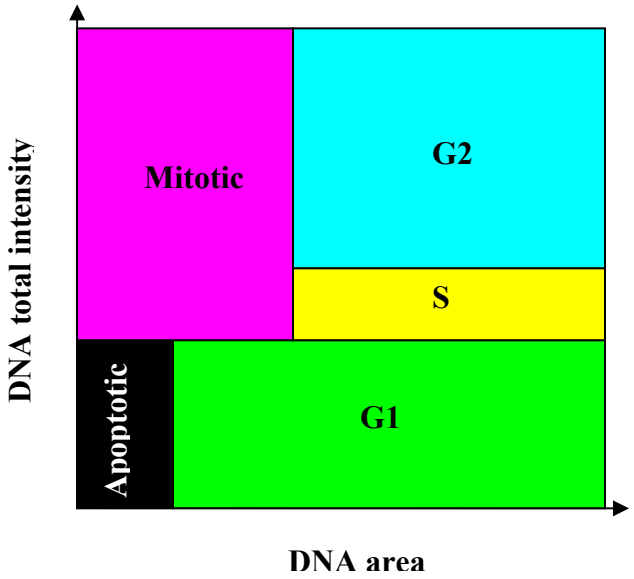
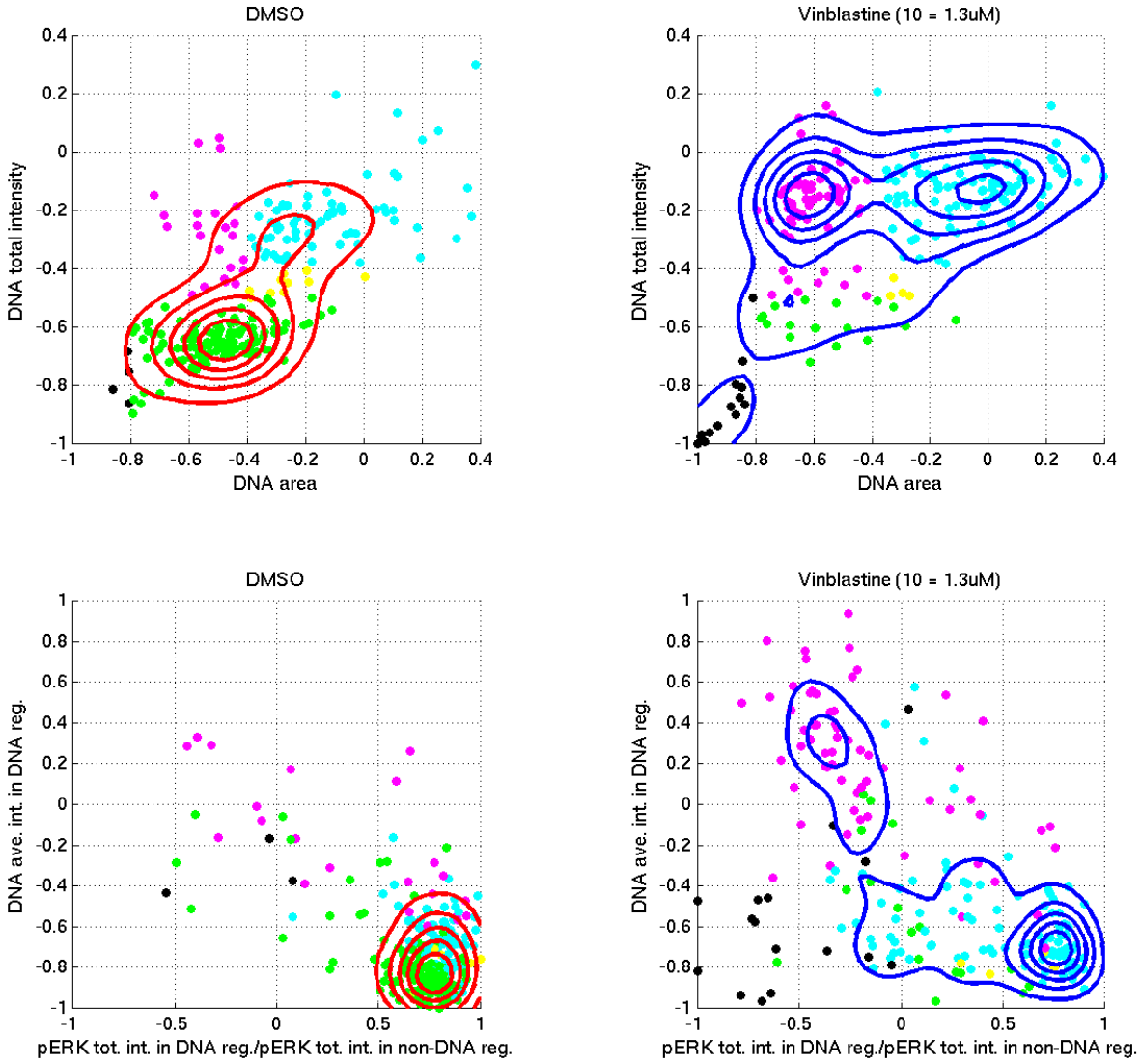
Supplementary Figure 3: Some of the common phenotypic changes are cell-cycle independent

