

References

- Abdelaal, T., Michielsen, L., Cats, D., Hoogduin, D., Mei, H., Reinders, M. J. T., and Mahfouz, A. (2019). A comparison of automatic cell identification methods for single-cell RNA sequencing data. *Genome Biology*, 20(1):194.
- Adam, M., Potter, A. S., and Potter, S. S. (2017). Psychrophilic proteases dramatically reduce single-cell RNA-seq artifacts: a molecular atlas of kidney development. *Development*, 144(19):3625–3632.
- Aevermann, B. D., Novotny, M., Bakken, T., Miller, J. A., Diehl, A. D., Osumi-Sutherland, D., Lasken, R. S., Lein, E. S., and Scheuermann, R. H. (2018). Cell type discovery using single-cell transcriptomics: implications for ontological representation. *Human Molecular Genetics*, 27(R1):R40–R47.
- Agace, W. W. (2006). Tissue-tropic effector T cells: generation and targeting opportunities. *Nature Reviews Immunology*, 6(9):682.
- Alavi, A., Ruffalo, M., Parvangada, A., Huang, Z., and Bar-Joseph, Z. (2018). A web server for comparative analysis of single-cell RNA-seq data. *Nature Communications*, 9(1):4768.
- Ali, N., Zirak, B., Rodriguez, R. S., Pauli, M. L., Truong, H.-A., Lai, K., Ahn, R., Corbin, K., Lowe, M. M., Scharschmidt, T. C., Taravati, K., Tan, M. R., Ricardo-Gonzalez, R. R., Nosbaum, A., Bertolini, M., Liao, W., Nestle, F. O., Paus, R., Cotsarelis, G., Abbas, A. K., and Rosenblum, M. D. (2017). Regulatory T Cells in Skin Facilitate Epithelial Stem Cell Differentiation. *Cell*, 169(6):1119–1129.e11.
- Alquicira-Hernández, J., Sathe, A., Ji, H. P., Nguyen, Q., and Powell, J. E. (2018). scPred: Cell type prediction at single-cell resolution. *bioRxiv*, page 369538.
- Altin, J. G. and Sloan, E. K. (1997). The role of CD45 and CD45-associated molecules in T cell activation. *Immunology and Cell Biology*, 75(5):430–445.
- Angermueller, C., Clark, S. J., Lee, H. J., Macaulay, I. C., Teng, M. J., Hu, T. X., Krueger, F., Smallwood, S. A., Ponting, C. P., Voet, T., Kelsey, G., Stegle, O., and Reik, W. (2016). Parallel single-cell sequencing links transcriptional and epigenetic heterogeneity. *Nature Methods*, 13(3):229–232.
- Aran, D., Camarda, R., Odegaard, J., Paik, H., Oskotsky, B., Krings, G., Goga, A., Sirota, M., and Butte, A. J. (2017). Comprehensive analysis of normal adjacent to tumor transcriptomes. *Nature Communications*, 8(1):1077.

- Aran, D., Looney, A. P., Liu, L., Wu, E., Fong, V., Hsu, A., Chak, S., Naikawadi, R. P., Wolters, P. J., Abate, A. R., Butte, A. J., and Bhattacharya, M. (2019). Reference-based analysis of lung single-cell sequencing reveals a transitional profibrotic macrophage. *Nature Immunology*, 20(2):163.
- Arzalluz-Luque, A. and Conesa, A. (2018). Single-cell RNAseq for the study of isoforms—how is that possible? *Genome Biology*, 19(1):110.
- Bagnoli, J. W., Ziegenhain, C., Janjic, A., Wange, L. E., Vieth, B., Parekh, S., Geuder, J., Hellmann, I., and Enard, W. (2018). Sensitive and powerful single-cell RNA sequencing using mcSCR-seq. *Nature Communications*, 9(1):1–8.
- Bandura, D. R., Baranov, V. I., Ornatsky, O. I., Antonov, A., Kinach, R., Lou, X., Pavlov, S., Vorobiev, S., Dick, J. E., and Tanner, S. D. (2009). Mass Cytometry: Technique for Real Time Single Cell Multitarget Immunoassay Based on Inductively Coupled Plasma Time-of-Flight Mass Spectrometry. *Analytical Chemistry*, 81(16):6813–6822.
- Barbosa-Morais, N. L., Irimia, M., Pan, Q., Xiong, H. Y., Gueroussov, S., Lee, L. J., Slobodeniuc, V., Kutter, C., Watt, S., Çolak, R., Kim, T., Misquitta-Ali, C. M., Wilson, M. D., Kim, P. M., Odom, D. T., Frey, B. J., and Blencowe, B. J. (2012). The Evolutionary Landscape of Alternative Splicing in Vertebrate Species. *Science*, 338(6114):1587–1593.
- Bard, J., Rhee, S. Y., and Ashburner, M. (2005). An ontology for cell types. *Genome Biology*, 6(2):R21.
- Barkas, N., Petukhov, V., Nikolaeva, D., Lozinsky, Y., Demharter, S., Khodosevich, K., and Kharchenko, P. V. (2019). Joint analysis of heterogeneous single-cell RNA-seq dataset collections. *Nature Methods*, 16(8):695–698.
- Baron, M., Veres, A., Wolock, S. L., Faust, A. L., Gaujoux, R., Vetere, A., Ryu, J. H., Wagner, B. K., Shen-Orr, S. S., Klein, A. M., Melton, D. A., and Yanai, I. (2016). A Single-Cell Transcriptomic Map of the Human and Mouse Pancreas Reveals Inter- and Intra-cell Population Structure. *Cell Systems*, 3(4):346–360.e4.
- Barreiro, L. B. and Quintana-Murci, L. (2010). From evolutionary genetics to human immunology: how selection shapes host defence genes. *Nature Reviews Genetics*, 11(1):17–30.
- Behjati, S., Lindsay, S., Teichmann, S. A., and Haniffa, M. (2018). Mapping human development at single-cell resolution. *Development*, 145(3):dev152561.
- Bernstein, M. N. and Dewey, C. N. (2019). Hierarchical cell type classification using mass, heterogeneous RNA-seq data from human primary cells. *bioRxiv*, page 634097.
- Bettelli, E., Carrier, Y., Gao, W., Korn, T., Strom, T. B., Oukka, M., Weiner, H. L., and Kuchroo, V. K. (2006). Reciprocal developmental pathways for the generation of pathogenic effector TH17 and regulatory T cells. *Nature*, 441(7090):235–238.

- Bjorklund, A. K., Forkel, M., Picelli, S., Konya, V., Theorell, J., Friberg, D., Sandberg, R., and Mjösberg, J. (2016). The heterogeneity of human CD127⁺ innate lymphoid cells revealed by single-cell RNA sequencing. *Nature Immunology*, 17(4):451–460.
- Blondel, V. D., Guillaume, J.-L., Lambiotte, R., and Lefebvre, E. (2008). Fast unfolding of communities in large networks. *Journal of Statistical Mechanics: Theory and Experiment*, 2008(10):P10008.
- Bollrath, J. and Powrie, F. M. (2013). Controlling the frontier: regulatory t-cells and intestinal homeostasis. *Semin. Immunol.*, 25(5):352–357.
- Bonner, W. A., Hulett, H. R., Sweet, R. G., and Herzenberg, L. A. (1972). Fluorescence Activated Cell Sorting. *Review of Scientific Instruments*, 43(3):404–409.
- Boufe, K., Seth, S., and Batada, N. N. (2019). scID: Identification of equivalent transcriptional cell populations across single cell RNA-seq data using discriminant analysis. *bioRxiv*, page 470203.
- Braga, F. A. V., Kar, G., Berg, M., Carpaij, O. A., Polanski, K., Simon, L. M., Brouwer, S., Gomes, T., Hesse, L., Jiang, J., Fasouli, E. S., Efremova, M., Vento-Tormo, R., Talavera-López, C., Jonker, M. R., Affleck, K., Palit, S., Strzelecka, P. M., Firth, H. V., Mahbubani, K. T., Cvejic, A., Meyer, K. B., Saeb-Parsy, K., Luinge, M., Brandsma, C.-A., Timens, W., Angelidis, I., Strunz, M., Koppelman, G. H., Oosterhout, A. J. v., Schiller, H. B., Theis, F. J., Berge, M. v. d., Nawijn, M. C., and Teichmann, S. A. (2019). A cellular census of human lungs identifies novel cell states in health and in asthma. *Nature Medicine*, 25(7):1153–1163.
- Brawand, D., Soumillon, M., Necsulea, A., Julien, P., Csárdi, G., Harrigan, P., Weier, M., Liechti, A., Aximu-Petri, A., Kircher, M., Albert, F. W., Zeller, U., Khaitovich, P., Grützner, F., Bergmann, S., Nielsen, R., Pääbo, S., and Kaessmann, H. (2011). The evolution of gene expression levels in mammalian organs. *Nature*, 478(7369):343–348.
- Brazovskaja, A., Treutlein, B., and Camp, J. G. (2019). High-throughput single-cell transcriptomics on organoids. *Current Opinion in Biotechnology*, 55:167–171.
- Brennecke, P., Anders, S., Kim, J. K., Kołodziejczyk, A. A., Zhang, X., Proserpio, V., Baying, B., Benes, V., Teichmann, S. A., Marioni, J. C., and Heisler, M. G. (2013). Accounting for technical noise in single-cell RNA-seq experiments. *Nature Methods*, 10(11):1093–1095.
- Brown, R. (1866). On the Organs and Mode of Fecundation of Orchidex and Asclepiadea. In *Miscellaneous Botanical Works, Vol. I*. London: Ray Society.
- Buenrostro, J. D., Wu, B., Litzenburger, U. M., Ruff, D., Gonzales, M. L., Snyder, M. P., Chang, H. Y., and Greenleaf, W. J. (2015). Single-cell chromatin accessibility reveals principles of regulatory variation. *Nature*, 523(7561):486–490.
- Buettner, F., Pratanwanich, N., McCarthy, D. J., Marioni, J. C., and Stegle, O. (2017). f-scLVM: scalable and versatile factor analysis for single-cell RNA-seq. *Genome Biology*, 18(1):212.

- Burzyn, D., Kuswanto, W., Kolodin, D., Shadrach, J. L., Cerletti, M., Jang, Y., Sefik, E., Tan, T. G., Wagers, A. J., Benoist, C., and Mathis, D. (2013). A Special Population of Regulatory T Cells Potentiates Muscle Repair. *Cell*, 155(6):1282–1295.
- Butler, A., Hoffman, P., Smibert, P., Papalexi, E., and Satija, R. (2018). Integrating single-cell transcriptomic data across different conditions, technologies, and species. *Nature Biotechnology*, 36(5):411–420.
- Büttner, M., Miao, Z., Wolf, F. A., Teichmann, S. A., and Theis, F. J. (2019). A test metric for assessing single-cell RNA-seq batch correction. *Nature Methods*, 16(1):43–49.
- Camp, J. G., Wollny, D., and Treutlein, B. (2018). Single-cell genomics to guide human stem cell and tissue engineering. *Nature Methods*, 15(9):661–667.
- Campbell, D. J. and Koch, M. A. (2011). Phenotypical and functional specialization of FOXP3+ regulatory T cells. *Nat. Rev. Immunol.*, 11(2):119–130.
- Campbell, K. R. and Yau, C. (2017). switchde: inference of switch-like differential expression along single-cell trajectories. *Bioinformatics*, 33(8):1241–1242.
- Cao, J., Packer, J. S., Ramani, V., Cusanovich, D. A., Huynh, C., Daza, R., Qiu, X., Lee, C., Furlan, S. N., Steemers, F. J., Adey, A., Waterston, R. H., Trapnell, C., and Shendure, J. (2017). Comprehensive single-cell transcriptional profiling of a multicellular organism. *Science*, 357(6352):661–667.
- Cao, J., Spielmann, M., Qiu, X., Huang, X., Ibrahim, D. M., Hill, A. J., Zhang, F., Mundlos, S., Christiansen, L., Steemers, F. J., Trapnell, C., and Shendure, J. (2019a). The single-cell transcriptional landscape of mammalian organogenesis. *Nature*, 566(7745):496.
- Cao, Z.-J., Wei, L., Lu, S., Yang, D.-C., and Gao, G. (2019b). Cell BLAST: Searching large-scale scRNA-seq database via unbiased cell embedding. *bioRxiv*, page 587360.
- Cebula, A., Seweryn, M., Rempala, G. A., Pabla, S. S., McIndoe, R. A., Denning, T. L., Bry, L., Kraj, P., Kisielow, P., and Ignatowicz, L. (2013). Thymus-derived regulatory T cells contribute to tolerance to commensal microbiota. *Nature*, 497(7448):258–262.
- Cepek, K. L., Shaw, S. K., Parker, C. M., Russell, G. J., Morrow, J. S., Rimm, D. L., and Brenner, M. B. (1994). Adhesion between epithelial cells and T lymphocytes mediated by e-cadherin and the $\alpha E\beta 7$ integrin. *Nature*, 372(6502):190–193.
- Chang, Q., Ornatsky, O. I., Siddiqui, I., Loboda, A., Baranov, V. I., and Hedley, D. W. (2017). Imaging Mass Cytometry. *Cytometry Part A*, 91(2):160–169.
- Chen, S., Park, J. H., Rivaud, P., Charles, E., Haliburton, J., Pichiorri, F., and Thomson, M. (2018). Dissecting heterogeneous cell-populations across signaling and disease conditions with PopAlign. *bioRxiv*, page 421354.

