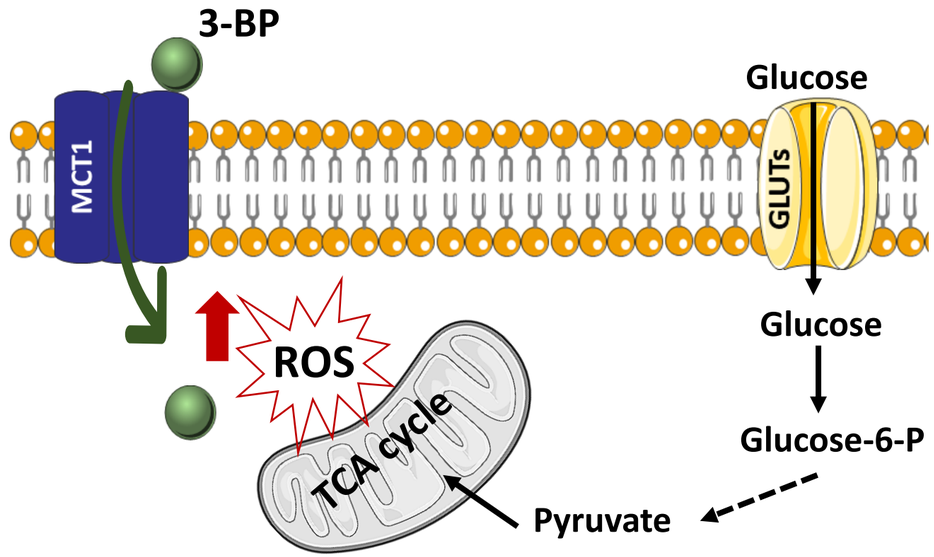
? 5µM 3-BP do not affect AML extracellular lactate levels, suggesting that non-toxic concentration of 3-BP may affect other metabolic pathway(s)

Figure 3. Characterization of 3-BP effect on AML glycolytic profile using commercial enzymatic colorimetric kits.
*p < 0.05; **p < 0.01; ns: not statistically significant

3.4

5µM 3-BP induce oxidative stress, increasing ROS levels in AML cells





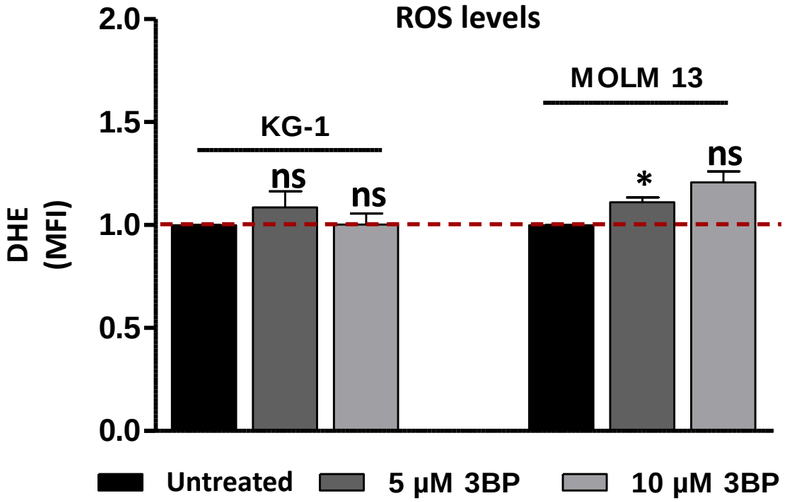


Figure 4. Characterization of mitochondrial activity and ROS levels of AML cells in the presence of 3-BP for 16 h. *p < 0.05; ns: no statistically significant.

