

Supplemental References:

84. C. D. Richardson, G. J. Ray, M. A. DeWitt, G. L. Curie, J. E. Corn, Enhancing homology-

- directed genome editing by catalytically active and inactive CRISPR-Cas9 using asymmetric donor DNA. *Nat. Biotechnol.* **34**, 339–344 (2016).
85. F. A. Ran, F. Ann Ran, L. Cong, W. X. Yan, D. A. Scott, J. S. Gootenberg, A. J. Kriz, B. Zetsche, O. Shalem, X. Wu, K. S. Makarova, E. V. Koonin, P. A. Sharp, F. Zhang, In vivo genome editing using *Staphylococcus aureus* Cas9. *Nature.* **520** (2015), pp. 186–191.
 86. D. B. Wheeler, R. Zoncu, D. E. Root, D. M. Sabatini, C. L. Sawyers, Identification of an oncogenic RAB protein. *Science.* **350**, 211–217 (2015).
 87. Terra platform, (available at <https://app.terra.bio/>).
 88. B. Li, J. Gould, Y. Yang, S. Sarkizova, M. Tabaka, O. Ashenberg, Y. Rosen, M. Slyper, M. S. Kowalczyk, A.-C. Villani, T. Tickle, N. Hacohen, O. Rozenblatt-Rosen, A. Regev, Cumulus provides cloud-based data analysis for large-scale single-cell and single-nucleus RNA-seq. *Nat. Methods.* **17**, 793–798 (2020).
 89. G. X. Y. Zheng, J. M. Terry, P. Belgrader, P. Ryvkin, Z. W. Bent, R. Wilson, S. B. Ziraldo, T. D. Wheeler, G. P. McDermott, J. Zhu, M. T. Gregory, J. Shuga, L. Montesclaros, J. G. Underwood, D. A. Masquelier, S. Y. Nishimura, M. Schnall-Levin, P. W. Wyatt, C. M. Hindson, R. Bharadwaj, A. Wong, K. D. Ness, L. W. Beppu, H. J. Deeg, C. McFarland, K. R. Loeb, W. J. Valente, N. G. Ericson, E. A. Stevens, J. P. Radich, T. S. Mikkelsen, B. J. Hindson, J. H. Bielas, Massively parallel digital transcriptional profiling of single cells. *Nat. Commun.* **8**, 14049 (2017).
 90. S. E. Hunt, W. McLaren, L. Gil, A. Thormann, H. Schuilenburg, D. Sheppard, A. Parton, I. M. Armean, S. J. Trevanion, P. Flicek, F. Cunningham, Ensembl variation resources. *Database* . **2018** (2018), doi:10.1093/database/bay119.
 91. S. J. Fleming, J. C. Marioni, M. Babadi, CellBender remove-background: a deep generative model for unsupervised removal of background noise from scRNA-seq datasets. *Cold Spring Harbor Laboratory* (2019), p. 791699.
 92. F. A. Wolf, P. Angerer, F. J. Theis, SCANPY: large-scale single-cell gene expression data analysis. *Genome Biol.* **19**, 15 (2018).
 93. O. Ursu, J. T. Neal, E. Shea, P. I. Thakore, L. Jerby-Arnon, L. Nguyen, D. Dionne, C. Diaz, J. Bauman, M. M. Mosaad, C. Fagre, A. O. Giacomelli, S. H. Ly, O. Rozenblatt-Rosen, W. C. Hahn, A. J. Aguirre, A. H. Berger, A. Regev, J. S. Boehm, Massively parallel phenotyping of variant impact in cancer with Perturb-seq reveals a shift in the spectrum of cell states induced by somatic mutations. *Cold Spring Harbor Laboratory* (2020), p. 2020.11.16.383307, , doi:10.1101/2020.11.16.383307.
 94. S. L. Wolock, R. Lopez, A. M. Klein, Scrublet: Computational Identification of Cell Doublets in Single-Cell Transcriptomic Data. *Cell Syst.* **8**, 281-291.e9 (2019).
 95. I. Korsunsky, N. Millard, J. Fan, K. Slowikowski, F. Zhang, K. Wei, Y. Baglaenko, M. Brenner, P.-R. Loh, S. Raychaudhuri, Fast, sensitive and accurate integration of single-cell

