

References

- Al Hawas, R., Ren, Q., Ye, S., Karim, Z. A., Filipovich, A. H., and Whiteheart, S. W. (2012). Munc18b/STXBP2 is required for platelet secretion. *Blood*, 120(12):2493–500.
- Alter, G., Malenfant, J. M., and Altfeld, M. (2004). CD107a as a functional marker for the identification of natural killer cell activity. *Journal of Immunological Methods*, 294(1-2):15–22.
- Ammann, S., Schulz, A., Krageloh-Mann, I., Dieckmann, N. M. G., Niethammer, K., Fuchs, S., Eckl, K. M., Plank, R., Werner, R., Altmuller, J., Thiele, H., Nurnberg, P., Bank, J., Strauss, A., von Bernuth, H., zur Stadt, U., Grieve, S., Griffiths, G. M., Lehmberg, K., Hennies, H. C., and Ehl, S. (2016). Mutations in AP3D1 associated with immunodeficiency and seizures define a new type of Hermansky-Pudlak syndrome. *Blood*, 127(8):997–1006.
- Anders, S. and Huber, W. (2010). Differential expression analysis for sequence count data. *Genome Biology*, 11(10):R106.
- Anders, S., McCarthy, D. J., Chen, Y., Okoniewski, M., Smyth, G. K., Huber, W., and Robinson, M. D. (2013). Count-based differential expression analysis of RNA sequencing data using R and Bioconductor. *Nature Protocols*, 8(9):1765–1786.
- Anders, S., Pyl, P. T., and Huber, W. (2015). HTSeq—a Python framework to work with high-throughput sequencing data. *Bioinformatics*, 31(2):166–169.
- Arneson, L. N., Brickshawana, A., Segovis, C. M., Schoon, R. A., Dick, C. J., and Leibson, P. J. (2007). Cutting edge: syntaxin 11 regulates lymphocyte-mediated secretion and cytotoxicity. *Journal of immunology (Baltimore, Md. : 1950)*, 179(6):3397–401.
- Baetz, K., Isaaz, S., and Griffiths, G. M. (1995). Loss of cytotoxic T lymphocyte function in Chediak-Higashi syndrome arises from a secretory defect that prevents lytic granule exocytosis. *Journal of immunology (Baltimore, Md. : 1950)*, 154(11):6122–31.
- Barbosa, M. D. F. S., Nguyen, Q. A., Tchernev, V. T., Ashley, J. A., Detter, J. C., Blaydes, S. M., Brandt, S. J., Chotai, D., Hodgman, C., Solari, R. C. E., Lovett, M., and Kingsmore, S. F. (1996). Identification of the homologous beige and Chediak–Higashi syndrome genes. *Nature*, 382(6588):262.
- Basu, R., Whitlock, B. M., Husson, J., Le Floc'h, A., Jin, W., Oyler-Yaniv, A., Dotiwala, F., Giannone, G., Hivroz, C., Biais, N., Lieberman, J., Kam, L. C., and Huse, M. (2016). Cytotoxic T Cells Use Mechanical Force to Potentiate Target Cell Killing. *Cell*, 165(1):100–110.

