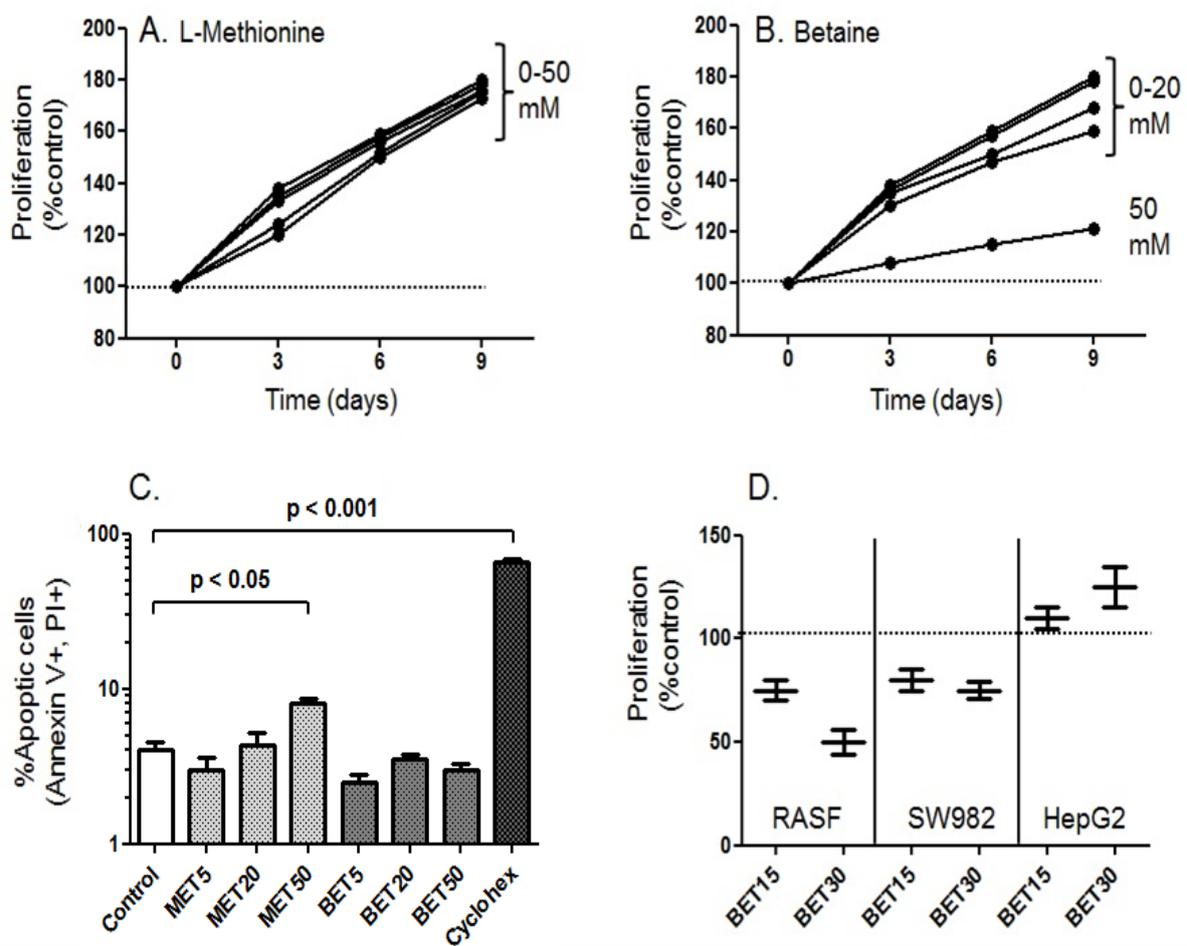
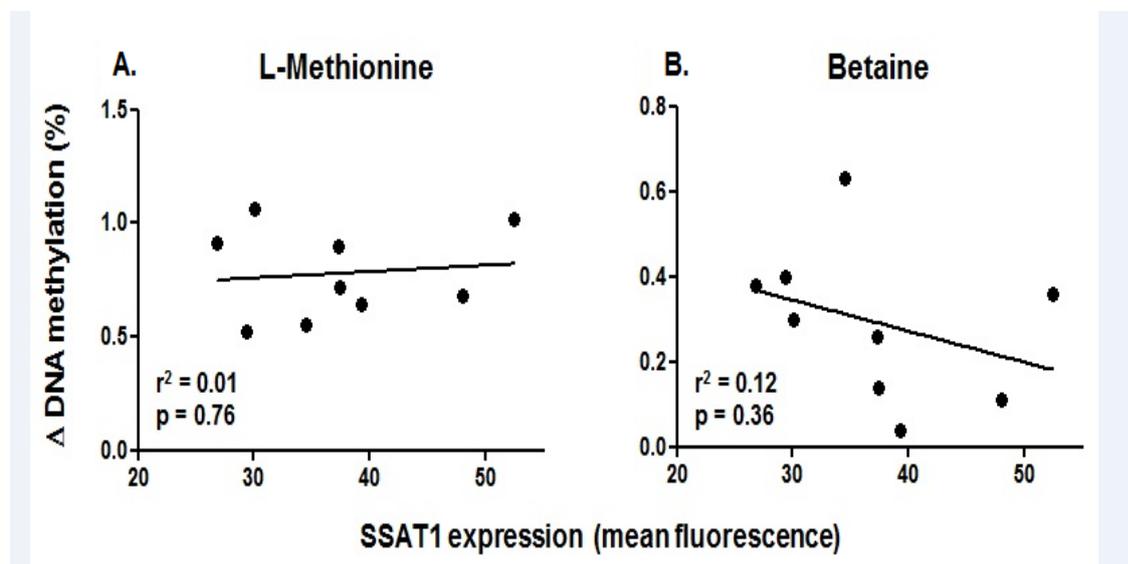