- Chen, X., Chen, S., and Jiang, R. (2019). EnClaSC: A novel ensemble approach for accurate and robust cell-type classification of single-cell transcriptomes. *bioRxiv*, page 754085.
- Chow, Z., Banerjee, A., and Hickey, M. J. (2015). Controlling the fire — tissue-specific mechanisms of effector regulatory t-cell homing. *Immunol. Cell Biol.*, 93(4):355–363.
- Cipolletta, D. (2014). Adipose tissue-resident regulatory T cells: phenotypic specialization, functions and therapeutic potential. *Immunology*, 142(4):517–525.
- Clark, S. J., Argelaguet, R., Kapourani, C.-A., Stubbs, T. M., Lee, H. J., Alda-Catalinas, C., Krueger, F., Sanguinetti, G., Kelsey, G., Marioni, J. C., Stegle, O., and Reik, W. (2018). scNMT-seq enables joint profiling of chromatin accessibility DNA methylation and transcription in single cells. *Nature Communications*, 9(1):781.
- Collins, P. and Billett, F. S. (1995). The terminology of early development: History, concepts, and current usage. *Clinical Anatomy*, 8(6):418–425.
- Consortium, T. G. (2015). The Genotype-Tissue Expression (GTEx) pilot analysis: Multitissue gene regulation in humans. *Science*, 348(6235):648–660.
- Coons, A. H., Creech, H. J., and Jones, R. N. (1941). Immunological Properties of an Antibody Containing a Fluorescent Group. *Proceedings of the Society for Experimental Biology and Medicine*, 47(2):200–202.
- Cretney, E., Xin, A., Shi, W., Minnich, M., Masson, F., Miasari, M., Belz, G. T., Smyth, G. K., Busslinger, M., Nutt, S. L., and Kallies, A. (2011). The transcription factors blimp-1 and IRF4 jointly control the differentiation and function of effector regulatory T cells. *Nat. Immunol.*, 12(4):304–311.
- Cusanovich, D. A., Hill, A. J., Aghamirzaie, D., Daza, R. M., Pliner, H. A., Berletch, J. B., Filippova, G. N., Huang, X., Christiansen, L., DeWitt, W. S., Lee, C., Regalado, S. G., Read, D. F., Steemers, F. J., Disteche, C. M., Trapnell, C., and Shendure, J. (2018). A Single-Cell Atlas of In Vivo Mammalian Chromatin Accessibility. *Cell*, 174(5):1309–1324.e18.
- Damianou, A., Ek, C., Titsias, M., and Lawrence, N. (2012). Manifold relevance determination. *arXiv*.
- Datlinger, P., Rendeiro, A. F., Schmidl, C., Krausgruber, T., Traxler, P., Klughammer, J., Schuster, L. C., Kuchler, A., Alpar, D., and Bock, C. (2017). Pooled CRISPR screening with single-cell transcriptome readout. *Nature Methods*, 14(3):297–301.
- de Kanter, J. K., Lijnzaad, P., Candelli, T., Margaritis, T., and Holstege, F. C. P. (2019). CHETAH: a selective, hierarchical cell type identification method for single-cell RNA sequencing. *Nucleic Acids Research*.
- De Simone, M., De Simone, M., Arrigoni, A., Rossetti, G., Gruarin, P., Ranzani, V., Politano, C., Bonnal, R. J. P., Provasi, E., Sarnicola, M. L., Panzeri, I., Moro, M., Crosti, M., Mazzara, S., Vaira, V., Bosari, S., Palleschi, A., Santambrogio, L.,

- Bovo, G., Zucchini, N., Totis, M., Gianotti, L., Cesana, G., Perego, R. A., Maroni, N., Ceretti, A. P., Opocher, E., De Francesco, R., Geginat, J., Stunnenberg, H. G., Abrignani, S., and Pagani, M. (2016). Transcriptional landscape of human tissue lymphocytes unveils uniqueness of Tumor-Infiltrating T regulatory cells. *Immunity*, 45(5):1135–1147.
- DePasquale, E. A., Dexheimer, P., Schnell, D., Ferchen, K., Hay, S., Valiente-Alandi, I., Blaxall, B. C., Grimes, H. L., and Salomonis, N. (2019). cellHarmony: Cell-level matching and holistic comparison of single-cell transcriptomes. *bioRxiv*, page 412080.
- DeRisi, J. L., Iyer, V. R., and Brown, P. O. (1997). Exploring the Metabolic and Genetic Control of Gene Expression on a Genomic Scale. *Science*, 278(5338):680–686.
- Di Palma, S. and Bodenmiller, B. (2015). Unraveling cell populations in tumors by single-cell mass cytometry. *Current Opinion in Biotechnology*, 31:122–129.
- DiSpirito, J. R., Zemmour, D., Ramanan, D., Cho, J., Zilionis, R., Klein, A. M., Benoist, C., and Mathis, D. (2018). Molecular diversification of regulatory T cells in nonlymphoid tissues. *Science Immunology*, 3(27).
- Dixit, A., Parnas, O., Li, B., Chen, J., Fulco, C. P., Jerby-Arnon, L., Marjanovic, N. D., Dionne, D., Burks, T., Raychowdhury, R., Adamson, B., Norman, T. M., Lander, E. S., Weissman, J. S., Friedman, N., and Regev, A. (2016). Perturb-Seq: Dissecting Molecular Circuits with Scalable Single-Cell RNA Profiling of Pooled Genetic Screens. *Cell*, 167(7):1853–1866.e17.
- Domanskyi, S., Szedlak, A., Hawkins, N. T., Wang, J., Paternostro, G., and Piermarocchi, C. (2019). Polled Digital Cell Sorter (p-DCS): Automatic identification of hematological cell types from single cell RNA-sequencing clusters. *BMC Bioinformatics*, 20(1):369.
- Dongen, S. V. (2000). Performance Criteria for Graph Clustering and Markov Cluster Experiments. Technical report, NATIONAL RESEARCH INSTITUTE FOR MATHEMATICS AND COMPUTER SCIENCE IN THE.
- Dunham, I., Kundaje, A., Aldred, S. F., Collins, P. J., Davis, C. A., Doyle, F., Epstein, C. B., Frietze, S., Harrow, J., Kaul, R., Khatun, J., Lajoie, B. R., Landt, S. G., Lee, B.-K., Pauli, F., Rosenbloom, K. R., Sabo, P., Safi, A., Sanyal, A., Shores, N., Simon, J. M., Song, L., Trinklein, N. D., Altshuler, R. C., Birney, E., Brown, J. B., Cheng, C., Djebali, S., Dong, X., Dunham, I., Ernst, J., Furey, T. S., Gerstein, M., Giardine, B., Greven, M., Hardison, R. C., Harris, R. S., Herrero, J., Hoffman, M. M., Iyer, S., Kellis, M., Khatun, J., Kheradpour, P., Kundaje, A., Lassmann, T., Li, Q., Lin, X., Marinov, G. K., Merkel, A., Mortazavi, A., Parker, S. C. J., Reddy, T. E., Rozowsky, J., Schlesinger, F., Thurman, R. E., Wang, J., Ward, L. D., Whitfield, T. W., Wilder, S. P., Wu, W., Xi, H. S., Yip, K. Y., Zhuang, J., Bernstein, B. E., Birney, E., Dunham, I., Green, E. D., Gunter, C., Snyder, M., Pazin, M. J., Lowdon, R. F., Dillon, L. A. L., Adams, L. B., Kelly, C. J., Zhang, J., Wexler, J. R., Green, E. D., Good, P. J., Feingold, E. A., Bernstein, B. E., Birney, E., Crawford, G. E., Dekker, J., Elnitski, L., Farnham, P. J., Gerstein, M., Giddings, M. C., Gingeras, T. R., Green, E. D., Guigó, R.,

- Hardison, R. C., Hubbard, T. J., Kellis, M., Kent, W. J., Lieb, J. D., Margulies, E. H., Myers, R. M., Snyder, M., Stamatoyannopoulos, J. A., Tenenbaum, S. A., Weng, Z., White, K. P., Wold, B., Khatun, J., Yu, Y., Wrobel, J., Risk, B. A., Gunawardena, H. P., Kuiper, H. C., Maier, C. W., Xie, L., Chen, X., Giddings, M. C., Bernstein, B. E., Epstein, C. B., Shores, N., Ernst, J., Kheradpour, P., Mikkelsen, T. S., Gillespie, S., Goren, A., Ram, O., Zhang, X., Wang, L., Issner, R., Coyne, M. J., Durham, T., Ku, M., Truong, T., Ward, L. D., Altshuler, R. C., Eaton, M. L., Kellis, M., Djebali, S., Davis, C. A., Merkel, A., Dobin, A., Lassmann, T., Mortazavi, A., Tanzer, A., Lagarde, J., Lin, W., Schlesinger, F., Xue, C., Marinov, G. K., Khatun, J., Williams, B. A., Zaleski, C., Rozowsky, J., Röder, M., Kokocinski, F., Abdelhamid, R. F., Alioto, T., Antoshechkin, I., Baer, M. T., Batut, P., Bell, I., Bell, K., Chakraborty, S., Chen, X., Chrast, J., Curado, J., Derrien, T., Drenkow, J., Dumais, E., Dumais, J., Duttagupta, R., Fastuca, M., Fejes-Toth, K., Ferreira, P., Foissac, S., Fullwood, M. J., Gao, H., Gonzalez, D., Gordon, A., Gunawardena, H. P., Howald, C., Jha, S., Johnson, R., Kapranov, P., King, B., Kingswood, C., Li, G., Luo, O. J., Park, E., Preall, J. B., Presaud, K., Ribeca, P., Risk, B. A., Robyr, D., Ruan, X., Sammeth, M., Sandhu, K. S., Schaeffer, L., See, L.-H., Shahab, A., Skancke, J., Suzuki, A. M., Takahashi, H., Tilgner, H., Trout, D., Walters, N., Wang, H., Wrobel, J., Yu, Y., Hayashizaki, Y., Harrow, J., Gerstein, M., Hubbard, T. J., Reymond, A., Antonarakis, S. E., Hannon, G. J., Giddings, M. C., Ruan, Y., Wold, B., Carninci, P., Guigó, R., Gingeras, T. R., Rosenbloom, K. R., Sloan, C. A., Learned, K., Malladi, V. S., Wong, M. C., Barber, G. P., Cline, M. S., Dreszer, T. R., Heitner, S. G., Karolchik, D., Kent, W. J., Kirkup, V. M., Meyer, L. R., Long, J. C., Maddren, M., Raney, B. J., Furey, T. S., Song, L., Grasfeder, L. L., Giressi, P. G., Lee, B.-K., Battenhouse, A., Sheffield, N. C., Simon, J. M., Showers, K. A., Safi, A., London, D., Bhinge, A. A., Shestak, C., Schaner, M. R., Ki Kim, S., Zhang, Z. Z., Mieczkowski, P. A., Mieczkowska, J. O., Liu, Z., McDaniel, R. M., Ni, Y., Rashid, N. U., Kim, M. J., Adar, S., Zhang, Z., Wang, T., Winter, D., Keefe, D., Birney, E., Iyer, V. R., Lieb, J. D., Crawford, G. E., Li, G., Sandhu, K. S., Zheng, M., Wang, P., Luo, O. J., Shahab, A., Fullwood, M. J., Ruan, X., Ruan, Y., Myers, R. M., Pauli, F., Williams, B. A., Gertz, J., Marinov, G. K., Reddy, T. E., Vielmetter, J., Partridge, E., Trout, D., Varley, K. E., Gasper, C., The ENCODE Project Consortium, Overall coordination (data analysis coordination), Data production leads (data production), Lead analysts (data analysis), Writing group, NHGRI project management (scientific management), Principal investigators (steering committee), Boise State University and University of North Carolina at Chapel Hill Proteomics groups (data production and analysis), Broad Institute Group (data production and analysis), Cold Spring Harbor, Center for Genomic Regulation, B. R. S. I. U. o. L. G. I. o. S. g. d. p. a. a. U. o. G., Data coordination center at UC Santa Cruz (production data coordination), Duke University, University of Texas, A. U. o. N. C.-C. H. g. d. p. a. a. E., Genome Institute of Singapore group (data production and analysis), and HudsonAlpha Institute, UC Irvine, S. g. d. p. a. a.-C. (2012). An integrated encyclopedia of DNA elements in the human genome. *Nature*, 489(7414):57–74.
- Durinck, S., Spellman, P. T., Birney, E., and Huber, W. (2009). Mapping identifiers for the integration of genomic datasets with the R/Bioconductor package biomaRt. *Nature Protocols*, 4(8):1184–1191.

- Efremova, M., Vento-Tormo, M., Teichmann, S. A., and Vento-Tormo, R. (2019). CellPhoneDB v2.0: Inferring cell-cell communication from combined expression of multi-subunit receptor-ligand complexes. *bioRxiv*, page 680926.
- Eisenberg, E. and Levanon, E. Y. (2013). Human housekeeping genes, revisited. *Trends in Genetics*, 29(10):569–574.
- Enard, W., Khaitovich, P., Klose, J., Zöllner, S., Heissig, F., Giavalisco, P., Nieselt-Struwe, K., Muchmore, E., Varki, A., Ravid, R., Doxiadis, G. M., Bontrop, R. E., and Pääbo, S. (2002). Intra- and Interspecific Variation in Primate Gene Expression Patterns. *Science*, 296(5566):340–343.
- Fagerberg, L., Hallström, B. M., Oksvold, P., Kampf, C., Djureinovic, D., Odeberg, J., Habuka, M., Tahmasebpoor, S., Danielsson, A., Edlund, K., Asplund, A., Sjöstedt, E., Lundberg, E., Szigartyo, C. A.-K., Skogs, M., Takanen, J. O., Berling, H., Tegel, H., Mulder, J., Nilsson, P., Schwenk, J. M., Lindskog, C., Danielsson, F., Mardinoglu, A., Sivertsson, A., von Feilitzen, K., Forsberg, M., Zwahlen, M., Olsson, I., Navani, S., Huss, M., Nielsen, J., Ponten, F., and Uhlén, M. (2014). Analysis of the human tissue-specific expression by genome-wide integration of transcriptomics and antibody-based proteomics. *Mol. Cell. Proteomics*, 13(2):397–406.
- Fincher, C. T., Wurtzel, O., Hoog, T. d., Kravarik, K. M., and Reddien, P. W. (2018). Cell type transcriptome atlas for the planarian *Schmidtea mediterranea*. *Science*, 360(6391):eaq1736.
- Franzén, O., Gan, L.-M., and Björkegren, J. L. M. (2019). PanglaoDB: a web server for exploration of mouse and human single-cell RNA sequencing data. *Database*, 2019.
- Gabanyi, I., Muller, P., Feighery, L., Oliveira, T., Costa-Pinto, F., and Mucida, D. (2016). Neuro-immune Interactions Drive Tissue Programming in Intestinal Macrophages. *Cell*, 164(3):378–391.
- Gao, X., Hu, D., Gogol, M., and Li, H. (2018). ClusterMap: Comparing analyses across multiple Single Cell RNA-Seq profiles. *bioRxiv*, page 331330.
- Geremia, A., Arancibia-Cárcamo, C. V., Fleming, M. P. P., Rust, N., Singh, B., Mortensen, N. J., Travis, S. P. L., and Powrie, F. (2011). IL-23-responsive innate lymphoid cells are increased in inflammatory bowel disease. *J. Exp. Med.*, 208(6):1127–1133.
- Gierahn, T. M., Wadsworth Ii, M. H., Hughes, T. K., Bryson, B. D., Butler, A., Satija, R., Fortune, S., Love, J. C., and Shalek, A. K. (2017). Seq-Well: portable, low-cost RNA sequencing of single cells at high throughput. *Nature Methods*, 14(4):395–398.
- Glusman, G., Rowen, L., Lee, I., Boysen, C., Roach, J. C., Smit, A. F. A., Wang, K., Koop, B. F., and Hood, L. (2001). Comparative Genomics of the Human and Mouse T Cell Receptor Loci. *Immunity*, 15(3):337–349.

