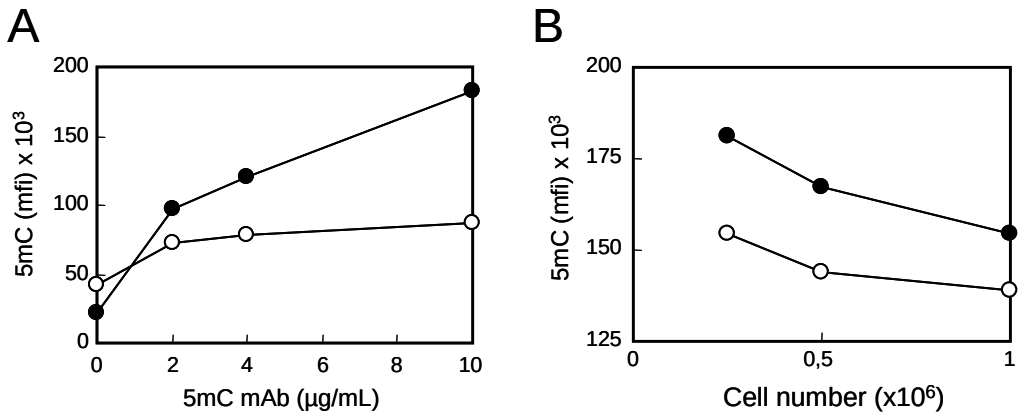
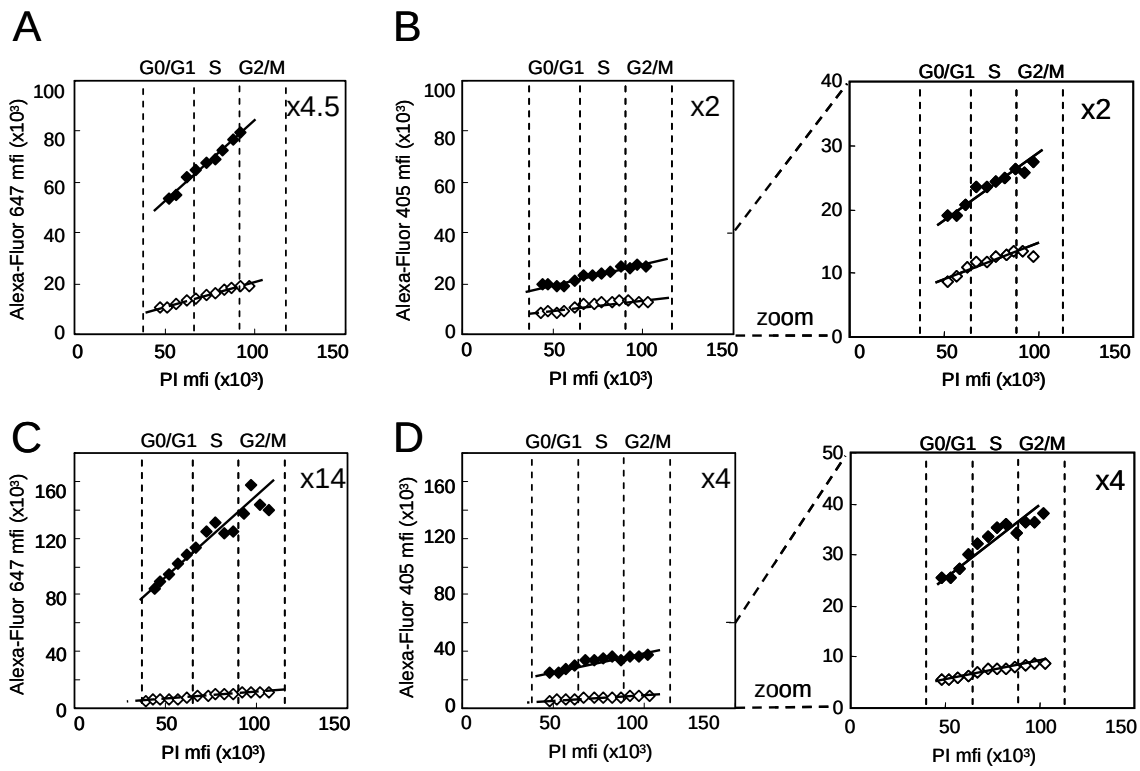
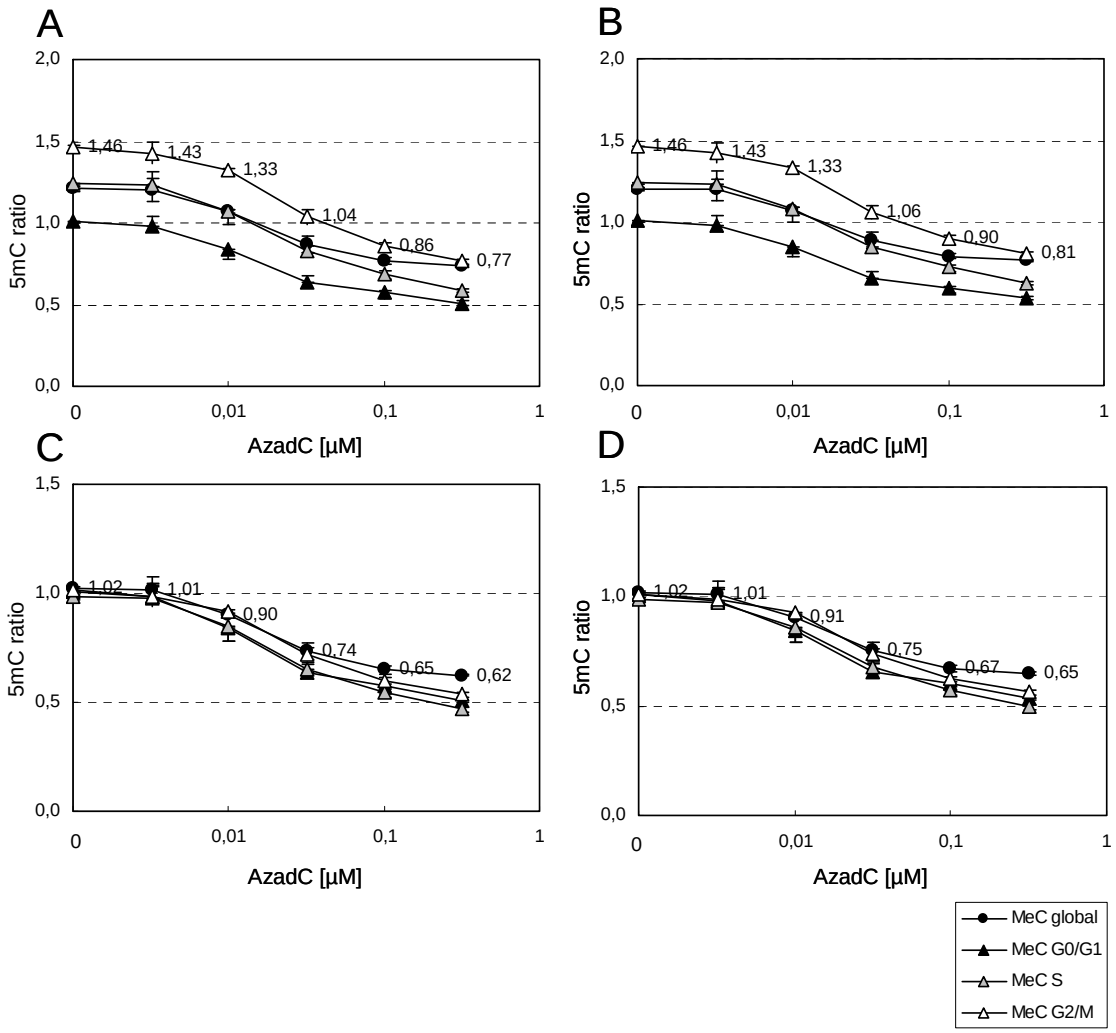