- Best, J. A., Blair, D. A., Knell, J., Yang, E., Mayya, V., Doedens, A., Dustin, M. L., Goldrath, A. W., and Immunological Genome Project Consortium (2013). Transcriptional insights into the CD8+ T cell response to infection and memory T cell formation. *Nature Immunology*, 14(4):404–412.
- Betts, M. R., Brenchley, J. M., Price, D. A., De Rosa, S. C., Douek, D. C., Roederer, M., and Koup, R. A. (2003). Sensitive and viable identification of antigen-specific CD8+ T cells by a flow cytometric assay for degranulation. *Journal of immunological methods*, 281(1-2):65–78.
- Bin, N.-R., Jung, C. H., Piggott, C., and Sugita, S. (2013). Crucial role of the hydrophobic pocket region of Munc18 protein in mast cell degranulation. *Proceedings of the National Academy of Sciences*, 110(12):4610–4615.
- Bossi, G. and Griffiths, G. (1999). Degranulation plays an essential part in regulating cell surface expression of Fas ligand in T cells and natural killer cells. *Nature Medicine*, 5(1):90–96.
- Bossi, G. and Griffiths, G. M. (2005). CTL secretory lysosomes: biogenesis and secretion of a harmful organelle. *Seminars in Immunology*, 17(1):87–94.
- Boswell, K. L., James, D. J., Esquibel, J. M., Bruinsma, S., Shirakawa, R., Horiuchi, H., and Martin, T. F. J. (2012). Munc13-4 reconstitutes calcium-dependent SNARE-mediated membrane fusion. *The Journal of cell biology*, 197(2):301–12.
- Bots, M. and Medema, J. P. (2006). Granzymes at a glance. *Journal of Cell Science*, 119(24):5011–5014.
- Bouabe, H. and Okkenhaug, K. (2013). Gene Targeting in Mice: A Review. In *Methods in molecular biology* (Clifton, N.J.), volume 1064, pages 315–336.
- Brownlie, R. J. and Zamoyska, R. (2013). T cell receptor signalling networks: branched, diversified and bounded. *Nature Reviews Immunology*, 13(4):257–269.
- Brunner, K. T., Mauel, J., Cerottini, J. C., and Chapuis, B. (1968). Quantitative assay of the lytic action of immune lymphoid cells on 51-Cr-labelled allogeneic target cells in vitro; inhibition by isoantibody and by drugs. *Immunology*, 14(2):181–96.
- Bryceson, Y. T., Pende, D., Maul-Pavicic, A., Gilmour, K. C., Ufheil, H., Vraetz, T., Chiang, S. C., Marcenaro, S., Meazza, R., Bondzio, I., Walshe, D., Janka, G., Lehmburg, K., Beutel, K., zur Stadt, U., Binder, N., Arico, M., Moretta, L., Henter, J.-I., and Ehl, S. (2012). A prospective evaluation of degranulation assays in the rapid diagnosis of familial hemophagocytic syndromes. *Blood*, 119(12):2754–2763.
- Bryceson, Y. T., Rudd, E., Zheng, C., Edner, J., Ma, D., Wood, S. M., Bechensteen, A. G., Boelens, J. J., Celkan, T., Farah, R. A., Hultenby, K., Winiarski, J., Roche, P. A., Nordenskjold, M., Henter, J.-I., Long, E. O., and Ljunggren, H.-G. (2007). Defective cytotoxic lymphocyte degranulation in syntaxin-11-deficient familial hemophagocytic lymphohistiocytosis 4 (FHL4) patients. *Blood*, 110(6):1906–1915.
- Cantrell, D. (2015). Signaling in Lymphocyte Activation. *Cold Spring Harbor Perspectives in Biology*, 7(6):a018788.

- Carisey, A. F., Mace, E. M., Saeed, M. B., Davis, D. M., and Orange, J. S. (2018). Nanoscale Dynamism of Actin Enables Secretory Function in Cytolytic Cells. *Current Biology*, 28(4):489–502.e9.
- Carr, C. M. and Rizo, J. (2010). At the junction of SNARE and SM protein function. *Current Opinion in Cell Biology*, 22(4):488–495.
- Cetica, V., Hackmann, Y., Grieve, S., Sieni, E., Ciambotti, B., Coniglio, M. L., Pende, D., Gilmour, K., Romagnoli, P., Griffiths, G. M., and Aricò, M. (2015). Patients with Griscelli syndrome and normal pigmentation identify RAB27A mutations that selectively disrupt MUNC13-4 binding. *The Journal of allergy and clinical immunology*, 135(5):1310–8.e1.
- Cetica, V., Santoro, A., Gilmour, K. C., Sieni, E., Beutel, K., Pende, D., Marcenaro, S., Koch, F., Grieve, S., Wheeler, R., Zhao, F., zur Stadt, U., Griffiths, G. M., and Arico, M. (2010). STXBP2 mutations in children with familial haemophagocytic lymphohistiocytosis type 5. *Journal of Medical Genetics*, 47(9):595–600.
- Cheng, J. and Haas, M. (1990). Frequent mutations in the p53 tumor suppressor gene in human leukemia T-cell lines. *Molecular and cellular biology*, 10(10):5502–9.
- Chiang, S. C. C., Theorell, J., Entesarian, M., Meeths, M., Mastafa, M., Al-Herz, W., Frisk, P., Gilmour, K. C., Ifversen, M., Langenskiold, C., Machaczka, M., Naqvi, A., Payne, J., Perez-Martinez, A., Sabel, M., Unal, E., Unal, S., Winiarski, J., Nordenskjold, M., Ljunggren, H.-G., Henter, J.-I., and Bryceson, Y. T. (2013). Comparison of primary human cytotoxic T-cell and natural killer cell responses reveal similar molecular requirements for lytic granule exocytosis but differences in cytokine production. *Blood*, 121(8):1345–1356.
- Chicaybam, L., Sodre, A. L., Curzio, B. A., and Bonamino, M. H. (2013). An Efficient Low Cost Method for Gene Transfer to T Lymphocytes. *PLoS ONE*, 8(3):e60298.
- Cho, S. W., Kim, S., Kim, J. M., and Kim, J.-S. (2013). Targeted genome engineering in human cells with the Cas9 RNA-guided endonuclease. *Nature Biotechnology*, 31(3):230–232.
- Chu, V. T., Graf, R., Wirtz, T., Weber, T., Favret, J., Li, X., Petsch, K., Tran, N. T., Sieweke, M. H., Berek, C., Kühn, R., and Rajewsky, K. (2016a). Efficient CRISPR-mediated mutagenesis in primary immune cells using CrispRGold and a C57BL/6 Cas9 transgenic mouse line. *Proceedings of the National Academy of Sciences*, 113(44):12514–12519.
- Chu, V. T., Weber, T., Graf, R., Sommermann, T., Petsch, K., Sack, U., Volchkov, P., Rajewsky, K., and Kühn, R. (2016b). Efficient generation of Rosa26 knock-in mice using CRISPR/Cas9 in C57BL/6 zygotes. *BMC Biotechnology*, 16(1):4.
- Clark, R. and Griffiths, G. M. (2003). Lytic granules, secretory lysosomes and disease. *Current Opinion in Immunology*, 15(5):516–521.
- Clark, R. H., Stinchcombe, J. C., Day, A., Blott, E., Booth, S., Bossi, G., Hamblin, T., Davies, E. G., and Griffiths, G. M. (2003). Adaptor protein 3-dependent microtubule-mediated movement of lytic granules to the immunological synapse. *Nature Immunology*, 4(11):1111–1120.