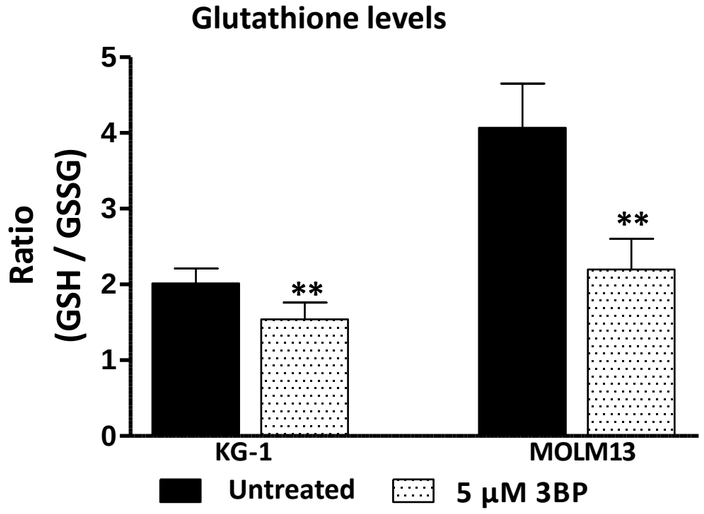
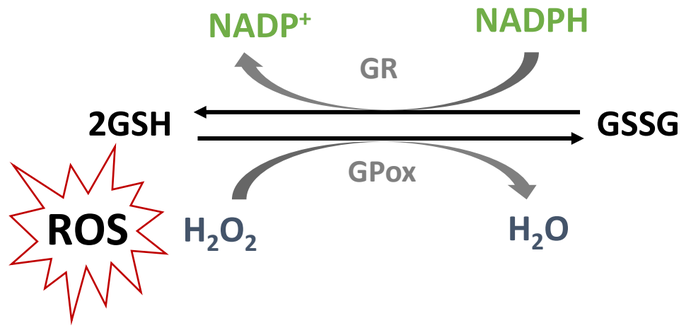


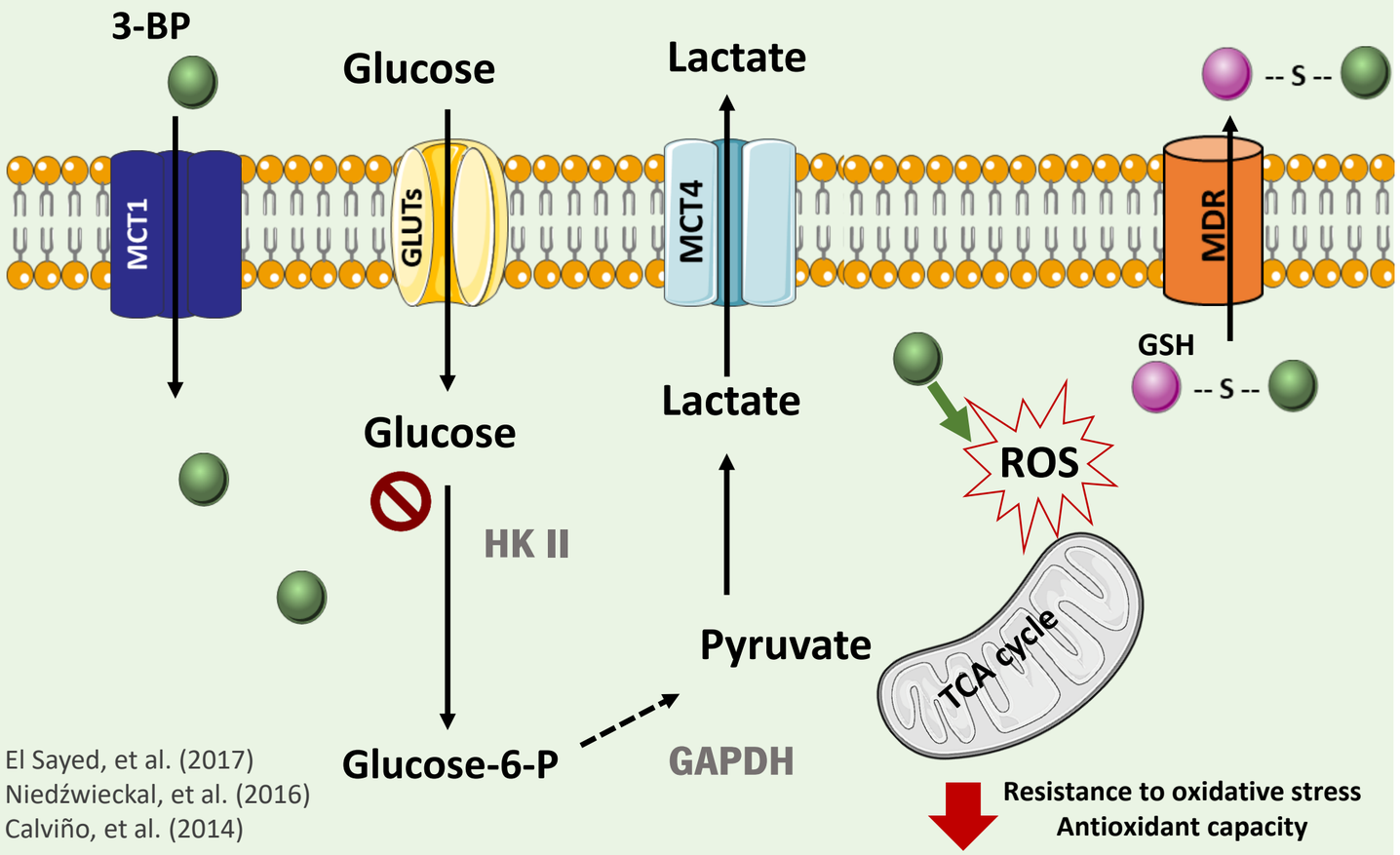
Figure 5. Characterization of 5µM of 3-BP effect on glutathione levels of MOLM13 and KG-1 cell lines. **p < 0.01.