- Goldstein, L. D., Chen, Y.-J. J., Dunne, J., Mir, A., Hubschle, H., Guillory, J., Yuan, W., Zhang, J., Stinson, J., Jaiswal, B., Pahuja, K. B., Mann, I., Schaal, T., Chan, L., Anandkrishnan, S., Lin, C.-w., Espinoza, P., Husain, S., Shapiro, H., Swaminathan, K., Wei, S., Srinivasan, M., Seshagiri, S., and Modrusan, Z. (2017). Massively parallel nanowell-based single-cell gene expression profiling. *BMC Genomics*, 18(1):519.
- Golgi, C. and Lipsky, N. G. (1989). On the structure of nerve cells. *Journal of Microscopy*, 155(1):3–7.
- Gomez Perdiguero, E., Klapproth, K., Schulz, C., Busch, K., Azzoni, E., Crozet, L., Garner, H., Trouillet, C., de Bruijn, M. F., Geissmann, F., and Rodewald, H.-R. (2015). Tissue-resident macrophages originate from yolk-sac-derived erythromyeloid progenitors. *Nature*, 518(7540):547–551.
- Gordon, S. and Martinez-Pomares, L. (2017). Physiological roles of macrophages. *Pflügers Archiv - European Journal of Physiology*, 469(3):365–374.
- Gorin, G., Svensson, V., and Pachter, L. (2019). RNA velocity and protein acceleration from single-cell multiomics experiments. *bioRxiv*, page 658401.
- Gosselin, D., Link, V. M., Romanoski, C., Fonseca, G., Eichenfield, D., Spann, N., Stender, J., Chun, H., Garner, H., Geissmann, F., and Glass, C. (2014). Environment Drives Selection and Function of Enhancers Controlling Tissue-Specific Macrophage Identities. *Cell*, 159(6):1327–1340.
- GTEx Consortium (2017). Genetic effects on gene expression across human tissues. *Nature*, 550(7675):204–213.
- Guo, J., Grow, E. J., Mlcochova, H., Maher, G. J., Lindskog, C., Nie, X., Guo, Y., Takei, Y., Yun, J., Cai, L., Kim, R., Carrell, D. T., Goriely, A., Hotaling, J. M., and Cairns, B. R. (2018). The adult human testis transcriptional cell atlas. *Cell Research*, 28(12):1141–1157.
- Gupta, I., Collier, P. G., Haase, B., Mahfouz, A., Joglekar, A., Floyd, T., Koopmans, F., Barres, B., Smit, A. B., Sloan, S. A., Luo, W., Fedrigo, O., Ross, M. E., and Tilgner, H. U. (2018). Single-cell isoform RNA sequencing characterizes isoforms in thousands of cerebellar cells. *Nature Biotechnology*, 36(12):1197–1202.
- Habib, N., Avraham-Davidi, I., Basu, A., Burks, T., Shekhar, K., Hofree, M., Choudhury, S. R., Aguet, F., Gelfand, E., Ardlie, K., Weitz, D. A., Rozenblatt-Rosen, O., Zhang, F., and Regev, A. (2017). Massively parallel single-nucleus RNA-seq with DroNc-seq. *Nature Methods*, 14(10):955–958.
- Hagai, T., Chen, X., Miragaia, R. J., Rostom, R., Gomes, T., Kunowska, N., Henriksson, J., Park, J.-E., Proserpio, V., Donati, G., Bossini-Castillo, L., Braga, F. A. V., Naamati, G., Fletcher, J., Stephenson, E., Vegh, P., Trynka, G., Kondova, I., Dennis, M., Haniffa, M., Nourmohammad, A., Lässig, M., and Teichmann, S. A. (2018). Gene expression variability across cells and species shapes innate immunity. *Nature*, 563(7730):197.

- Haghverdi, L., Lun, A. T. L., Morgan, M. D., and Marioni, J. C. (2018). Batch effects in single-cell RNA-sequencing data are corrected by matching mutual nearest neighbors. *Nature Biotechnology*, 36(5):421–427.
- Halle, S., Halle, O., and Förster, R. (2017). Mechanisms and Dynamics of T Cell-Mediated Cytotoxicity In Vivo. *Trends in Immunology*, 38(6):432–443.
- Han, X., Wang, R., Zhou, Y., Fei, L., Sun, H., Lai, S., Saadatpour, A., Zhou, Z., Chen, H., Ye, F., Huang, D., Xu, Y., Huang, W., Jiang, M., Jiang, X., Mao, J., Chen, Y., Lu, C., Xie, J., Fang, Q., Wang, Y., Yue, R., Li, T., Huang, H., Orkin, S. H., Yuan, G.-C., Chen, M., and Guo, G. (2018). Mapping the Mouse Cell Atlas by Microwell-Seq. *Cell*, 172(5):1091–1107.e17.
- Haribhai, D., Lin, W., Relland, L. M., Truong, N., Williams, C. B., and Chatila, T. A. (2007). Regulatory T cells dynamically control the primary immune response to foreign antigen. *J. Immunol.*, 178(5):2961–2972.
- Hashimshony, T., Senderovich, N., Avital, G., Klochendler, A., de Leeuw, Y., Anavy, L., Gennert, D., Li, S., Livak, K. J., Rozenblatt-Rosen, O., Dor, Y., Regev, A., and Yanai, I. (2016). CEL-Seq2: sensitive highly-multiplexed single-cell RNA-Seq. *Genome Biology*, 17(1):77.
- Hashimshony, T., Wagner, F., Sher, N., and Yanai, I. (2012). CEL-Seq: Single-Cell RNA-Seq by Multiplexed Linear Amplification. *Cell Reports*, 2(3):666–673.
- Hayashi, T., Ozaki, H., Sasagawa, Y., Umeda, M., Danno, H., and Nikaido, I. (2018). Single-cell full-length total RNA sequencing uncovers dynamics of recursive splicing and enhancer RNAs. *Nature Communications*, 9(1):1–16.
- Henry, G. H., Malewska, A., Joseph, D. B., Malladi, V. S., Lee, J., Torrealba, J., Mauck, R. J., Gahan, J. C., Raj, G. V., Roehrborn, C. G., Hon, G. C., MacConmara, M. P., Reese, J. C., Hutchinson, R. C., Vezina, C. M., and Strand, D. W. (2018). A Cellular Anatomy of the Normal Adult Human Prostate and Prostatic Urethra. *Cell Reports*, 25(12):3530–3542.e5.
- Hie, B., Bryson, B., and Berger, B. (2019a). Efficient integration of heterogeneous single-cell transcriptomes using Scanorama. *Nature Biotechnology*, 37(6):685–691.
- Hie, B., Cho, H., DeMeo, B., Bryson, B., and Berger, B. (2019b). Geometric Sketching Compactly Summarizes the Single-Cell Transcriptomic Landscape. *Cell Systems*, 8(6):483–493.e7.
- Hoadley, K. A., Yau, C., Hinoue, T., Wolf, D. M., Lazar, A. J., Drill, E., Shen, R., Taylor, A. M., Cherniack, A. D., Thorsson, V., Akbani, R., Bowlby, R., Wong, C. K., Wiznerowicz, M., Sanchez-Vega, F., Robertson, A. G., Schneider, B. G., Lawrence, M. S., Noushmehr, H., Malta, T. M., Caesar-Johnson, S. J., Demchok, J. A., Felau, I., Kasapi, M., Ferguson, M. L., Hutter, C. M., Sofia, H. J., Tarnuzzer, R., Wang, Z., Yang, L., Zenklusen, J. C., Zhang, J. J., Chudamani, S., Liu, J., Lolla, L., Naresh, R., Pihl, T., Sun, Q., Wan, Y., Wu, Y., Cho, J., DeFreitas, T., Frazer, S., Gehlenborg, N., Getz, G., Heiman, D. I., Kim, J., Lawrence, M. S., Lin, P., Meier, S., Noble, M. S., Saksena, G., Voet, D., Zhang, H., Bernard, B., Chambwe, N., Dhankani,

V., Knijnenburg, T., Kramer, R., Leinonen, K., Liu, Y., Miller, M., Reynolds, S., Shmulevich, I., Thorsson, V., Zhang, W., Akbani, R., Broom, B. M., Hegde, A. M., Ju, Z., Kanchi, R. S., Korkut, A., Li, J., Liang, H., Ling, S., Liu, W., Lu, Y., Mills, G. B., Ng, K.-S., Rao, A., Ryan, M., Wang, J., Weinstein, J. N., Zhang, J., Abeshouse, A., Armenia, J., Chakravarty, D., Chatila, W. K., Bruijn, I. d., Gao, J., Gross, B. E., Heins, Z. J., Kundra, R., La, K., Ladanyi, M., Luna, A., Nissan, M. G., Ochoa, A., Phillips, S. M., Reznik, E., Sanchez-Vega, F., Sander, C., Schultz, N., Sheridan, R., Sumer, S. O., Sun, Y., Taylor, B. S., Wang, J., Zhang, H., Anur, P., Peto, M., Spellman, P., Benz, C., Stuart, J. M., Wong, C. K., Yau, C., Hayes, D. N., Parker, J. S., Wilkerson, M. D., Ally, A., Balasundaram, M., Bowlby, R., Brooks, D., Carlsen, R., Chuah, E., Dhalla, N., Holt, R., Jones, S. J. M., Kasaian, K., Lee, D., Ma, Y., Marra, M. A., Mayo, M., Moore, R. A., Mungall, A. J., Mungall, K., Robertson, A. G., Sadeghi, S., Schein, J. E., Sipahimalani, P., Tam, A., Thiessen, N., Tse, K., Wong, T., Berger, A. C., Beroukhi, R., Cherniack, A. D., Cibulskis, C., Gabriel, S. B., Gao, G. F., Ha, G., Meyerson, M., Schumacher, S. E., Shih, J., Kucherlapati, M. H., Kucherlapati, R. S., Baylin, S., Cope, L., Danilova, L., Bootwalla, M. S., Lai, P. H., Maglinte, D. T., Berg, D. J. V. D., Weisenberger, D. J., Auman, J. T., Balu, S., Bodenheimer, T., Fan, C., Hoadley, K. A., Hoyle, A. P., Jefferys, S. R., Jones, C. D., Meng, S., Mieczkowski, P. A., Mose, L. E., Perou, A. H., Perou, C. M., Roach, J., Shi, Y., Simons, J. V., Skelly, T., Soloway, M. G., Tan, D., Veluvolu, U., Fan, H., Hinoue, T., Laird, P. W., Shen, H., Zhou, W., Bellair, M., Chang, K., Covington, K., Creighton, C. J., Dinh, H., Doddapaneni, H., Donehower, L. A., Drummond, J., Gibbs, R. A., Glenn, R., Hale, W., Han, Y., Hu, J., Korchina, V., Lee, S., Lewis, L., Li, W., Liu, X., Morgan, M., Morton, D., Muzny, D., Santibanez, J., Sheth, M., Shinbrot, E., Wang, L., Wang, M., Wheeler, D. A., Xi, L., Zhao, F., Hess, J., Appelbaum, E. L., Bailey, M., Cordes, M. G., Ding, L., Fronick, C. C., Fulton, L. A., Fulton, R. S., Kandoth, C., Mardis, E. R., McLellan, M. D., Miller, C. A., Schmidt, H. K., Wilson, R. K., Crain, D., Curley, E., Gardner, J., Lau, K., Mallery, D., Morris, S., Paulauskis, J., Penny, R., Shelton, C., Shelton, T., Sherman, M., Thompson, E., Yena, P., Bowen, J., Gastier-Foster, J. M., Gerken, M., Leraas, K. M., Lichtenberg, T. M., Ramirez, N. C., Wise, L., Zmuda, E., Corcoran, N., Costello, T., Hovens, C., Carvalho, A. L., Carvalho, A. C. d., Fregnani, J. H., Longatto-Filho, A., Reis, R. M., Scapulatempo-Neto, C., Silveira, H. C. S., Vidal, D. O., Burnette, A., Eschbacher, J., Hermes, B., Noss, A., Singh, R., Anderson, M. L., Castro, P. D., Ittmann, M., Huntsman, D., Kohl, B., Le, X., Thorp, R., Andry, C., Duffy, E. R., Lyadov, V., Paklina, O., Setdikova, G., Shabunin, A., Tavobilov, M., McPherson, C., Warnick, R., Berkowitz, R., Cramer, D., Feltmate, C., Horowitz, N., Kibel, A., Muto, M., Raut, C. P., Malykh, A., Barnholtz-Sloan, J. S., Barrett, W., Devine, K., Fulop, J., Ostrom, Q. T., Shimmel, K., Wolinsky, Y., Sloan, A. E., Rose, A. D., Giuliante, F., Goodman, M., Karlan, B. Y., Hagedorn, C. H., Eckman, J., Harr, J., Myers, J., Tucker, K., Zach, L. A., Deyarmin, B., Hu, H., Kvecher, L., Larson, C., Mural, R. J., Somiari, S., Vicha, A., Zelinka, T., Bennett, J., Iacocca, M., Rabeno, B., Swanson, P., Latour, M., Lacombe, L., Têtu, B., Bergeron, A., McGraw, M., Staugaitis, S. M., Chabot, J., Hibshoosh, H., Sepulveda, A., Su, T., Wang, T., Potapova, O., Voronina, O., Desjardins, L., Mariani, O., Roman-Roman, S., Sastre, X., Stern, M.-H., Cheng, F., Signoretti, S., Berchuck, A., Bigner, D., Lipp, E., Marks, J., McCall, S., McLendon, R., Secord, A., Sharp, A., Behera, M., Brat, D. J., Chen, A., Delman, K., Force, S., Khuri, F., Magliocca, K., Maithel, S., Olson, J. J., Owonikoko, T., Pickens, A., Ramalingam, S., Shin, D. M., Sica, G., Meir, E. G. V., Zhang, H.,

