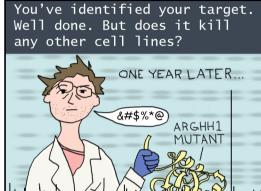
Correlating chemical sensitivity and basal gene expression reveals mechanism of action

Matthew G. Rees, Brinton Seashore-Ludlow, Jaime H. Cheah, Drew J. Adams, Edmund V. Price, Shubhroz Gill, Sarah Javaid, Matthew E. Coletti, Victor L Jones, Nicole E. Bodycombe, Christian K. Soule, Benjamin Alexander, Ava Li, Philip Montgomery, Joanne D. Kotz, C Suk-Yee Hon, Benito Munoz, Ted Liefeld, Vlado Dančík, Daniel A. Haber, Clary B Clish, Joshua A. Bittker, Michelle Palmer, Bridget K Wagner, Paul A. Clemons, Alykhan F Shamji & Stuart L Schreiber Nat Chem Biol. 2016 Feb;12(2):109-16. doi: 10.1038/nchembio.1986. Epub 2015 Dec 14.

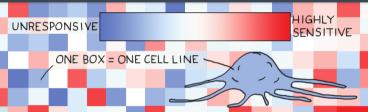
The scenario below is completely fictional but highlights real strategies including the one introduced in this paper.







Why don't you try giving the compound to 823 different cancer cell lines from various lineages (ie. skin, lung, etc.) and figure out how sensitive each one is. May help predict patient response.

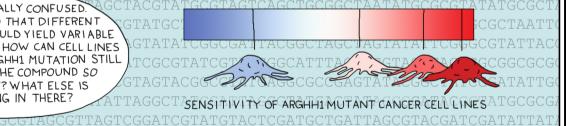


OKAY, SO LUNG CANCER CELLS ARE PARTICULARLY SENSITIVE. BUT WHY IS THERE SO MUCH VARIABILITY?



Thanks to some massive parallel sequencing efforts there is a lot of sequence information on these cell lines. You could narrow down to cell lines with genetic variants of ARGHH1.





What if you could correlate the sensitivity of these cancer cell lines with up or down-regulation of particular genes? Not as a *result* of treatment, I'm talking about *basal* transcription levels. If a gene's expression correlates to sensitivity, it may play a role in drug's mechanism of action.

