SUPPLEMENTARY INFORMATION
MATERIALS AND METHODS

Bioinformatic analysis. Microarray data analysis was performed using GeneSpring v7.1 (Agilent Technologies UK Limited, Stockport, UK). For both 5-FU and oxaliplatin, two independent experiments were created. Firstly, to analyse drug-inducible gene expression in HCT116 parental cells, all genes on each array were normalised to the median signal intensity of that array. Secondly, each gene on the 6, 12 and 24h sample arrays was normalised to the median signal intensity of the respective gene on the 0h (control) array. The GeneSpring Cross Gene Error Model was then applied to the experiment, with the average base/proportional values calculated from the replicated conditions of the experiment. Genes were filtered using three parameters. Firstly, all genes that displayed an Affymetrix present or marginal flag call in all samples were retained. The gene list was subsequently filtered using the average base/proportional values calculated from the cross gene error model, with genes displaying control values greater than the average base/proportional value being retained (this was required in all samples for any gene). Finally, the list was filtered using a 2-fold cut-off for each gene relative to the 0h control, with genes meeting this criterion in at least 1 of the 3 timepoints being retained. The genes passing these 3 filters were considered to be drug-inducible.

The second experiment created aimed to compare basal gene expression in the HCT116 parental cell line relative to both the 5-FU- and oxaliplatin-resistant daughter lines. As described above, all genes on each array were initially normalised to the median signal intensity of that array. Each gene was then normalised to the median signal intensity of the respective gene on all arrays. The data was filtered as described
above with genes required to demonstrate a 2-fold up- or down regulation in the resistant cell line relative to the parental line. The resultant lists of genes were considered transcriptionally dysregulated in drug-resistant cells relative to parental cells.

In order to generate a list of genes which were both constitutively dysregulated in the drug-resistant cell lines and induced or repressed in the parental cell line following acute exposure to chemotherapy, the two gene lists described above were combined using the Venn diagram functionality in GeneSpring. The genes that were common to both lists and appeared in the intersection of the diagram were subsequently retained.