Eijckenboom, W., Gillis, A., Korpershoek, E., Looijenga, L., Oosterhuis, W., Stoop, H., Kessel, K. E. v., Zwarthoff, E. C., Calatozzolo, C., Cuppini, L., Cuzzubbo, S., DiMeco, F., Finocchiaro, G., Mattei, L., Perin, A., Pollo, B., Chen, C., Houck, J., Lohavanichbutr, P., Hartmann, A., Stoehr, C., Stoehr, R., Taubert, H., Wach, S., Wullich, B., Kycler, W., Murawa, D., Wiznerowicz, M., Chung, K., Edenfield, W. J., Martin, J., Baudin, E., Bubley, G., Bueno, R., Rienzo, A. D., Richards, W. G., Kalkanis, S., Mikkelsen, T., Noushmehr, H., Scarpace, L., Girard, N., Aymerich, M., Campo, E., Giné, E., Guillermo, A. L., Bang, N. V., Hanh, P. T., Phu, B. D., Tang, Y., Colman, H., Evason, K., Dottino, P. R., Martignetti, J. A., Gabra, H., Juhl, H., Akeredolu, T., Stepa, S., Hoon, D., Ahn, K., Kang, K. J., Beuschlein, F., Breggia, A., Birrer, M., Bell, D., Borad, M., Bryce, A. H., Castle, E., Chandan, V., Cheville, J., Copland, J. A., Farnell, M., Flotte, T., Giama, N., Ho, T., Kendrick, M., Kocher, J.-P., Kopp, K., Moser, C., Nagorney, D., O'Brien, D., O'Neill, B. P., Patel, T., Petersen, G., Que, F., Rivera, M., Roberts, L., Smallridge, R., Smyrk, T., Stanton, M., Thompson, R. H., Torbenson, M., Yang, J. D., Zhang, L., Brimo, F., Ajani, J. A., Gonzalez, A. M. A., Behrens, C., Bondaruk, O., Broaddus, R., Czerniak, B., Esmaeli, B., Fujimoto, J., Gershenwald, J., Guo, C., Lazar, A. J., Logothetis, C., Meric-Bernstam, F., Moran, C., Ramondetta, L., Rice, D., Sood, A., Tamboli, P., Thompson, T., Troncoso, P., Tsao, A., Wistuba, I., Carter, C., Haydu, L., Hersey, P., Jakrot, V., Kakavand, H., Kefford, R., Lee, K., Long, G., Mann, G., Quinn, M., Saw, R., Scolyer, R., Shannon, K., Spillane, A., Stretch, J., Synott, M., Thompson, J., Wilmott, J., Al-Ahmadie, H., Chan, T. A., Ghossein, R., Gopalan, A., Levine, D. A., Reuter, V., Singer, S., Singh, B., Tien, N. V., Broudy, T., Mirsaidi, C., Nair, P., Drwiega, P., Miller, J., Smith, J., Zaren, H., Park, J.-W., Hung, N. P., Kebebew, E., Linehan, W. M., Metwalli, A. R., Pacak, K., Pinto, P. A., Schiffman, M., Schmidt, L. S., Vocke, C. D., Wentzensen, N., Worrell, R., Yang, H., Moncrieff, M., Goparaju, C., Melamed, J., Pass, H., Botnariuc, N., Caraman, I., Cernat, M., Chemencedji, I., Clipca, A., Doruc, S., Gorincioi, G., Mura, S., Pirtac, M., Stancul, I., Tcaciuc, D., Albert, M., Alexopoulou, I., Arnaout, A., Bartlett, J., Engel, J., Gilbert, S., Parfitt, J., Sekhon, H., Thomas, G., Rassl, D. M., Rintoul, R. C., Bifulco, C., Tamakawa, R., Urba, W., Hayward, N., Timmers, H., Antenucci, A., Facciolo, F., Grazi, G., Marino, M., Merola, R., Krijger, R. d., Gimenez-Roqueplo, A.-P., Piché, A., Chevalier, S., McKercher, G., Birsoy, K., Barnett, G., Brewer, C., Farver, C., Naska, T., Pennell, N. A., Raymond, D., Schilero, C., Smolenski, K., Williams, F., Morrison, C., Borgia, J. A., Liptay, M. J., Pool, M., Seder, C. W., Junker, K., Omberg, L., Dinkin, M., Manikhas, G., Alvaro, D., Bragazzi, M. C., Cardinale, V., Carpino, G., Gaudio, E., Chesla, D., Cottingham, S., Dubina, M., Moiseenko, F., Dhanasekaran, R., Becker, K.-F., Janssen, K.-P., Slotta-Huspenina, J., Abdel-Rahman, M. H., Aziz, D., Bell, S., Cebulla, C. M., Davis, A., Duell, R., Elder, J. B., Hilty, J., Kumar, B., Lang, J., Lehman, N. L., Mandt, R., Nguyen, P., Pilarski, R., Rai, K., Schoenfield, L., Senecal, K., Wakely, P., Hansen, P., Lechan, R., Powers, J., Tischler, A., Grizzle, W. E., Sexton, K. C., Kastl, A., Henderson, J., Porten, S., Waldmann, J., Fassnacht, M., Asa, S. L., Schadendorf, D., Couce, M., Graefen, M., Huland, H., Sauter, G., Schlomm, T., Simon, R., Tennstedt, P., Olabode, O., Nelson, M., Bathe, O., Carroll, P. R., Chan, J. M., Disaia, P., Glenn, P., Kelley, R. K., Landen, C. N., Phillips, J., Prados, M., Simko, J., Smith-McCune, K., VandenBerg, S., Roggin, K., Fehrenbach, A., Kandler, A., Sifri, S., Steele, R., Jimeno, A., Carey, F., Forgie, I., Mannelli, M., Carney, M., Hernandez, B., Campos, B., Herold-Mende, C., Jungk, C., Unterberg, A., Deimling, A. v., Bossler, A., Galbraith, J., Jacobus, L., Knudson,

- M., Knutson, T., Ma, D., Milhem, M., Sigmund, R., Godwin, A. K., Madan, R., Rosenthal, H. G., Adebamowo, C., Adebamowo, S. N., Boussioutas, A., Beer, D., Giordano, T., Mes-Masson, A.-M., Saad, F., Bocklage, T., Landrum, L., Mannel, R., Moore, K., Moxley, K., Postier, R., Walker, J., Zuna, R., Feldman, M., Valdivieso, F., Dhir, R., Luketich, J., Pinero, E. M. M., Quintero-Aguilo, M., Carlotti, C. G., Santos, J. S. D., Kemp, R., Sankarankuty, A., Tirapelli, D., Catto, J., Agnew, K., Swisher, E., Creaney, J., Robinson, B., Shelley, C. S., Godwin, E. M., Kendall, S., Shipman, C., Bradford, C., Carey, T., Haddad, A., Moyer, J., Peterson, L., Prince, M., Rozek, L., Wolf, G., Bowman, R., Fong, K. M., Yang, I., Korst, R., Rathmell, W. K., Fantacone-Campbell, J. L., Hooke, J. A., Kovatich, A. J., Shriver, C. D., DiPersio, J., Drake, B., Govindan, R., Heath, S., Ley, T., Tine, B. V., Westervelt, P., Rubin, M. A., Lee, J. I., Aredes, N. D., Mariamidze, A., Stuart, J. M., Benz, C. C., and Laird, P. W. (2018). Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000 Tumors from 33 Types of Cancer. *Cell*, 173(2):291–304.e6.
- Hooke, R. (1667). *Micrographia: Or, Some Physiological Descriptions of Minute Bodies Made by Magnifying Glasses, with Observations and Inquiries Thereupon*. History of microscopy series. Science Heritage.
- Hori, S., Nomura, T., and Sakaguchi, S. (2003). Control of Regulatory T Cell Development by the Transcription Factor Foxp3. *Science*, 299(5609):1057–1061.
- Hou, R., Denisenko, E., and Forrest, A. R. R. (2019). scMatch: a single-cell gene expression profile annotation tool using reference datasets. *Bioinformatics*.
- Hoyer, F. F., Naxerova, K., Schloss, M. J., Hulsmans, M., Nair, A. V., Dutta, P., Calcagno, D. M., Herisson, F., Anzai, A., Sun, Y., Wojtkiewicz, G., Rohde, D., Frodermann, V., Vandoorne, K., Courties, G., Iwamoto, Y., Garris, C. S., Williams, D. L., Breton, S., Brown, D., Whalen, M., Libby, P., Pittet, M. J., King, K. R., Weissleder, R., Swirski, F. K., and Nahrendorf, M. (2019). Tissue-Specific Macrophage Responses to Remote Injury Impact the Outcome of Subsequent Local Immune Challenge. *Immunity*, 51(5):899–914.e7.
- Hu, H., Miao, Y.-R., Jia, L.-H., Yu, Q.-Y., Zhang, Q., and Guo, A.-Y. (2019). AnimalTFDB 3.0: a comprehensive resource for annotation and prediction of animal transcription factors. *Nucleic Acids Research*, 47(D1):D33–D38.
- Hu, Z.-Q. and Zhao, W.-H. (2015). The IL-33/ST2 axis is specifically required for development of adipose tissue-resident regulatory T cells. *Cell. Mol. Immunol.*, 12(5):521–524.
- Huehn, J., Siegmund, K., Lehmann, J. C. U., Siewert, C., Haubold, U., Feuerer, M., Debes, G. F., Lauber, J., Frey, O., Przybylski, G. K., Niesner, U., Rosa, M. d. l., Schmidt, C. A., Bräuer, R., Buer, J., Scheffold, A., and Hamann, A. (2004). Developmental Stage, Phenotype, and Migration Distinguish Naive- and Effector/Memory-like CD4+ Regulatory T Cells. *Journal of Experimental Medicine*, 199(3):303–313.
- Hughes, T. K., Wadsworth, M. H., Gierahn, T. M., Do, T., Weiss, D., Andrade, P. R., Ma, F., Silva, B. J. d. A., Shao, S., Tsoi, L. C., Ordovas-Montanes, J., Gudjonsson, J. E.,

- Modlin, R. L., Love, J. C., and Shalek, A. K. (2019). Highly Efficient, Massively-Parallel Single-Cell RNA-Seq Reveals Cellular States and Molecular Features of Human Skin Pathology. *bioRxiv*, page 689273.
- Ikebuchi, R., Teraguchi, S., Vandenbon, A., Honda, T., Shand, F. H. W., Nakanishi, Y., Watanabe, T., and Tomura, M. (2016). A rare subset of skin-tropic regulatory T cells expressing Il10/Gzmb inhibits the cutaneous immune response. *Sci. Rep.*, 6:35002.
- Islam, S., Kjällquist, U., Moliner, A., Zajac, P., Fan, J.-B., Lönnerberg, P., and Linnarsson, S. (2011). Characterization of the single-cell transcriptional landscape by highly multiplex RNA-seq. *Genome Research*, 21(7):1160–1167.
- Ivanov, I. I., Frutos, R. d. L., Manel, N., Yoshinaga, K., Rifkin, D. B., Sartor, R. B., Finlay, B. B., and Littman, D. R. (2008). Specific microbiota direct the differentiation of IL-17-producing t-helper cells in the mucosa of the small intestine. *Cell Host Microbe*, 4(4):337–349.
- Izcue, A., Coombes, J. L., and Powrie, F. (2009). Regulatory lymphocytes and intestinal inflammation. *Annu. Rev. Immunol.*, 27(1):313–338.
- Jaitin, D. A., Adlung, L., Thaiss, C. A., Weiner, A., Li, B., Descamps, H., Lundgren, P., Bleriot, C., Liu, Z., Deczkowska, A., Keren-Shaul, H., David, E., Zmora, N., Eldar, S. M., Lubezky, N., Shibolet, O., Hill, D. A., Lazar, M. A., Colonna, M., Ginhoux, F., Shapiro, H., Elinav, E., and Amit, I. (2019). Lipid-Associated Macrophages Control Metabolic Homeostasis in a Trem2-Dependent Manner. *Cell*, 178(3):686–698.e14.
- James, K. R., Gomes, T., Elmentaite, R., Kumar, N., Gulliver, E. L., King, H. W., Stares, M. D., Bareham, B. R., Ferdinand, J. R., Petrova, V. N., Polanski, K., Forster, S. C., Jarvis, L. B., Suchanek, O., Howlett, S., James, L. K., Jones, J. L., Meyer, K. B., Clatworthy, M. R., Saeb-Parsy, K., Lawley, T. D., and Teichmann, S. A. (2019). Distinct microbial and immune niches of the human colon. *bioRxiv*, page 2019.12.12.871657.
- Johnson, W. E., Li, C., and Rabinovic, A. (2007). Adjusting batch effects in microarray expression data using empirical Bayes methods. *Biostatistics*, 8(1):118–127.
- Josefowicz, S. Z., Lu, L.-F., and Rudensky, A. Y. (2012). Regulatory T cells: mechanisms of differentiation and function. *Annu. Rev. Immunol.*, 30:531–564.
- Julius, M. H., Masuda, T., and Herzenberg, L. A. (1972). Demonstration That Antigen-Binding Cells Are Precursors of Antibody-Producing Cells After Purification with a Fluorescence-Activated Cell Sorter. *Proceedings of the National Academy of Sciences of the United States of America*, 69(7):1934–1938.
- Kaya-Okur, H. S., Wu, S. J., Codomo, C. A., Pledger, E. S., Bryson, T. D., Henikoff, J. G., Ahmad, K., and Henikoff, S. (2019). CUT&Tag for efficient epigenomic profiling of small samples and single cells. *Nature Communications*, 10(1):1930.
- Keren-Shaul, H., Kenigsberg, E., Jaitin, D. A., David, E., Paul, F., Tanay, A., and Amit, I. (2019). MARS-seq2.0: an experimental and analytical pipeline for indexed sorting combined with single-cell RNA sequencing. *Nature Protocols*, 14(6):1841–1862.

