

LDHA and LDHB are dispensable for aerobic glycolysis in neuroblastoma cells while promoting their aggressiveness

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Ždravlević *et al.* (1) show that LDHA and LDHB are redundant in the Warburg effect. These data are in line with recent findings in neuroblastoma cells, where both LDHA and LDHB were found to be dispensable for aerobic glycolysis (2). In contrast to the results of Ždravlević *et al.*, however, concomitant depletion of LDHA and LDHB in neuroblastoma cells did not abrogate the Warburg effect. Also in contrast, depletion of either LDHA or LDHB in neuroblastoma cells decreased their aggressiveness, showing that LDHA and LDHB can have cancer-promoting effects independent of aerobic glycolysis. Along this line, LDHA expression was shown to be an independent prognostic marker in neuroblastoma patients. While the contrasting findings may be explained in part by cell type-specific

differences in the function of LDHA and LDHB, or by methodological differences, both papers question a nonredundant role of LDHA in aerobic glycolysis and delineate the limitations of therapeutically targeting the Warburg effect in general, and LDHA and LDHB in particular.

References

1. Ždravlević, M., Brand, A., Di Ianni, L., Dettmer, K., Reinders, J., Singer, K., Peter, K., Schnell, A., Bruss, C., Decking, S. M., Koehl, G., Felipe-Abrio, B., Durivault, J., Bayer, P., Evangelista, M., O'Brien, T., Oefner, P. J., Renner, K., Pouyssegur, J., and Kreutz, M. (2018) Double genetic disruption of lactate dehydrogenases A and B is required to ablate the "Warburg effect" restricting tumor growth to oxidative metabolism. *J. Biol. Chem.* **293**, 15947–15961 [CrossRef Medline](#)
2. Dorneburg, C., Fischer, M., Barth, T. F. E., Mueller-Klieser, W., Hero, B., Gecht, J., Carter, D. R., de Preter, K., Mayer, B., Christner, L., Speleman, F., Marshall, G. M., Debatin, K. M., and Beltinger, C. (2018) LDHA in neuroblastoma is associated with poor outcome and its depletion decreases neuroblastoma growth independent of aerobic glycolysis. *Clin. Cancer Res.* **24**, 5772–5783 [CrossRef Medline](#)

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