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L-glutamate delays aspirin-induced apoptosis of redox-compromised yeast cells by restoring the GSH/GSSG ratio and the mitochondrial respiratory rate

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Introduction: We showed that aspirin induces apoptosis in *Saccharomyces cerevisiae* EG110 cells deficient in manganese superoxide dismutase (MnSOD) cultivated in ethanol medium, but not in wild-type EG103 cells. Our microarray study revealed an aspirin-induced downregulation of *SNO1* and *SNZ1* in the mutant strain. Together, these genes encode a glutamine amidotransferase complex that produces glutamate: a key metabolite involved in synthesising the antioxidant glutathione (GSH) and the tricarboxylic acid (TCA) cycle intermediate, α-ketoglutarate.

Methods: Upon confirmation of gene expression by RT-qPCR, the growth of aspirin-treated EG110 cells supplemented with L-glutamate was monitored via optical density measurements (OD600). The effect of glutamate was confirmed by viability studies, based on colony forming units (CFUs) and flow-cytometric analysis. Further experiments involved the measurement of intracellular GSH and GSSG levels, as well as respirometry measurements.

Results: We observed that aspirin-induced apoptosis of EG110 cells is significantly delayed by the addition of 200mM L-glutamate. Furthermore, we show that this rescuing effect is due to a restored GSH/GSSG ratio, as well as a restored mitochondrial respiratory rate.

Conclusion: The influence of aspirin on glutamate metabolism in our redox-compromised cells, suggests that their death is preceded by redox imbalance, as shown by a lowered GSH/GSSG ratio and oxidative stress accompanied by decreased respiratory rate. Rescuing by exogenous glutamate is likely mediated by increased synthesis of cellular GSH and the anaplerotic supply of α -ketoglutarate to the TCA cycle. This aspirin-induced effect on glutamate metabolism may help us better understand the antineoplastic effect of aspirin on early-stage cancer cells which are also redox-compromised.

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Tracing Maltese genetic origins

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Introduction: Malta has a rich demographic history. Historical records trace population origins to the Temple people. However, contemporary Maltese are descendants from those who re-populated the islands at the turn of the first millennium AD.

Methods: Maltese mitochondrial DNA (mtDNA) and Y chromosome data are not publicly available. High-quality datasets were generated to evaluate Maltese lineages: mtDNA control region (CR) and Y-STR chromosome markers. A total of 798 samples were collected randomly Maltese mitochondrial DNA (mtDNA) and Y chromosome data are not publicly available. High-quality datasets were generated to evaluate Maltese lineages: mtDNA control region (CR) and Y-STR chromosome markers. A total of 798 samples were collected randomly with associated ancestry data from Malta and Gozo. The dataset is archived in the Malta BioBank (BBMRI.mt). The EMPOP protocol was used to amplify and sequence a subset of 300 samples with a minimum of four EMPOP sequencing primers. mtDNA haplotypes were checked on EMPOP and Phylotree and haplogroup frequencies were calculated. The PowerPlex® Y23 system was used to analyse 400 unrelated males. NevGen was used to predict Y-STR haplogroups. SNP analysis by HRM was used to confirm Y haplogroups.

Results: The major Maltese mtDNAs and Y haplogroups could be attributed to West Eurasian haplogroups. mtDNA: H (35%), T (18%), K (12%), J (5%), U (5%), X (1%), W (1%); predicted Y chromosome clades: R1 (29%), J2 (22%), E1b1b (12%), G (12%), and I (10%). African mtDNA lineages were also present: L1 (0.4%), L2 (10%), L3 (1%), M1 (0.4%).

Conclusion: The genetic profile obtained from the population of Malta and Gozo provides a first insight into the origins of the Maltese. The datasets can be used as the first national reference database for mtDNA and Y chromosome applications in forensic and population genetic studies.

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