Supplementary Figure S1. Analysis of the 5-methylcytosine (5mC) content in WM266-4 cells by flow cytometry.

A. The 5mC labeling intensity was measured on cells treated 30 min with 2 N HCl either at 37°C (closed symbols) or at room temperature (open symbols), prior labeling with increasing concentrations of anti-5mC antibody.
B. The 5mC labeling intensity was measured on increasing numbers of cells with 10 µg/mL of 5mC antibody.



Supplementary Figure S2. FACS analysis of 5mC labeling in WM266-4 cells and KG1 cells using a secondary antibody coupled to Alexa-Fluor 647 and Alexa-Fluor 405.
WM266-4 melanoma cells ($1x10^6$ cells) (A, B) and KG1 leukemia cells ($0.5x10^6$ cells) (C, D) were labeled with the anti-5mC monoclonal antibody, then with a secondary antibody coupled to Alexa-Fluor 647 (A,C) or Alexa-Fluor 405 (B,D) prior to DNA staining with propidium iodide (PI). Flow cytometry analysis was performed with the corresponding PMTs set-up in order to obtain similar means of fluorescence intensities(mfis) for both isotypic controls. As in figure 1F, graphs report the mfi of labeling according to PI contents of cells (R2) included in contiguous regions of 5x1000 mfi units on the PI scale.
Close symbols are for labeling with the anti-5mC antibody. Open symbols are for isotypic controls. The reported values indicate the ratio between mfis obtained from the anti-5mC labeling and the corresponding isotypic control.



Supplementary Figure S3. Comparison of FACS data normalization methods.
Raw data from main figure 4D (KG1 cells) were either corrected by subtracting the isotypic control values (A, C) or divided by the isotypic control values (B, D). In order to calculate the variations induced by the treatment, these corrected values were reported to the value calculated for the G0/G1 cells in the non-treated sample (A, B). This allows to distinguish the different cell cycle phases by their relative methylation level. Alternatively, the corrected values were reported to the value calculated in their corresponding cell cycle phase in the non-treated sample (C, D).