- Kim, S. V., Xiang, W. V., Kwak, C., Yang, Y., Lin, X. W., Ota, M., Sarpel, U., Rifkin, D. B., Xu, R., and Littman, D. R. (2013). GPR15-mediated homing controls immune homeostasis in the large intestine mucosa. *Science*, 340(6139):1456–1459.
- Kimpton, W. G., Washington, E. A., Cahill, R. N. P., and Miyasaka, M. (1995). Virgin $\alpha\beta$ and $\gamma\delta$ T cells recirculate extensively through peripheral tissues and skin during normal development of the fetal immune system. *Int. Immunol.*, 7(10):1567–1577.
- Kiselev, V. Y., Yiu, A., and Hemberg, M. (2018). scmap: projection of single-cell RNA-seq data across data sets. *Nature Methods*, 15(5):359–362.
- Klein, A. M., Mazutis, L., Akartuna, I., Tallapragada, N., Veres, A., Li, V., Peshkin, L., Weitz, D. A., and Kirschner, M. W. (2015). Droplet Barcoding for Single-Cell Transcriptomics Applied to Embryonic Stem Cells. *Cell*, 161(5):1187–1201.
- Korsunsky, I., Fan, J., Slowikowski, K., Zhang, F., Wei, K., Baglaenko, Y., Brenner, M., Loh, P.-R., and Raychaudhuri, S. (2018). Fast, sensitive, and accurate integration of single cell data with Harmony. *bioRxiv*, page 461954.
- Krangel, M. S. (2009). Mechanics of T cell receptor gene rearrangement. *Current Opinion in Immunology*, 21(2):133–139.
- Kryuchkova-Mostacci, N. and Robinson-Rechavi, M. (2017). A benchmark of gene expression tissue-specificity metrics. *Briefings in Bioinformatics*, 18(2):205–214.
- Kumar, B. V., Connors, T. J., and Farber, D. L. (2018). Human T Cell Development, Localization, and Function throughout Life. *Immunity*, 48(2):202–213.
- Köhler, N. D., Büttner, M., and Theis, F. J. (2019). Deep learning does not outperform classical machine learning for cell-type annotation. *bioRxiv*, page 653907.
- La Manno, G., Gyllborg, D., Codeluppi, S., Nishimura, K., Salto, C., Zeisel, A., Borm, L. E., Stott, S. R. W., Toledo, E. M., Villaescusa, J. C., Lönnerberg, P., Ryge, J., Barker, R. A., Arenas, E., and Linnarsson, S. (2016). Molecular Diversity of Midbrain Development in Mouse, Human, and Stem Cells. *Cell*, 167(2):566–580.e19.
- Laurent, P., Jolivel, V., Manicki, P., Chiu, L., Contin-Bordes, C., Truchetet, M.-E., and Pradeu, T. (2017). Immune-Mediated Repair: A Matter of Plasticity. *Frontiers in Immunology*, 8.
- Lavin, Y., Winter, D., Blecher-Gonen, R., David, E., Keren-Shaul, H., Merad, M., Jung, S., and Amit, I. (2014). Tissue-Resident Macrophage Enhancer Landscapes Are Shaped by the Local Microenvironment. *Cell*, 159(6):1312–1326.
- Leeuwenhoeck M (1674). Microscopical observations from Leeuwenhoeck, concerning blood, milk, bones, the brain, spittle, and cuticula, &c. communicated by the said observer to the Publisher in a letter, dated June 1. 1674. *Philosophical Transactions of the Royal Society of London*, 9(106):121–131.
- Leeuwenhoek Antoni Van (1677). Observationes D. Anthonii Lewenhoeck, de natis'e semine genitali animalculis. *Philosophical Transactions of the Royal Society of London*, 12(142):1040–1046.

- Li, C., DiSpirito, J. R., Zemmour, D., Spallanzani, R. G., Kuswanto, W., Benoist, C., and Mathis, D. (2018a). TCR transgenic mice reveal stepwise, multi-site acquisition of the distinctive Fat-Treg phenotype. *Cell*, 174(2):285–299.e12.
- Li, C., Liu, B., Kang, B., Liu, Z., Liu, Y., Ren, X., and Zhang, Z. (2019a). SciBet: a fast classifier for cell type identification using single cell RNA sequencing data. *bioRxiv*, page 645358.
- Li, J., Tan, J., Martino, M. M., and Lui, K. O. (2018b). Regulatory T-Cells: Potential Regulator of Tissue Repair and Regeneration. *Frontiers in Immunology*, 9.
- Li, J. J., Huang, H., Bickel, P. J., and Brenner, S. E. (2014). Comparison of *D. melanogaster* and *C. elegans* developmental stages, tissues, and cells by modENCODE RNA-seq data. *Genome Research*, 24(7):1086–1101.
- Li, N., Unen, V. v., Abdelaal, T., Guo, N., Kasatskaya, S. A., Ladell, K., McLaren, J. E., Egorov, E. S., Izraelson, M., Lopes, S. M. C. d. S., Höllt, T., Britanova, O. V., Eggermont, J., Miranda, N. F. C. C. d., Chudakov, D. M., Price, D. A., Lelieveldt, B. P. F., and Koning, F. (2019b). Memory CD4 + T cells are generated in the human fetal intestine. *Nature Immunology*, 20(3):301–312.
- Lieberman, Y., Rokach, L., and Shay, T. (2018). CaSTLe – Classification of single cells by transfer learning: Harnessing the power of publicly available single cell RNA sequencing experiments to annotate new experiments. *PLOS ONE*, 13(10):e0205499.
- Lin, Y., Cao, Y., Kim, H. J., Salim, A., Speed, T. P., Lin, D., Yang, P., and Yang, J. Y. H. (2019). scClassify: hierarchical classification of cells. *bioRxiv*, page 776948.
- Lindeman, I., Emerton, G., Mamanova, L., Snir, O., Polanski, K., Qiao, S.-W., Sollid, L. M., Teichmann, S. A., and Stubbington, M. J. T. (2018). BraCeR: B-cell-receptor reconstruction and clonality inference from single-cell RNA-seq. *Nature Methods*, 15(8):563–565.
- Liston, A. and Gray, D. H. D. (2014). Homeostatic control of regulatory T cell diversity. *Nature Reviews Immunology*, 14(3):154–165.
- Lonsdale, J., Thomas, J., Salvatore, M., Phillips, R., Lo, E., Shad, S., Hasz, R., Walters, G., Garcia, F., Young, N., Foster, B., Moser, M., Karasik, E., Gillard, B., Ramsey, K., Sullivan, S., Bridge, J., Magazine, H., Syron, J., Fleming, J., Siminoff, L., Traino, H., Mosavel, M., Barker, L., Jewell, S., Rohrer, D., Maxim, D., Filkins, D., Harbach, P., Cortadillo, E., Berghuis, B., Turner, L., Hudson, E., Feenstra, K., Sobin, L., Robb, J., Branton, P., Korzeniewski, G., Shive, C., Tabor, D., Qi, L., Groch, K., Nampally, S., Buia, S., Zimmerman, A., Smith, A., Burges, R., Robinson, K., Valentino, K., Bradbury, D., Cosentino, M., Diaz-Mayoral, N., Kennedy, M., Engel, T., Williams, P., Erickson, K., Ardlie, K., Winckler, W., Getz, G., DeLuca, D., MacArthur, D., Kellis, M., Thomson, A., Young, T., Gelfand, E., Donovan, M., Meng, Y., Grant, G., Mash, D., Marcus, Y., Basile, M., Liu, J., Zhu, J., Tu, Z., Cox, N. J., Nicolae, D. L., Gamazon, E. R., Im, H. K., Konkashbaev, A., Pritchard, J., Stevens, M., Flutre, T., Wen, X., Dermitzakis, E. T., Lappalainen, T., Guigo, R., Monlong, J., Sammeth, M., Koller, D., Battle, A., Mostafavi, S., McCarthy, M., Rivas, M., Maller, J., Rusyn, I., Nobel, A., Wright, F., Shabalina, A., Feolo, M., Sharopova, N., Sturcke, A., Paschal, J., Anderson,

- J. M., Wilder, E. L., Derr, L. K., Green, E. D., Struewing, J. P., Temple, G., Volpi, S., Boyer, J. T., Thomson, E. J., Guyer, M. S., Ng, C., Abdallah, A., Colantuoni, D., Insel, T. R., Koester, S. E., Little, A. R., Bender, P. K., Lehner, T., Yao, Y., Compton, C. C., Vaught, J. B., Sawyer, S., Lockhart, N. C., Demchok, J., and Moore, H. F. (2013). The Genotype-Tissue Expression (GTEx) project. *Nature Genetics*, 45:580–585.
- Lopez, R., Regier, J., Cole, M. B., Jordan, M. I., and Yosef, N. (2018). Deep generative modeling for single-cell transcriptomics. *Nature Methods*, 15(12):1053.
- Lotfollahi, M., Wolf, F. A., and Theis, F. J. (2018). Generative modeling and latent space arithmetics predict single-cell perturbation response across cell types, studies and species. *bioRxiv*, page 478503.
- Luckheeram, R. V., Zhou, R., Verma, A. D., and Xia, B. (2012). CD4+T Cells: Differentiation and Functions. *Clinical and Developmental Immunology*, 2012.
- Luecken, M. D. and Theis, F. J. (2019). Current best practices in single-cell RNA-seq analysis: a tutorial. *Molecular Systems Biology*, 15(6):e8746.
- Lönnerberg, T., Svensson, V., James, K. R., Fernandez-Ruiz, D., Sebina, I., Montandon, R., Soon, M. S. F., Fogg, L. G., Nair, A. S., Liligeto, U. N., Stubbington, M. J. T., Ly, L.-H., Bagger, F. O., Zwiessle, M., Lawrence, N. D., Souza-Fonseca-Guimaraes, F., Bunn, P. T., Engwerda, C. R., Heath, W. R., Billker, O., Stegle, O., Haque, A., and Teichmann, S. A. (2017). Single-cell RNA-seq and computational analysis using temporal mixture modeling resolves TH1/TFH fate bifurcation in malaria. *Science Immunology*, 2(9):eaal2192.
- Ma, F. and Pellegrini, M. (2019). Automated identification of Cell Types in Single Cell RNA Sequencing. *bioRxiv*, page 532093.
- Macosko, E. Z., Basu, A., Satija, R., Nemesh, J., Shekhar, K., Goldman, M., Tirosh, I., Bialas, A. R., Kamitaki, N., Martersteck, E. M., Trombetta, J. J., Weitz, D. A., Sanes, J. R., Shalek, A. K., Regev, A., and McCarroll, S. A. (2015). Highly Parallel Genome-wide Expression Profiling of Individual Cells Using Nanoliter Droplets. *Cell*, 161(5):1202–1214.
- Madisson, E., Wilbrey-Clark, A., Miragaia, R. J., Saeb-Parsy, K., Mahbubani, K., Georgakopoulos, N., Harding, P., Polanski, K., Nowicki-Osuch, K., Fitzgerald, R. C., Loudon, K. W., Ferdinand, J. R., Clatworthy, M. R., Tsingene, A., Dongen, S. V., Dabrowska, M., Patel, M., Stubbington, M. J. T., Teichmann, S., Stegle, O., and Meyer, K. B. (2019). Lung, spleen and oesophagus tissue remains stable for scRNAseq in cold preservation. *bioRxiv*, page 741405.
- Malhotra, N., Leyva-Castillo, J. M., Jadhav, U., Barreiro, O., Kam, C., O'Neill, N. K., Meylan, F., Chambon, P., von Andrian, U. H., Siegel, R. M., Wang, E. C., Shivdasani, R., and Geha, R. S. (2018). Ror α -expressing T regulatory cells restrain allergic skin inflammation. *Science Immunology*, 3(21):eaao6923.
- Malik, B. T., Byrne, K. T., Vella, J. L., Zhang, P., Shabaneh, T. B., Steinberg, S. M., Molodtsov, A. K., Bowers, J. S., Angeles, C. V., Paulos, C. M., Huang, Y. H., and Turk, M. J. (2017). Resident memory T cells in the skin mediate durable immunity to melanoma. *Sci Immunol*, 2(10).

- Manno, G. L., Soldatov, R., Zeisel, A., Braun, E., Hochgerner, H., Petukhov, V., Lidschreiber, K., Kastrioti, M. E., Lönnerberg, P., Furlan, A., Fan, J., Borm, L. E., Liu, Z., Bruggen, D. v., Guo, J., He, X., Barker, R., Sundström, E., Castelo-Branco, G., Cramer, P., Adameyko, I., Linnarsson, S., and Kharchenko, P. V. (2018). RNA velocity of single cells. *Nature*, 560(7719):494.
- Masuda, T., Sankowski, R., Staszewski, O., Böttcher, C., Amann, L., Sagar, Scheiwe, C., Nessler, S., Kunz, P., Loo, G. v., Coenen, V. A., Reinacher, P. C., Michel, A., Sure, U., Gold, R., Grün, D., Priller, J., Stadelmann, C., and Prinz, M. (2019). Spatial and temporal heterogeneity of mouse and human microglia at single-cell resolution. *Nature*, 566(7744):388–392.
- Matsushima, H. and Takashima, A. (2010). Bidirectional homing of tregs between the skin and lymph nodes. *J. Clin. Invest.*, 120(3):653–656.
- Mazzarello, P. (1999). A unifying concept: the history of cell theory. *Nature Cell Biology*, 1(1):E13.
- McCarthy, D. J., Campbell, K. R., Lun, A. T. L., and Wills, Q. F. (2017). Scater: pre-processing, quality control, normalization and visualization of single-cell RNA-seq data in R. *Bioinformatics*, 33(8):1179–1186.
- McInnes, L., Healy, J., and Melville, J. (2018). UMAP: Uniform Manifold Approximation and Projection for Dimension Reduction. *arXiv:1802.03426 [cs, stat]*. arXiv: 1802.03426.
- Melé, M., Ferreira, P. G., Reverter, F., DeLuca, D. S., Monlong, J., Sammeth, M., Young, T. R., Goldmann, J. M., Pervouchine, D. D., Sullivan, T. J., Johnson, R., Segrè, A. V., Djebali, S., Niarchou, A., Consortium, T. G., Wright, F. A., Lappalainen, T., Calvo, M., Getz, G., Dermitzakis, E. T., Ardlie, K. G., and Guigó, R. (2015). The human transcriptome across tissues and individuals. *Science*, 348(6235):660–665.
- Menon, R., Otto, E. A., Kokoruda, A., Zhou, J., Zhang, Z., Yoon, E., Chen, Y.-C., Troyanskaya, O., Spence, J. R., Kretzler, M., and Cebrián, C. (2018). Single-cell analysis of progenitor cell dynamics and lineage specification in the human fetal kidney. *Development*, 145(16):dev164038.
- Mereu, E., Iacono, G., Guillaumet-Adkins, A., Moutinho, C., Lunazzi, G., Santos, C., Miguel-Escalada, I., Ferrer, J., Real, F. X., Gut, I., and Heyn, H. (2018). matchScore: Matching Single-Cell Phenotypes Across Tools and Experiments. *bioRxiv*, page 314831.
- Mereu, E., Lafzi, A., Moutinho, C., Ziegenhain, C., MacCarthy, D. J., Alvarez, A., Batlle, E., Sagar, Grün, D., Lau, J. K., Boutet, S. C., Sanada, C., Ooi, A., Jones, R. C., Kaihara, K., Brampton, C., Talaga, Y., Sasagawa, Y., Tanaka, K., Hayashi, T., Nikaido, I., Fischer, C., Sauer, S., Trefzer, T., Conrad, C., Adiconis, X., Nguyen, L. T., Regev, A., Levin, J. Z., Parekh, S., Janjic, A., Wange, L. E., Bagnoli, J. W., Enard, W., Gut, M., Sandberg, R., Gut, I., Stegle, O., and Heyn, H. (2019). Benchmarking Single-Cell RNA Sequencing Protocols for Cell Atlas Projects. *bioRxiv*, page 630087.

