ADDENDUM

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Addendum: The Cancer Cell Line Encyclopedia enables predictive modelling of anticancer drug sensitivity

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In the Supplementary Information of this Letter, the use of distinct data normalization and directionality methods for pharmacological response calculations caused minor inconsistencies. We have therefore updated Supplementary Table 11 and some of the Supplementary Figures to resolve any confusion (see the Supplementary Information to this Addendum). We also wish to describe the relevant drug sensitivity normalization and response score calculations more completely.

Two versions of the drug response data were generated. First, raw activity values were calculated at each dose as $A = 100(T/U - 1)$, in which T represents the Cell Titer Glo (CTG) level measured for the compound-treated well, and U is the median level of the untreated wells across the plate. This raw A is 0% with no drug and 100% for fully active compounds, when no CTG is detected. Second, the data were adjusted to a plate surface pattern and normalized to the MG132 positive control, as described in the Supplementary Methods. This normalized A is also 0% with no drug, but 100% corresponds to the median MG132 response on that plate. Although normalized drug responses were used to determine EC_{50}, IC_{50} and A_{max} values, we used the raw drug responses for calculating the activity area (AA). This distinction is now clear in the corrected Supplementary Table 11 (the two AA measures, derived from raw or normalized data, correlate closely: $r = 0.98$).

The activity is the sum of differences between the measured A_i at concentration i and $A = 0$, excluding positive A values: $AA = \sum i\{0 - \min(0, A_i/100)\}$. This AA has a value of 0 with no drug, and +8 for a compound inhibiting at $A = 100\%$ at all eight drug concentrations, as illustrated in Fig. 2b of the original Letter. We hope that this definition eliminates any confusion that may have existed in the original Supplementary Methods (page 13) and enables others to reproduce our AA results starting from the raw drug sensitivity data. As a further means of clarification, we have added three columns to Supplementary Table 11 showing the raw (non-normalized) response data necessary to calculate AA, MG132 activity, and AA derived from normalized response data.

In addition, although all computational analyses used the above AA formula, a few Supplementary Figures (Supplementary Figs 6, 11, 9 and 14b) used a scale showing 8 − AA. This value was used for display purposes, so that low values corresponded to sensitive cell lines and the visualization remained consistent with other sensitivity metrics (IC_{50}, A_{max}). This specification was noted in Supplementary Fig. 8 but had been inadvertently cut off the Supplementary Fig. 9 legend. We have therefore updated the Supplementary Fig. 9 legend to clarify where an inverted scale was used, and updated the scale of Supplementary Figs 6, 11 and 14b to reflect our definition of AA (noted above).

These changes do not affect the analyses, results or scientific conclusions presented in the paper. The authors are indebted to B. Yadav, who alerted them to these inconsistencies.

Supplementary Information is available in the online version of the Addendum.