Cancer cells convert glucose preferentially to lactate even in the presence of oxygen (aerobic glycolysis-Warburg effect). New concepts in cancer treatment aim at inhibition of aerobic glycolysis. Pyruvate dehydrogenase converts pyruvate to acetylCoA thus preventing lactate formation. Therefore, the aim of this study was to evaluate compounds that could activate pyruvate dehydrogenase in cancer cells. We investigated the effects of (R)-(+-)-?-lipoic acid (LPA) and dichloroacetate (DCA), possible activators of pyruvate dehydrogenase, on suppression of aerobic glycolysis and induction of cell death. The neuroblastoma cell lines Kelly, SK-N-SH, Neuro-2a and the breast cancer cell line SkBr3 were incubated with different concentrations (0.1-30 mM) of LPA and DCA. The effects of both compounds on cell viability/proliferation (WST-1 assay), [18F]-FDG uptake, lactate production and induction of apoptosis (flow cytometric detection of caspase-3) were evaluated. Furthermore, NMRI nu/nu mice that had been inoculated s.c. with SkBr3 cells were treated daily for four weeks with LPA (i.p., 18.5 mg/kg) starting at day 7 p.i.. Tumor development was measured with a sliding caliper and monitored via [18F]-FDG-PET. Residual tumors after therapy were examined histopathologically. These data suggests that LPA can reduce (1) cell viability/proliferation, (2) uptake of [18F]-FDG and (3) lactate production.
and increase apoptosis in all investigated cell lines. In contrast, DCA was almost ineffective. In the mouse xenograft model with s.c. SkBr3 cells, daily treatment with LPA retarded tumor progression. Therefore, LPA seems to be a promising compound for cancer treatment.