- Miragaia, R. J., Gomes, T., Chomka, A., Jardine, L., Riedel, A., Hegazy, A. N., Whibley, N., Tucci, A., Chen, X., Lindeman, I., Emerton, G., Krausgruber, T., Shields, J., Haniffa, M., Powrie, F., and Teichmann, S. A. (2019). Single-Cell Transcriptomics of Regulatory T Cells Reveals Trajectories of Tissue Adaptation. *Immunity*, 50(2):493–504.e7.
- Montoro, D. T., Haber, A. L., Biton, M., Vinarsky, V., Lin, B., Birket, S. E., Yuan, F., Chen, S., Leung, H. M., Villoria, J., Rogel, N., Burgin, G., Tsankov, A. M., Waghray, A., Slyper, M., Waldman, J., Nguyen, L., Dionne, D., Rozenblatt-Rosen, O., Tata, P. R., Mou, H., Shivaraju, M., Bihler, H., Mense, M., Tearney, G. J., Rowe, S. M., Engelhardt, J. F., Regev, A., and Rajagopal, J. (2018). A revised airway epithelial hierarchy includes CFTR-expressing ionocytes. *Nature*, 560(7718):319.
- Mortazavi, A., Williams, B. A., McCue, K., Schaeffer, L., and Wold, B. (2008). Mapping and quantifying mammalian transcriptomes by RNA-Seq. *Nature Methods*, 5(7):621–628.
- Mosmann, T. R., Cherwinski, H., Bond, M. W., Giedlin, M. A., and Coffman, R. L. (1986). Two types of murine helper T cell clone. I. Definition according to profiles of lymphokine activities and secreted proteins. *The Journal of Immunology*, 136(7):2348–2357.
- Muraro, M. J., Dharmadhikari, G., Grün, D., Groen, N., Dielen, T., Jansen, E., van Gorp, L., Engelse, M. A., Carlotti, F., de Koning, E. J. P., and van Oudenaarden, A. (2016). A Single-Cell Transcriptome Atlas of the Human Pancreas. *Cell Systems*, 3(4):385–394.e3.
- Nagar, M., Jacob-Hirsch, J., Vernitsky, H., Berkun, Y., Ben-Horin, S., Amariglio, N., Bank, I., Kloog, Y., Rechavi, G., and Goldstein, I. (2010). TNF Activates a NF- κ B-Regulated Cellular Program in Human CD45ra⁻ Regulatory T Cells that Modulates Their Suppressive Function. *The Journal of Immunology*, 184(7):3570–3581.
- Nitta, N., Sugimura, T., Isozaki, A., Mikami, H., Hiraki, K., Sakuma, S., Iino, T., Arai, F., Endo, T., Fujiwaki, Y., Fukuzawa, H., Hase, M., Hayakawa, T., Hiramatsu, K., Hoshino, Y., Inaba, M., Ito, T., Karakawa, H., Kasai, Y., Koizumi, K., Lee, S., Lei, C., Li, M., Maeno, T., Matsusaka, S., Murakami, D., Nakagawa, A., Oguchi, Y., Oikawa, M., Ota, T., Shiba, K., Shintaku, H., Shirasaki, Y., Suga, K., Suzuki, Y., Suzuki, N., Tanaka, Y., Tezuka, H., Toyokawa, C., Yalikul, Y., Yamada, M., Yamagishi, M., Yamano, T., Yasumoto, A., Yatomi, Y., Yazawa, M., Di Carlo, D., Hosokawa, Y., Uemura, S., Ozeki, Y., and Goda, K. (2018). Intelligent Image-Activated Cell Sorting. *Cell*, 175(1):266–276.e13.
- Nowakowski, T. J., Bhaduri, A., Pollen, A. A., Alvarado, B., Mostajo-Radji, M. A., Lullo, E. D., Haeussler, M., Sandoval-Espinosa, C., Liu, S. J., Velmeshev, D., Ounadjela, J. R., Shuga, J., Wang, X., Lim, D. A., West, J. A., Leyrat, A. A., Kent, W. J., and Kriegstein, A. R. (2017). Spatiotemporal gene expression trajectories reveal developmental hierarchies of the human cortex. *Science*, 358(6368):1318–1323.

- Ohnmacht, C., Park, J.-H., Cording, S., Wing, J. B., Atarashi, K., Obata, Y., Gaboriau-Routhiau, V., Marques, R., Dulauroy, S., Fedoseeva, M., Busslinger, M., Cerf-Bensussan, N., Boneca, I. G., Voehringer, D., Hase, K., Honda, K., Sakaguchi, S., and Eberl, G. (2015). MUCOSAL IMMUNOLOGY. the microbiota regulates type 2 immunity through ROR γ ⁺ T cells. *Science*, 349(6251):989–993.
- Panduro, M., Benoist, C., and Mathis, D. (2016). Tissue tregs. *Annu. Rev. Immunol.*, 34:609–633.
- Park, J.-E., Polański, K., Meyer, K., and Teichmann, S. A. (2018). Fast Batch Alignment of Single Cell Transcriptomes Unifies Multiple Mouse Cell Atlases into an Integrated Landscape. *bioRxiv*, page 397042.
- Patro, R., Duggal, G., Love, M. I., Irizarry, R. A., and Kingsford, C. (2017). Salmon provides fast and bias-aware quantification of transcript expression. *Nat. Methods*, 14(4):417–419.
- Pedregosa, F., Varoquaux, G., Gramfort, A., Michel, V., Thirion, B., Grisel, O., Blondel, M., Prettenhofer, P., Weiss, R., Dubourg, V., Vanderplas, J., Passos, A., Cournapeau, D., Brucher, M., Perrot, M., and Duchesnay, E. (2011). Scikit-learn: Machine learning in Python. *Journal of Machine Learning Research*, 12:2825–2830.
- Picelli, S., Faridani, O. R., Bjorklund, A. K., Winberg, G., Sagasser, S., and Sandberg, R. (2014). Full-length RNA-seq from single cells using Smart-seq2. *Nature Protocols*, 9(1):171–181.
- Plass, M., Solana, J., Wolf, F. A., Ayoub, S., Misios, A., Glažar, P., Obermayer, B., Theis, F. J., Kocks, C., and Rajewsky, N. (2018). Cell type atlas and lineage tree of a whole complex animal by single-cell transcriptomics. *Science*, 360(6391):eaq1723.
- Pliner, H. A., Shendure, J., and Trapnell, C. (2019). Supervised classification enables rapid annotation of cell atlases. *bioRxiv*, page 538652.
- Plitas, G., Konopacki, C., Wu, K., Bos, P. D., Morrow, M., Putintseva, E. V., Chudakov, D. M., and Rudensky, A. Y. (2016). Regulatory T cells exhibit distinct features in human breast cancer. *Immunity*, 45(5):1122–1134.
- Polański, K., Park, J. E., Young, M. D., Miao, Z., Meyer, K. B., and Teichmann, S. A. (2019). BBKNN: Fast Batch Alignment of Single Cell Transcriptomes. *Bioinformatics (Oxford, England)*.
- Popescu, D.-M., Botting, R. A., Stephenson, E., Green, K., Jardine, L., Calderbank, E. F., Efremova, M., Acres, M., Maunder, D., Vegh, P., Goh, I., Gitton, Y., Park, J., Polanski, K., Vento-Tormo, R., Miao, Z., Rowell, R., McDonald, D., Fletcher, J., Dixon, D., Poyner, E., Reynolds, G., Mather, M., Moldovan, C., Mamanova, L., Greig, F., Young, M., Meyer, K., Lisgo, S., Bacardit, J., Fuller, A., Millar, B., Innes, B., Lindsay, S., Stubbington, M. J. T., Kowalczyk, M. S., Li, B., Ashenbrg, O., Tabaka, M., Dionne, D., Tickle, T. L., Slyper, M., Rozenblatt-Rosen, O., Filby, A., Villani, A.-C., Roy, A., Regev, A., Chedotal, A., Roberts, I., Göttgens, B., Laurenti, E., Behjati, S., Teichmann, S. A., and Haniffa, M. (2019). Decoding the development of the blood and immune systems during human fetal liver haematopoiesis. *bioRxiv*, page 654210.

- Prasad, A. and Alizadeh, E. (2019). Cell Form and Function: Interpreting and Controlling the Shape of Adherent Cells. *Trends in Biotechnology*, 37(4):347–357.
- Qiu, X., Zhang, Y., Yang, D., Hosseinzadeh, S., Wang, L., Yuan, R., Xu, S., Ma, Y., Replogle, J., Darmanis, S., Xing, J., and Weissman, J. S. (2019). Mapping Vector Field of Single Cells. *bioRxiv*, page 696724.
- Ramsköld, D., Luo, S., Wang, Y.-C., Li, R., Deng, Q., Faridani, O. R., Daniels, G. A., Khrebtkova, I., Loring, J. F., Laurent, L. C., Schroth, G. P., and Sandberg, R. (2012). Full-length mRNA-Seq from single-cell levels of RNA and individual circulating tumor cells. *Nature Biotechnology*, 30(8):777–782.
- Regev, A., Teichmann, S. A., Lander, E. S., Amit, I., Benoist, C., Birney, E., Bodenmiller, B., Campbell, P., Carninci, P., Clatworthy, M., Clevers, H., Deplancke, B., Dunham, I., Eberwine, J., Eils, R., Enard, W., Farmer, A., Fugger, L., Göttgens, B., Hacohen, N., Haniffa, M., Hemberg, M., Kim, S., Klenerman, P., Kriegstein, A., Lein, E., Linnarsson, S., Lundberg, E., Lundberg, J., Majumder, P., Marioni, J. C., Merad, M., Mhlanga, M., Nawijn, M., Netea, M., Nolan, G., Pe'er, D., Phillipakis, A., Ponting, C. P., Quake, S., Reik, W., Rozenblatt-Rosen, O., Sanes, J., Satija, R., Schumacher, T. N., Shalek, A., Shapiro, E., Sharma, P., Shin, J. W., Stegle, O., Stratton, M., Stubbington, M. J. T., Theis, F. J., Uhlen, M., van Oudenaarden, A., Wagner, A., Watt, F., Weissman, J., Wold, B., Xavier, R., Yosef, N., and Human Cell Atlas Meeting Participants (2017). The Human Cell Atlas. *eLife*, 6:e27041.
- Reimand, J., Arak, T., Adler, P., Kolberg, L., Reisberg, S., Peterson, H., and Vilo, J. (2016). g:profiler-a web server for functional interpretation of gene lists (2016 update). *Nucleic Acids Res.*, 44(W1):W83–9.
- Reinherz, E. L. (2014). Revisiting the Discovery of the $\alpha\beta$ TCR Complex and Its Co-Receptors. *Frontiers in Immunology*, 5.
- Rhodes, D. R., Yu, J., Shanker, K., Deshpande, N., Varambally, R., Ghosh, D., Barrette, T., Pandey, A., and Chinnaiyan, A. M. (2004). Large-scale meta-analysis of cancer microarray data identifies common transcriptional profiles of neoplastic transformation and progression. *Proceedings of the National Academy of Sciences*, 101(25):9309–9314.
- Riedel, A., Shorthouse, D., Haas, L., Hall, B. A., and Shields, J. (2016). Tumor-induced stromal reprogramming drives lymph node transformation. *Nat. Immunol.*, 17(9):1118–1127.
- Ritchie, M. E., Phipson, B., Wu, D., Hu, Y., Law, C. W., Shi, W., and Smyth, G. K. (2015). limma powers differential expression analyses for RNA-sequencing and microarray studies. *Nucleic Acids Research*, 43(7):e47–e47.
- Rodrigues, S. G., Stickels, R. R., Goeva, A., Martin, C. A., Murray, E., Vanderburg, C. R., Welch, J., Chen, L. M., Chen, F., and Macosko, E. Z. (2019). Slide-seq: A scalable technology for measuring genome-wide expression at high spatial resolution. *Science*, 363(6434):1463–1467.