- data with Harmony. *Nat. Methods*. **16**, 1289–1296 (2019).
96. R Core Team, “R: A Language and Environment for Statistical Computing” (R Foundation for Statistical Computing, Vienna, Austria, 2017), (available at <https://www.R-project.org/>).
 97. Z. Gu, R. Eils, M. Schlesner, Complex heatmaps reveal patterns and correlations in multidimensional genomic data. *Bioinformatics*. **32**, 2847–2849 (2016).
 98. inferCNV of the Trinity CTAT Project, (available at <https://github.com/broadinstitute/inferCNV>).
 99. B. M. Broom, M. C. Ryan, R. E. Brown, F. Ikeda, M. Stucky, D. W. Kane, J. Melott, C. Wakefield, T. D. Casasent, R. Akbani, J. N. Weinstein, A Galaxy Implementation of Next-Generation Clustered Heatmaps for Interactive Exploration of Molecular Profiling Data. *Cancer Res*. **77**, e23–e26 (2017).
 100. M. Stephens, False discovery rates: a new deal. *Biostatistics*. **18**, 275–294 (2017).
 101. J. A. Mumford, T. Nichols, Simple group fMRI modeling and inference. *Neuroimage*. **47**, 1469–1475 (2009).
 102. J. W. Squair, M. Gautier, C. Kathe, M. A. Anderson, N. D. James, T. H. Hutson, R. Hudelle, T. Qaiser, K. J. E. Matson, Q. Barraud, A. J. Levine, G. La Manno, M. A. Skinnider, G. Courtine, Confronting false discoveries in single-cell differential expression. *Nat. Commun*. **12**, 5692 (2021).
 103. J. Atchison, S. M. Shen, Logistic-normal distributions: Some properties and uses. *Biometrika*. **67**, 261–272 (1980).
 104. A. Gelman, Prior distributions for variance parameters in hierarchical models (comment on article by Browne and Draper). *ba*. **1**, 515–534 (2006).
 105. M. D. Hoffman, A. Gelman, The No-U-Turn Sampler: Adaptively Setting Path Lengths in Hamiltonian Monte Carlo. *J. Mach. Learn. Res*. **15**, 1593–1623 (2014).
 106. D. Phan, N. Pradhan, M. Jankowiak, Composable Effects for Flexible and Accelerated Probabilistic Programming in NumPyro. *arXiv [stat.ML]* (2019), (available at <http://arxiv.org/abs/1912.11554>).
 107. E. Bingham, J. P. Chen, M. Jankowiak, F. Obermeyer, N. Pradhan, T. Karaletsos, R. Singh, P. Szerlip, P. Horsfall, N. D. Goodman, Pyro: Deep universal probabilistic programming. *J. Mach. Learn. Res*. **20**, 973–978 (2019).
 108. D. Makowski, M. S. Ben-Shachar, S. H. A. Chen, D. Lüdtke, Indices of Effect Existence and Significance in the Bayesian Framework. *Front. Psychol*. **10**, 2767 (2019).
 109. R. Kumar, C. Carroll, A. Hartikainen, O. Martin, ArviZ a unified library for exploratory analysis of Bayesian models in Python. *J. Open Source Softw*. **4**, 1143 (2019).

110. Y. Drier, M. S. Lawrence, S. L. Carter, C. Stewart, S. B. Gabriel, E. S. Lander, M. Meyerson, R. Beroukhi, G. Getz, Somatic rearrangements across cancer reveal classes of samples with distinct patterns of DNA breakage and rearrangement-induced hypermutability. *Genome Res.* **23**, 228–235 (2013).
111. M. F. Berger, M. S. Lawrence, F. Demichelis, Y. Drier, K. Cibulskis, A. Y. Sivachenko, A. Sboner, R. Esgueva, D. Pflueger, C. Sougnez, R. Onofrio, S. L. Carter, K. Park, L. Habegger, L. Ambrogio, T. Fennell, M. Parkin, G. Saksena, D. Voet, A. H. Ramos, T. J. Pugh, J. Wilkinson, S. Fisher, W. Winckler, S. Mahan, K. Ardlie, J. Baldwin, J. W. Simons, N. Kitabayashi, T. Y. MacDonald, P. W. Kantoff, L. Chin, S. B. Gabriel, M. B. Gerstein, T. R. Golub, M. Meyerson, A. Tewari, E. S. Lander, G. Getz, M. A. Rubin, L. A. Garraway, The genomic complexity of primary human prostate cancer. *Nature.* **470**, 214–220 (2011).
112. L. D. Trucco, P. A. Mundra, K. Hogan, P. Garcia-Martinez, A. Viros, A. K. Mandal, N. Macagno, C. Gaudy-Marqueste, D. Allan, F. Baenke, M. Cook, C. McManus, B. Sanchez-Laorden, N. Dhomen, R. Marais, Ultraviolet radiation–induced DNA damage is prognostic for outcome in melanoma. *Nat. Med.* **25**, 221–224 (2018).
113. S. Berg, D. Kutra, T. Kroeger, C. N. Straehle, B. X. Kausler, C. Haubold, M. Schiegg, J. Ales, T. Beier, M. Rudy, K. Eren, J. I. Cervantes, B. Xu, F. Beuttenmueller, A. Wolny, C. Zhang, U. Koethe, F. A. Hamprecht, A. Kreshuk, ilastik: interactive machine learning for (bio)image analysis. *Nat. Methods.* **16**, 1226–1232 (2019).
114. A. Goode, B. Gilbert, J. Harkes, D. Jukic, M. Satyanarayanan, OpenSlide: A vendor-neutral software foundation for digital pathology. *J. Pathol. Inform.* **4**, 27 (2013).
115. K. Nazeri, A. Aminpour, M. Ebrahimi, in *Lecture Notes in Computer Science* (Springer International Publishing, Cham, 2018), *Lecture notes in computer science*, pp. 717–726.