3.5

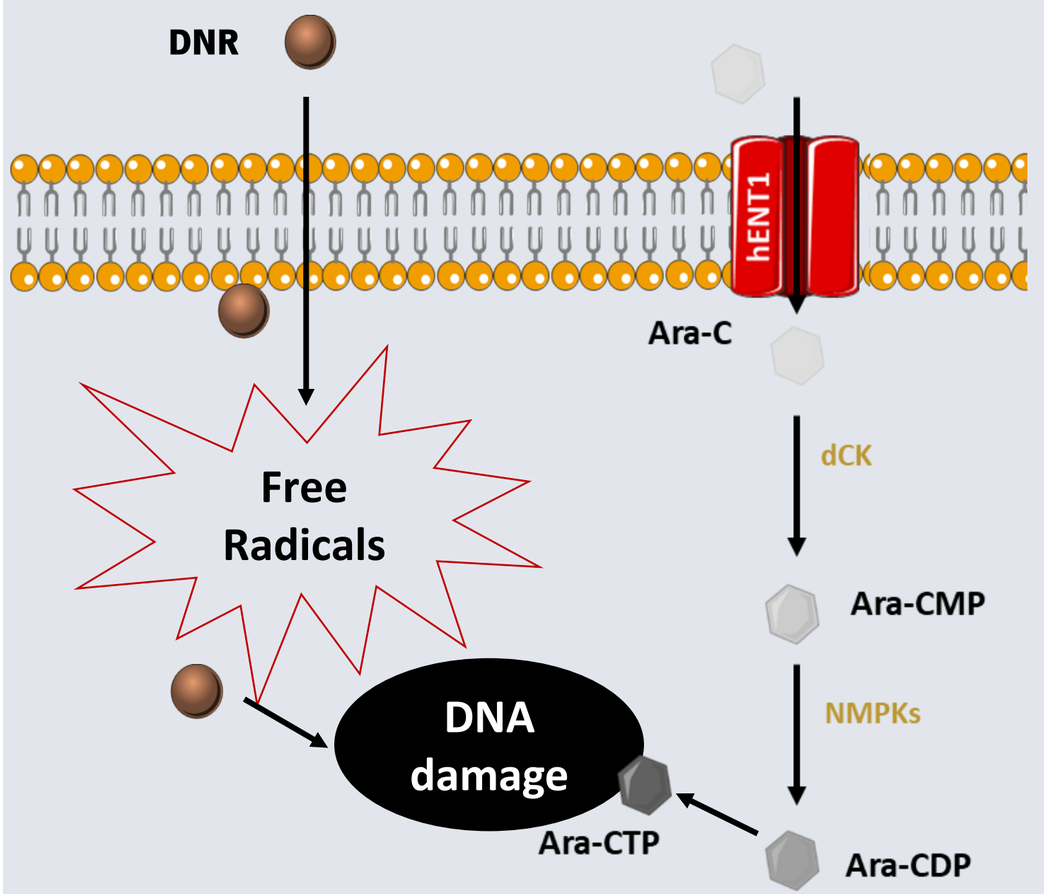
5µM 3-BP decrease the redox potential of AML cells, increasing oxidized glutathione (GSSG)

Effect of PT with 5µM 3-BP



El Sayed, et al. (2017)
Niedźwieckal, et al. (2016)
Calviño, et al. (2014)

Boost of the chemotherapy effect



Pre-treatment with a non-toxic concentration of 3-BP boosts effect of chemotherapy in AML cell lines as result of combined mechanisms

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