- Rosenberg, A. B., Roco, C. M., Muscat, R. A., Kuchina, A., Sample, P., Yao, Z., Graybuck, L. T., Peeler, D. J., Mukherjee, S., Chen, W., Pun, S. H., Sellers, D. L., Tasic, B., and Seelig, G. (2018). Single-cell profiling of the developing mouse brain and spinal cord with split-pool barcoding. *Science*, 360(6385):176–182.
- Rostom, R., Svensson, V., Teichmann, S. A., and Kar, G. (2017). Computational approaches for interpreting scRNA-seq data. *FEBS Letters*, 591(15):2213–2225.
- Saelens, W., Cannoodt, R., Todorov, H., and Saeys, Y. (2019). A comparison of single-cell trajectory inference methods. *Nature Biotechnology*, 37(5):547.
- Sakaguchi, S. (2004). Naturally arising CD4⁺ regulatory t cells for immunologic self-tolerance and negative control of immune responses. *Annu. Rev. Immunol.*, 22:531–562.
- Sakaguchi, S., Sakaguchi, N., Asano, M., Itoh, M., and Toda, M. (1995). Immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor alpha-chains (CD25). Breakdown of a single mechanism of self-tolerance causes various autoimmune diseases. *The Journal of Immunology*, 155(3):1151–1164.
- Sasagawa, Y., Danno, H., Takada, H., Ebisawa, M., Tanaka, K., Hayashi, T., Kurisaki, A., and Nikaido, I. (2018). Quartz-Seq2: a high-throughput single-cell RNA-sequencing method that effectively uses limited sequence reads. *Genome Biology*, 19(1):29.
- Satija, R., Farrell, J. A., Gennert, D., Schier, A. F., and Regev, A. (2015). Spatial reconstruction of single-cell gene expression data. *Nat. Biotechnol.*, 33(5):495–502.
- Schiering, C., Krausgruber, T., Chomka, A., Fröhlich, A., Adelman, K., Wohlfert, E. A., Pott, J., Griseri, T., Bollrath, J., Hegazy, A. N., Harrison, O. J., Owens, B. M. J., Löhning, M., Belkaid, Y., Fallon, P. G., and Powrie, F. (2014). The alarmin IL-33 promotes regulatory t-cell function in the intestine. *Nature*, 513(7519):564–568.
- Schmitt, N. and Ueno, H. (2015). Regulation of human helper T cell subset differentiation by cytokines. *Current Opinion in Immunology*, 34:130–136.
- Schwann, T. (1847). *Microscopical researches into the accordance in the structure and growth of animals and plants*. Sydenham Society.
- Scialdone, A., Natarajan, K. N., Saraiva, L. R., Proserpio, V., Teichmann, S. A., Stegle, O., Marioni, J. C., and Buettner, F. (2015). Computational assignment of cell-cycle stage from single-cell transcriptome data. *Methods*, 85:54–61.
- Scialdone, A., Tanaka, Y., Jawaid, W., Moignard, V., Wilson, N. K., Macaulay, I. C., Marioni, J. C., and Göttgens, B. (2016). Resolving early mesoderm diversification through single-cell expression profiling. *Nature*, 535(7611):289–293.
- Scott, C. L., T’Jonck, W., Martens, L., Todorov, H., Sichien, D., Soen, B., Bonnardel, J., Prijck, S. D., Vandamme, N., Cannoodt, R., Saelens, W., Vanneste, B., Toussaint, W., Bleser, P. D., Takahashi, N., Vandenabeele, P., Henri, S., Pridans, C., Hume, D. A., Lambrecht, B. N., Baetselier, P. D., Milling, S. W. F., Ginderachter, J. A. V., Malissen,

- B., Berx, G., Beschin, A., Saeys, Y., and Guillems, M. (2018). The Transcription Factor ZEB2 Is Required to Maintain the Tissue-Specific Identities of Macrophages. *Immunity*, 49(2):312–325.e5.
- Sefik, E., Geva-Zatorsky, N., Oh, S., Konnikova, L., Zemmour, D., McGuire, A. M., Burzyn, D., Ortiz-Lopez, A., Lobera, M., Yang, J., Ghosh, S., Earl, A., Snapper, S. B., Jupp, R., Kasper, D., Mathis, D., and Benoist, C. (2015). MUCOSAL IMMUNOLOGY. individual intestinal symbionts induce a distinct population of rory⁺ regulatory T cells. *Science*, 349(6251):993–997.
- Segal, J. M., Kent, D., Wesche, D. J., Ng, S. S., Serra, M., Oulès, B., Kar, G., Emerton, G., Blackford, S. J. I., Darmanis, S., Miquel, R., Luong, T. V., Yamamoto, R., Bonham, A., Jassem, W., Heaton, N., Vigilante, A., King, A., Sancho, R., Teichmann, S., Quake, S. R., Nakauchi, H., and Rashid, S. T. (2019). Single cell analysis of human foetal liver captures the transcriptional profile of hepatobiliary hybrid progenitors. *Nature Communications*, 10(1):1–14.
- Segerstolpe, A., Palasantza, A., Eliasson, P., Andersson, E.-M., Andreasson, A.-C., Sun, X., Picelli, S., Sabirsh, A., Clausen, M., Bjursell, M. K., Smith, D. M., Kasper, M., Ämmälä, C., and Sandberg, R. (2016). Single-Cell Transcriptome Profiling of Human Pancreatic Islets in Health and Type 2 Diabetes. *Cell Metabolism*, 24(4):593–607.
- Sharma, A. and Rudra, D. (2018). Emerging Functions of Regulatory T Cells in Tissue Homeostasis. *Frontiers in Immunology*, 9.
- Sharma, M. D., Huang, L., Choi, J.-H., Lee, E.-J., Wilson, J. M., Lemos, H., Pan, F., Blazar, B. R., Pardoll, D. M., Mellor, A. L., Shi, H., and Munn, D. H. (2013). An inherently bifunctional subset of foxp3⁺ T helper cells is controlled by the transcription factor eos. *Immunity*, 38(5):998–1012.
- Shekhar, K., Lapan, S. W., Whitney, I. E., Tran, N. M., Macosko, E. Z., Kowalczyk, M., Adiconis, X., Levin, J. Z., Nemesh, J., Goldman, M., McCarroll, S. A., Cepko, C. L., Regev, A., and Sanes, J. R. (2016). Comprehensive Classification of Retinal Bipolar Neurons by Single-Cell Transcriptomics. *Cell*, 166(5):1308–1323.e30.
- Sherwood, A. M., Emerson, R. O., Scherer, D., Habermann, N., Buck, K., Staffa, J., Desmarais, C., Halama, N., Jaeger, D., Schirmacher, P., Herpel, E., Kloor, M., Ulrich, A., Schneider, M., Ulrich, C. M., and Robins, H. (2013). Tumor-infiltrating lymphocytes in colorectal tumors display a diversity of T cell receptor sequences that differ from the T cells in adjacent mucosal tissue. *Cancer Immunol. Immunother.*, 62(9):1453–1461.
- Shin, D., Lee, W., Lee, J. H., and Bang, D. (2019). Multiplexed single-cell RNA-seq via transient barcoding for simultaneous expression profiling of various drug perturbations. *Science Advances*, 5(5):eaav2249.
- Shulse, C. N., Cole, B. J., Ciobanu, D., Lin, J., Yoshinaga, Y., Gouran, M., Turco, G. M., Zhu, Y., O'Malley, R. C., Brady, S. M., and Dickel, D. E. (2019). High-Throughput Single-Cell Transcriptome Profiling of Plant Cell Types. *Cell Reports*, 27(7):2241–2247.e4.

- Shyamsundar, R., Kim, Y. H., Higgins, J. P., Montgomery, K., Jorden, M., Sethuraman, A., van de Rijn, M., Botstein, D., Brown, P. O., and Pollack, J. R. (2005). A DNA microarray survey of gene expression in normal human tissues. *Genome Biology*, 6(3):R22.
- Simoës, A. E., Di Lorenzo, B., and Silva-Santos, B. (2018). Molecular Determinants of Target Cell Recognition by Human $\gamma\delta$ T Cells. *Frontiers in Immunology*, 9.
- Smillie, C. S., Biton, M., Ordovas-Montanes, J., Sullivan, K. M., Burgin, G., Graham, D. B., Herbst, R. H., Rogel, N., Slyper, M., Waldman, J., Sud, M., Andrews, E., Velonias, G., Haber, A. L., Jagadeesh, K., Vickovic, S., Yao, J., Stevens, C., Dionne, D., Nguyen, L. T., Villani, A.-C., Hofree, M., Creasey, E. A., Huang, H., Rozenblatt-Rosen, O., Garber, J. J., Khalili, H., Desch, A. N., Daly, M. J., Ananthakrishnan, A. N., Shalek, A. K., Xavier, R. J., and Regev, A. (2019). Intra- and Inter-cellular Rewiring of the Human Colon during Ulcerative Colitis. *Cell*, 178(3):714–730.e22.
- Sohni, A., Tan, K., Song, H.-W., Burow, D., de Rooij, D. G., Laurent, L., Hsieh, T.-C., Rabah, R., Hammoud, S. S., Vicini, E., and Wilkinson, M. F. (2019). The Neonatal and Adult Human Testis Defined at the Single-Cell Level. *Cell Reports*, 26(6):1501–1517.e4.
- Sonawane, A. R., Platig, J., Fagny, M., Chen, C.-Y., Paulson, J. N., Lopes-Ramos, C. M., DeMeo, D. L., Quackenbush, J., Glass, K., and Kuijjer, M. L. (2017). Understanding Tissue-Specific Gene Regulation. *Cell Reports*, 21(4):1077–1088.
- Soneson, C. and Robinson, M. D. (2018). Bias, robustness and scalability in single-cell differential expression analysis. *Nature Methods*, 15(4):255–261.
- Stein-O'Brien, G. L., Clark, B. S., Sherman, T., Zibetti, C., Hu, Q., Sealfon, R., Liu, S., Qian, J., Colantuoni, C., Blackshaw, S., Goff, L. A., and Fertig, E. J. (2019). Decomposing Cell Identity for Transfer Learning across Cellular Measurements, Platforms, Tissues, and Species. *Cell Systems*, 8(5):395–411.e8.
- Stoeckius, M., Hafemeister, C., Stephenson, W., Houck-Loomis, B., Chattopadhyay, P. K., Swerdlow, H., Satija, R., and Smibert, P. (2017). Simultaneous epitope and transcriptome measurement in single cells. *Nature Methods*, 14(9):865–868.
- Stoeckius, M., Zheng, S., Houck-Loomis, B., Hao, S., Yeung, B. Z., Mauck, W. M., Smibert, P., and Satija, R. (2018). Cell Hashing with barcoded antibodies enables multiplexing and doublet detection for single cell genomics. *Genome Biology*, 19(1):224.
- Stuart, T., Butler, A., Hoffman, P., Hafemeister, C., Papalexi, E., Mauck, W. M., Hao, Y., Stoeckius, M., Smibert, P., and Satija, R. (2019). Comprehensive Integration of Single-Cell Data. *Cell*, 177(7):1888–1902.e21.
- Stubbington, M. J. T., Lönnberg, T., Proserpio, V., Clare, S., Speak, A. O., Dougan, G., and Teichmann, S. A. (2016). T cell fate and clonality inference from single-cell transcriptomes. *Nature Methods*, 13(4):329–332.

- Subramanian, A., Tamayo, P., Mootha, V. K., Mukherjee, S., Ebert, B. L., Gillette, M. A., Paulovich, A., Pomeroy, S. L., Golub, T. R., Lander, E. S., and Mesirov, J. P. (2005). Gene set enrichment analysis: A knowledge-based approach for interpreting genome-wide expression profiles. *Proceedings of the National Academy of Sciences*, 102(43):15545–15550.
- Svensson, V. and Beltrame, E. d. V. (2019). A curated database reveals trends in single cell transcriptomics. *bioRxiv*, page 742304.
- Svensson, V., Beltrame, E. d. V., and Pachter, L. (2019). Quantifying the tradeoff between sequencing depth and cell number in single-cell RNA-seq. *bioRxiv*, page 762773.
- Svensson, V., Vento-Tormo, R., and Teichmann, S. A. (2018). Exponential scaling of single-cell RNA-seq in the past decade. *Nature Protocols*, 13(4):599–604.
- Takeda, A., Hollmén, M., Dermadi, D., Pan, J., Brulois, K. F., Kaukonen, R., Lönnberg, T., Boström, P., Koskivuo, I., Irjala, H., Miyasaka, M., Salmi, M., Butcher, E. C., and Jalkanen, S. (2019). Single-Cell Survey of Human Lymphatics Unveils Marked Endothelial Cell Heterogeneity and Mechanisms of Homing for Neutrophils. *Immunity*.
- Tan, Y. and Cahan, P. (2018). SingleCellNet: a computational tool to classify single cell RNA-Seq data across platforms and across species. *bioRxiv*, page 508085.
- Tang, F., Barbacioru, C., Wang, Y., Nordman, E., Lee, C., Xu, N., Wang, X., Bodeau, J., Tuch, B. B., Siddiqui, A., Lao, K., and Surani, M. A. (2009). mRNA-Seq whole-transcriptome analysis of a single cell. *Nature Methods*, 6(5):377–382.
- Taylor, D. M., Aronow, B. J., Tan, K., Bernt, K., Salomonis, N., Greene, C. S., Frolova, A., Henrickson, S. E., Wells, A., Pei, L., Jaiswal, J. K., Whitsett, J., Hamilton, K. E., MacParland, S. A., Kelsen, J., Heuckeroth, R. O., Potter, S. S., Vella, L. A., Terry, N. A., Ghanem, L. R., Kennedy, B. C., Helbig, I., Sullivan, K. E., Castelo-Soccio, L., Kreigstein, A., Herse, F., Nawijn, M. C., Koppelman, G. H., Haendel, M., Harris, N. L., Rokita, J. L., Zhang, Y., Regev, A., Rozenblatt-Rosen, O., Rood, J. E., Tickle, T. L., Vento-Tormo, R., Alimohamed, S., Lek, M., Mar, J. C., Loomes, K. M., Barrett, D. M., Uapinyoying, P., Beggs, A. H., Agrawal, P. B., Chen, Y.-W., Muir, A. B., Garmire, L. X., Snapper, S. B., Nazarian, J., Seeholzer, S. H., Fazelinia, H., Singh, L. N., Faryabi, R. B., Raman, P., Dawany, N., Xie, H. M., Devkota, B., Diskin, S. J., Anderson, S. A., Rappaport, E. F., Peranteau, W., Wikenheiser-Brokamp, K. A., Teichmann, S., Wallace, D., Peng, T., Ding, Y.-y., Kim, M. S., Xing, Y., Kong, S. W., Bönnemann, C. G., Mandl, K. D., and White, P. S. (2019). The Pediatric Cell Atlas: Defining the Growth Phase of Human Development at Single-Cell Resolution. *Developmental Cell*, 49(1):10–29.
- The Cancer Genome Atlas Research Network, Weinstein, J. N., Collisson, E. A., Mills, G. B., Shaw, K. R. M., Ozenberger, B. A., Ellrott, K., Shmulevich, I., Sander, C., and Stuart, J. M. (2013). The Cancer Genome Atlas Pan-Cancer analysis project. *Nature Genetics*, 45:1113–1120.

