Sensitivity of polyamine metabolism to glucose deprivation is increased in neuroblastoma cells with N-myc amplification

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Ornithine-derived polyamines are essential for cell proliferation, and their levels are elevated in many human tumors. Neuroblastoma, the most frequent extra-cranial solid tumor in children, harbors amplification of *n-myc* oncogene (which enhances polyamine metabolism) in 25% of the cases. In the present communication, the relevance of *n-myc* amplification in several metabolic features of human neuroblastoma cell lines is studied. A previously unknown linkage between glycolysis impairment and polyamine reduction, related to *n-myc* amplification, is unveiled. Results show that glycolysis inhibition is able to trigger signaling events leading to the reduction of N-Myc protein levels and subsequent decrease of both ornithine decarboxylase expression and polyamine levels, accompanied by cell cycle blockade preceding cell death. Metabolism-targeted therapies are emerging as new approaches for cancer treatment. New anti-tumor strategies could take advantage of the direct relationship between glucose deprivation and PA metabolism impairment leading to cell death described in the present work, and its apparent dependence on *n-myc* amplification in the case of neuroblastoma. Combined therapies targeting glucose metabolism and polyamine synthesis could be effective in the treatment of *n-myc* amplified tumors.

[This work has been funded by Grants SAF2011-26518 (Ministerio de Economía y Competitividad, Spain), Excellence Projects CTS-1507 and CVI-06585 (Junta de Andalucía, Spain) and BIO-267 (fondos PAIDI, Junta de Andalucía, Spain). MVRP was the recipient of a FPU long-term fellowship (Ministerio de Educación, Cultura y Deporte, Spain) and a “III Plan Propio de Investigación” short-term fellowship (University of Málaga). CIBERER is an initiative of Instituto de Salud Carlos III. This communication has the support of a travel grant "Universidad de Málaga. Campus de Excelencia Internacional Andalucía Tech". We want to thank Dr Esther Melgarejo-Páez for her assistance with real-time PCR and Dr. Tuomo Keinänen and the technician Anne Karppinen for helping MVRP during ODC activity measurements].