

CORRECTION

Correction: Combined MEK and ERK inhibition overcomes therapy-mediated pathway reactivation in *RAS* mutant tumors

Mark Merchant, John Moffat, Gabriele Schaefer, Jocelyn Chan, Xi Wang, Christine Orr, Jason Cheng, Thomas Hunsaker, Lily Shao, Stephanie J. Wang, Marie-Claire Wagle, Eva Lin, Peter M. Haverty, Sheerin Shahidi-Latham, Hai Ngu, Margaret Solon, Jeffrey Eastham-Anderson, Hartmut Koeppen, Shih-Min A. Huang, Jacob Schwarz, Marcia Belvin, Daniel Kirouac, Melissa R. Junttila

[Fig 5a](#) is incorrect. The authors have provided a corrected version here.



OPEN ACCESS

Citation: Merchant M, Moffat J, Schaefer G, Chan J, Wang X, Orr C, et al. (2018) Correction: Combined MEK and ERK inhibition overcomes therapy-mediated pathway reactivation in *RAS* mutant tumors. PLoS ONE 13(1): e0192059. <https://doi.org/10.1371/journal.pone.0192059>

Published: January 25, 2018

Copyright: © 2018 Merchant et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

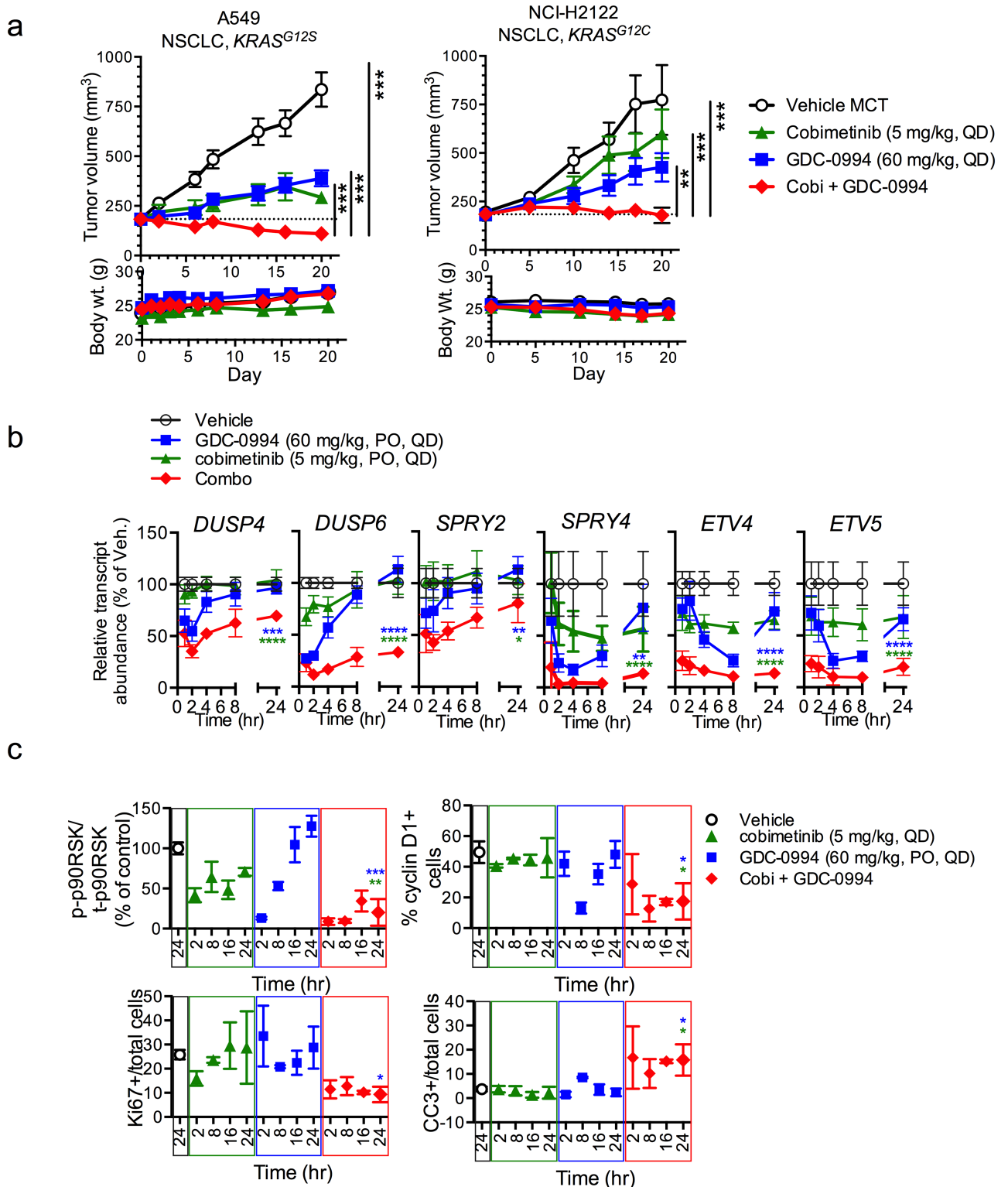


Fig 5. Combination of MEK and ERK inhibitors results in stronger suppression of KRAS mutant tumor growth due to improved suppression of MAPK output. (a) Combination of cobimetinib and GDC-0994 demonstrates significantly greater anti-tumor activity in multiple KRAS mutant tumor models A549 and NCI-H2122 (cobimetinib at 5 mg/kg, PO, QD + GDC-0994 at 60 mg/kg, PO, QD) compared to single agent (upper panels). Mean tumor volume is plotted \pm SEM (n = 10 mice per group). Study was terminated on day 20. All treatments were tolerated with minimal body weight loss (lower panels), One way ANOVA, * p<0.05, ** p<0.01, *** p<0.005, **** p<0.001. (b) A549 (NSCLC, KRAS^{G12S}) tumor-bearing mice (n = 3 per time

point) were treated with GDC-0994 (60 mg/kg, PO, QDx4), cobimetinib (GDC-0994; 5 mg/kg, PO, QDx4) or the combination and then MAPK target genes expression was assessed in tumor samples (Nanostring[®]) and the quantified results are plotted for each individual gene over time. The combination results in deeper, more prolonged suppression of multiple MAPK target genes, including *DUSP4*, *DUSP6*, *SPRY2*, *SPRY4*, *ETV4*, and *ETV5*. Student's t test at the 24 hr time point, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$, **** $p < 0.001$. (c) The combination of cobimetinib and GDC-0994 results in stronger and more prolonged suppression of p-p90RSK/total p90RSK phosphorylation (as determined by quantitative western blot), cyclin D1 and Ki-67, as well as increased induction of cleaved caspase 3 (CC3) (as determined by IHC) in A549 xenograft tumors treated for 4 days (values were quantified from $n = 4$ mice/time point). Student's t test at the 24 hr time point, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$.

<https://doi.org/10.1371/journal.pone.0192059.g001>

Reference

1. Merchant M, Moffat J, Schaefer G, Chan J, Wang X, Orr C, et al. (2017) Combined MEK and ERK inhibition overcomes therapy-mediated pathway reactivation in *RAS* mutant tumors. *PLoS ONE* 12(10): e0185862. <https://doi.org/10.1371/journal.pone.0185862> PMID: 28982154