- The ENCODE Project Consortium (2012). An integrated encyclopedia of DNA elements in the human genome. *Nature*, 489(7414):57–74.
- Thome, J. J. C., Bickham, K. L., Ohmura, Y., Kubota, M., Matsuoka, N., Gordon, C., Granot, T., Griesemer, A., Lerner, H., Kato, T., and Farber, D. L. (2015). Early-life compartmentalization of human T cell differentiation and regulatory function in mucosal and lymphoid tissues. *Nat. Med.*, 22(1):72–77.
- Titsias, M. K. and Lawrence, N. D. (2010). Bayesian gaussian process latent variable model. *Artif. Intell.*, 9:844–851.
- Traag, V. A., Waltman, L., and Eck, N. J. v. (2019). From Louvain to Leiden: guaranteeing well-connected communities. *Scientific Reports*, 9(1):5233.
- Trapnell, C., Cacchiarelli, D., Grimsby, J., Pokharel, P., Li, S., Morse, M., Lennon, N. J., Livak, K. J., Mikkelsen, T. S., and Rinn, J. L. (2014). The dynamics and regulators of cell fate decisions are revealed by pseudotemporal ordering of single cells. *Nature Biotechnology*, 32(4):381–386.
- Trzpis, M., McLaughlin, P. M., de Leij, L. M., and Harmsen, M. C. (2007). Epithelial Cell Adhesion Molecule. *The American Journal of Pathology*, 171(2):386–395.
- Uhlig, H. H., Coombes, J., Mottet, C., Izcue, A., Thompson, C., Fanger, A., Tannapfel, A., Fontenot, J. D., Ramsdell, F., and Powrie, F. (2006). Characterization of Foxp3+CD4+CD25+ and IL-10-secreting CD4+CD25+ T cells during cure of colitis. *J. Immunol.*, 177(9):5852–5860.
- van den Brink, S. C., Sage, F., Vértesy, Á., Spanjaard, B., Peterson-Maduro, J., Baron, C. S., Robin, C., and van Oudenaarden, A. (2017). Single-cell sequencing reveals dissociation-induced gene expression in tissue subpopulations. *Nat. Methods*, 14(10):935–936.
- Various (2017). What Is Your Conceptual Definition of “Cell Type” in the Context of a Mature Organism? *Cell Systems*, 4(3):255–259.
- Various (2018). Single-cell transcriptomics of 20 mouse organs creates a Tabula Muris. *Nature*, 562(7727):367.
- Vasanthakumar, A., Liao, Y., Teh, P., Pascutti, M. F., Oja, A. E., Garnham, A. L., Gloury, R., Tempany, J. C., Sidwell, T., Cuadrado, E., Tuijnenburg, P., Kuijpers, T. W., Lalaoui, N., Mielke, L. A., Bryant, V. L., Hodgkin, P. D., Silke, J., Smyth, G. K., Nolte, M. A., Shi, W., and Kallies, A. (2017). The TNF receptor Superfamily-NF- κ B axis is critical to maintain effector regulatory T cells in lymphoid and non-lymphoid tissues. *Cell Rep.*, 20(12):2906–2920.
- Vasanthakumar, A., Moro, K., Xin, A., Liao, Y., Gloury, R., Kawamoto, S., Fagarasan, S., Mielke, L. A., Afshar-Sterle, S., Masters, S. L., Nakae, S., Saito, H., Wentworth, J. M., Li, P., Liao, W., Leonard, W. J., Smyth, G. K., Shi, W., Nutt, S. L., Koyasu, S., and Kallies, A. (2015). The transcriptional regulators IRF4, BATF and IL-33 orchestrate development and maintenance of adipose tissue-resident regulatory T cells. *Nat. Immunol.*, 16(3):276–285.

- Veiga-Fernandes, H. and Mucida, D. (2016). Neuro-Immune Interactions at Barrier Surfaces. *Cell*, 165(4):801–811.
- Vento-Tormo, R., Efremova, M., Botting, R. A., Turco, M. Y., Vento-Tormo, M., Meyer, K. B., Park, J.-E., Stephenson, E., Polański, K., Goncalves, A., Gardner, L., Holmqvist, S., Henriksson, J., Zou, A., Sharkey, A. M., Millar, B., Innes, B., Wood, L., Wilbrey-Clark, A., Payne, R. P., Ivarsson, M. A., Lisgo, S., Filby, A., Rowitch, D. H., Bulmer, J. N., Wright, G. J., Stubbington, M. J. T., Haniffa, M., Moffett, A., and Teichmann, S. A. (2018). Single-cell reconstruction of the early maternal–fetal interface in humans. *Nature*, 563(7731):347.
- Verboom, K., Everaert, C., Bolduc, N., Livak, K. J., Yigit, N., Rombaut, D., Anckaert, J., Lee, S., Venø, M. T., Kjems, J., Speleman, F., Mestdagh, P., and Vandesompele, J. (2019). SMARTer single cell total RNA sequencing. *Nucleic Acids Research*, 47(16):e93–e93.
- Vickovic, S., Eraslan, G., Salmén, F., Klughammer, J., Stenbeck, L., Äijö, T., Bonneau, R., Bergensträhle, L., Navarro, J. F., Gould, J., Ronaghi, M., Frisén, J., Lundeberg, J., Regev, A., and Ståhl, P. L. (2019). High-density spatial transcriptomics arrays for in situ tissue profiling. *bioRxiv*, page 563338.
- Villani, A.-C., Satija, R., Reynolds, G., Sarkizova, S., Shekhar, K., Fletcher, J., Griesbeck, M., Butler, A., Zheng, S., Lazo, S., Jardine, L., Dixon, D., Stephenson, E., Nilsson, E., Grundberg, I., McDonald, D., Filby, A., Li, W., Jager, P. L. D., Rozenblatt-Rosen, O., Lane, A. A., Haniffa, M., Regev, A., and Hacohen, N. (2017). Single-cell RNA-seq reveals new types of human blood dendritic cells, monocytes, and progenitors. *Science*, 356(6335):eaah4573.
- Wagner, F. and Yanai, I. (2018). Moana: A robust and scalable cell type classification framework for single-cell RNA-Seq data. *bioRxiv*, page 456129.
- Wang, C.-C., Jamal, L., and Janes, K. A. (2012). Normal morphogenesis of epithelial tissues and progression of epithelial tumors. *Wiley interdisciplinary reviews. Systems biology and medicine*, 4(1):51–78.
- Wang, J., Agarwal, D., Huang, M., Hu, G., Zhou, Z., Conley, V. B., MacMullan, H., and Zhang, N. R. (2018). Transfer learning in single-cell transcriptomics improves data denoising and pattern discovery. *bioRxiv*, page 457879.
- Wang, Y., Hoinka, J., and Przytycka, T. M. (2019). Subpopulation Detection and Their Comparative Analysis across Single-Cell Experiments with scPopCorn. *Cell Systems*, 8(6):506–513.e5.
- Wang, Y. J., Schug, J., Won, K.-J., Liu, C., Naji, A., Avrahami, D., Golson, M. L., and Kaestner, K. H. (2016). Single-Cell Transcriptomics of the Human Endocrine Pancreas. *Diabetes*, 65(10):3028–3038.
- Wang, Z., Gerstein, M., and Snyder, M. (2009). RNA-Seq: a revolutionary tool for transcriptomics. *Nature Reviews Genetics*, 10(1):57–63.
- Watcham, S., Kucinski, I., and Gottgens, B. (2019). New Insights into Haematopoietic Differentiation Landscapes from scRNA-seq. *Blood*, pages blood–2018–08–835355.

- Weaver, C. T., Elson, C. O., Fouser, L. A., and Kolls, J. K. (2013). The Th17 Pathway and Inflammatory Diseases of the Intestines, Lungs, and Skin. *Annual Review of Pathology: Mechanisms of Disease*, 8(1):477–512.
- Welch, J. D., Kozareva, V., Ferreira, A., Vanderburg, C., Martin, C., and Macosko, E. Z. (2019). Single-Cell Multi-omic Integration Compares and Contrasts Features of Brain Cell Identity. *Cell*, 177(7):1873–1887.e17.
- Wheaton, J. D. and Ciofani, M. (2019). JunB controls intestinal effector programs in regulatory T cells. *bioRxiv*, page 772194.
- Wolf, F. A., Angerer, P., and Theis, F. J. (2018). SCANPY: large-scale single-cell gene expression data analysis. *Genome Biology*, 19(1):15.
- Wong, M. T., Ong, D. E. H., Lim, F. S. H., Teng, K. W. W., McGovern, N., Narayanan, S., Ho, W. Q., Cerny, D., Tan, H. K. K., Anicete, R., Tan, B. K., Lim, T. K. H., Chan, C. Y., Cheow, P. C., Lee, S. Y., Takano, A., Tan, E.-H., Tam, J. K. C., Tan, E. Y., Chan, J. K. Y., Fink, K., Bertolotti, A., Ginhoux, F., Curotto de Lafaille, M. A., and Newell, E. W. (2016a). A High-Dimensional Atlas of Human T Cell Diversity Reveals Tissue-Specific Trafficking and Cytokine Signatures. *Immunity*, 45(2):442–456.
- Wong, S. C., Gatt, A., Stamatescu, V., and McDonnell, M. D. (2016b). Understanding data augmentation for classification: when to warp? *arXiv:1609.08764 [cs]*. arXiv:1609.08764.
- Wu, Y. E., Pan, L., Zuo, Y., Li, X., and Hong, W. (2017). Detecting activated cell populations using Single-Cell RNA-Seq. *Neuron*, 96(2):313–329.e6.
- Xie, P., Gao, M., Wang, C., Zhang, J., Noel, P., Yang, C., Von Hoff, D., Han, H., Zhang, M. Q., and Lin, W. (2019). SuperCT: a supervised-learning framework for enhanced characterization of single-cell transcriptomic profiles. *Nucleic Acids Research*, 47(8):e48–e48.
- Yanai, I., Benjamin, H., Shmoish, M., Chalifa-Caspi, V., Shklar, M., Ophir, R., Bar-Even, A., Horn-Saban, S., Safran, M., Domany, E., Lancet, D., and Shmueli, O. (2005). Genome-wide midrange transcription profiles reveal expression level relationships in human tissue specification. *Bioinformatics*, 21(5):650–659.
- Yin, Y., Wang, X. X., and Mariuzza, R. A. (2012). Crystal structure of a complete ternary complex of T-cell receptor, peptide–MHC, and CD4. *Proceedings of the National Academy of Sciences*, 109(14):5405–5410.
- Young, M. D., Mitchell, T. J., Braga, F. A. V., Tran, M. G. B., Stewart, B. J., Ferdinand, J. R., Collord, G., Botting, R. A., Popescu, D.-M., Loudon, K. W., Vento-Tormo, R., Stephenson, E., Cagan, A., Farndon, S. J., Velasco-Herrera, M. D. C., Guzzo, C., Richoz, N., Mamanova, L., Aho, T., Armitage, J. N., Riddick, A. C. P., Mushtaq, I., Farrell, S., Rampling, D., Nicholson, J., Filby, A., Burge, J., Lisgo, S., Maxwell, P. H., Lindsay, S., Warren, A. Y., Stewart, G. D., Sebire, N., Coleman, N., Haniffa, M., Teichmann, S. A., Clatworthy, M., and Behjati, S. (2018). Single-cell transcriptomes from human kidneys reveal the cellular identity of renal tumors. *Science*, 361(6402):594–599.

- Yu, Y., Ma, X., Gong, R., Zhu, J., Wei, L., and Yao, J. (2018). Recent advances in CD8+ regulatory T cell research (Review). *Oncology Letters*, 15(6):8187–8194.
- Zemmour, D., Zilionis, R., Kiner, E., Klein, A. M., Mathis, D., and Benoist, C. (2018). Single-cell gene expression reveals a landscape of regulatory T cell phenotypes shaped by the TCR. *Nature Immunology*, 19(3):291–301.
- Zhang, A. W., O’Flanagan, C., Chavez, E., Lim, J. L., McPherson, A., Wiens, M., Walters, P., Chan, T., Hewitson, B., Lai, D., Mottok, A., Sarkozy, C., Chong, L., Aoki, T., Wang, X., Weng, A. P., McAlpine, J. N., Aparicio, S., Steidl, C., Campbell, K. R., and Shah, S. P. (2019a). Probabilistic cell type assignment of single-cell transcriptomic data reveals spatiotemporal microenvironment dynamics in human cancers. *bioRxiv*, page 521914.
- Zhang, H., Kong, H., Zeng, X., Guo, L., Sun, X., and He, S. (2014). Subsets of regulatory T cells and their roles in allergy. *Journal of Translational Medicine*, 12(1):125.
- Zhang, L., Yu, X., Zheng, L., Zhang, Y., Li, Y., Fang, Q., Gao, R., Kang, B., Zhang, Q., Huang, J. Y., Konno, H., Guo, X., Ye, Y., Gao, S., Wang, S., Hu, X., Ren, X., Shen, Z., Ouyang, W., and Zhang, Z. (2018). Lineage tracking reveals dynamic relationships of T cells in colorectal cancer. *Nature*, 564(7735):268–272.
- Zhang, Z., Luo, D., Zhong, X., Choi, J. H., Ma, Y., Mahrt, E., Guo, W., Stawiski, E. W., Wang, S., Modrusan, Z., Seshagiri, S., Kapur, P., Wang, X., Hon, G. C., Brugarolas, J., and Wang, T. (2019b). SCINA: Semi-Supervised Analysis of Single Cells in silico. *bioRxiv*, page 559872.
- Zheng, G. X. Y., Terry, J. M., Belgrader, P., Ryvkin, P., Bent, Z. W., Wilson, R., Ziraldo, S. B., Wheeler, T. D., McDermott, G. P., Zhu, J., Gregory, M. T., Shuga, J., Montesclaros, L., Underwood, J. G., Masquelier, D. A., Nishimura, S. Y., Schnall-Levin, M., Wyatt, P. W., Hindson, C. M., Bharadwaj, R., Wong, A., Ness, K. D., Beppu, L. W., Deeg, H. J., McFarland, C., Loeb, K. R., Valente, W. J., Ericson, N. G., Stevens, E. A., Radich, J. P., Mikkelsen, T. S., Hindson, B. J., and Bielas, J. H. (2017). Massively parallel digital transcriptional profiling of single cells. *Nature Communications*, 8:14049.
- Zimmermann, B., Robert, N. S. M., Technau, U., and Simakov, O. (2019). Ancient animal genome architecture reflects cell type identities. *Nature Ecology & Evolution*, 3(9):1289–1293.