Supplementary Figures

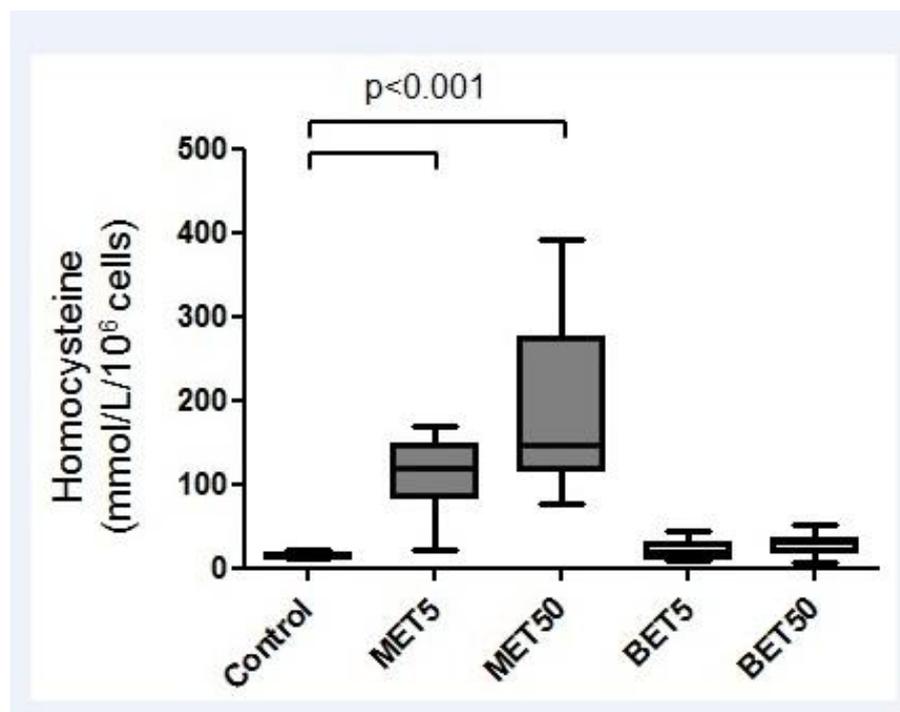
Supplementary Figure 1. A-B. Proliferation time-course (days 0-9) of RASF in presence of increasing doses of L-methionine (A.) or betaine (B.). The highest concentration of betaine appeared cytostatic. **C.** Late apoptotic RASF (i.e., annexin V+, propidium iodide+) within 3 days in presence of L-methionine (MET5, 20, 50: 5 to 50 mM) or betaine (BET5, 20, 50: 5 to 50 mM) (mean \pm standard deviation, $n = 5$ RASF). For comparison, apoptosis obtained within 24 hours upon 5 μ M cycloheximide (mean \pm standard deviation of 3 independent experiments). The highest dose of L-methionine triggers apoptosis in a few cells, but this was not the case for betaine (log scale). Statistics: Wilcoxon signed rank tests. **D.** Comparison in the proliferation of RASF within 9 days (mean \pm standard deviation, $n = 6$), SW982 sarcoma cells and HepG2 cells within 3 days (mean \pm standard deviation of 3 independent experiments) in presence of betaine (BET15, 15mM, and BET30, 30mM).



Supplementary Figure 2. A-B. In RASF, the increases in DNA methylation occurring upon treatment with L-methionine or betaine are not significantly associated with changes in SSAT1 protein expression (measured by flow cytometry in permeabilized cells). Statistics: Spearman's rank correlation coefficient.



Supplementary Figure 3. A-B. Comparison between SSAT1 levels determined by flow cytometry and ELISA (A.), as well as by a SSAT1 activity assay in RASF (n = 9). **C.** SSAT1 ex vivo enzyme kinetic according to a Lineweaver-Burk double reciprocal plot; compared were 3 protein extracts from OASF (pooled) to 3 protein extracts from RASF (separate). Compared with OASF, the activity of SSAT1 in RASF appears limited by competitive and/or mixed intracellular inhibitions.



Supplementary Figure 4. Dose-dependent and highly significant ($p < 0.001$) increase of homocysteine released in the cell culture supernatant in presence of L-methionine (MET5, 5mM, and MET50, 50 nM). In comparison, betaine did not increase homocysteine levels (BET5, 5mM, and BET50, 50 mM). Statistics: Wilcoxon signed rank test.