a) Cell cycle detector

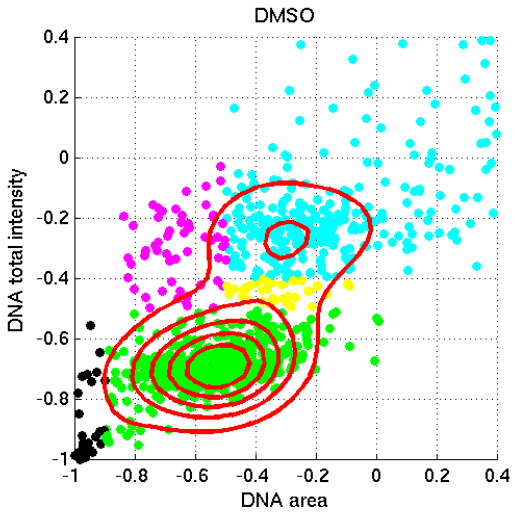


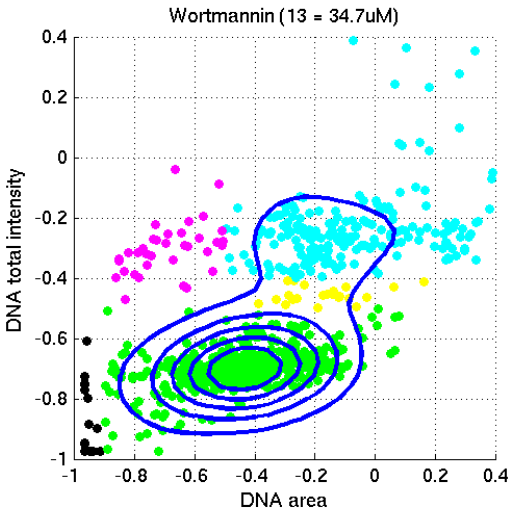
Supplementary Figure 3 (cont.)
b) Vinblastine

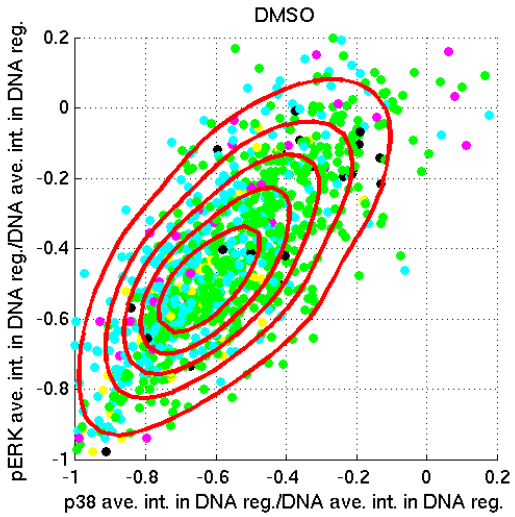


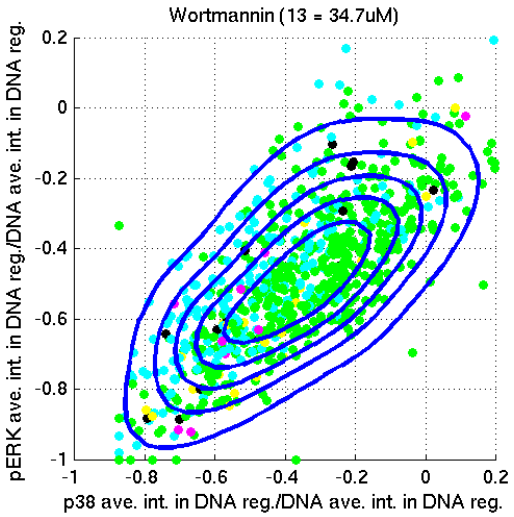
Supplementary Figure 3 (cont.)

c) Wortmanin









Supplementary Figure 3 (cont.)

Supplementary Figure 3: Some of the common phenotypic changes are cell-cycle independent

A simple cell cycle detector was implemented to examine if the common phenotypic changes detected by our approach were related to changes in cell cycle phase. **a)** The cell cycle detector had as input two cell cycle related features: the DNA total intensity and DNA area. The domain of these two features was heuristically divided into 5 regions according to 5 cellular states: apoptotic (black, lower left), G1 (green, lower right), S (yellow, middle right), G2 (light blue, upper right), and mitotic (cyan, upper left). **b-c)** For a selected compound, the thresholds for the divisions were determined from the control population (upper left panel), which shows a 2-dimensional, bi-modal empirical probability distribution (red contour lines). The same threshold was used for the treated population (upper right panel, blue contour lines: empirical distribution for the treated population). After every cell on the control and treated populations was assigned to a cellular state based on its location in the feature space, the control and treated populations were plotted using the two most discriminative features selected by our approach (**Common phenotypic change detection** in main text) for the compound's category (lower panels, red contour lines: the control empirical distribution, blue contour lines: the treated empirical distribution). By comparing the two plots, we could examine how the distribution of the population was changed in response to the compound perturbation. Furthermore, by comparing the changes detected by the two most discriminative features to the changes detected by the cell cycle features, we could find out the correlation between the most discriminative features and the cell cycle features. Examples were provided for **b)** vinblastine (cell-cycle dependent), and **c)** wortmannin (cell-cycle independent) on the DNA-pp38-pERK marker set.