- Cong, L., Ran, F. A., Cox, D., Lin, S., Barretto, R., Habib, N., Hsu, P. D., Wu, X., Jiang, W., Marraffini, L. A., and Zhang, F. (2013). Multiplex Genome Engineering Using CRISPR/Cas Systems. *Science*, 339(6121):819–823.
- Cooper, M. D. and Herrin, B. R. (2010). How did our complex immune system evolve? *Nature Reviews Immunology*, 10(1):2–3.
- Cornetta, K. and Anderson, W. F. (1989). Protamine sulfate as an effective alternative to polybrene in retroviral-mediated gene-transfer: implications for human gene therapy. *Journal of virological methods*, 23(2):187–94.
- Cornu, T. I., Mussolini, C., and Cathomen, T. (2017). Refining strategies to translate genome editing to the clinic. *Nature Medicine*, 23(4):415–423.
- Corrigan-Curay, J., Kiem, H.-P., Baltimore, D., O'Reilly, M., Brentjens, R. J., Cooper, L., Forman, S., Gottschalk, S., Greenberg, P., Junghans, R., Heslop, H., Jensen, M., Mackall, C., June, C., Press, O., Powell, D., Ribas, A., Rosenberg, S., Sadelain, M., Till, B., Patterson, A. P., Jambou, R. C., Rosenthal, E., Gargiulo, L., Montgomery, M., and Kohn, D. B. (2014). T-Cell Immunotherapy: Looking Forward. *Molecular Therapy*, 22(9):1564–1574.
- Côte, M., Ménager, M. M., Burgess, A., Mahlaoui, N., Picard, C., Schaffner, C., Al-Manjomi, F., Al-Harbi, M., Alangari, A., Le Deist, F., Gennery, A. R., Prince, N., Cariou, A., Nitschke, P., Blank, U., El-Ghazali, G., Ménasché, G., Latour, S., Fischer, A., and de Saint Basile, G. (2009). Munc18-2 deficiency causes familial hemophagocytic lymphohistiocytosis type 5 and impairs cytotoxic granule exocytosis in patient NK cells. *Journal of Clinical Investigation*, 119(12):3765–3773.
- Coulie, P. G., Van den Eynde, B. J., van der Bruggen, P., and Boon, T. (2014). Tumour antigens recognized by T lymphocytes: at the core of cancer immunotherapy. *Nature Reviews Cancer*, 14(2):135–146.
- Crozat, K., Hoebe, K., Ugolini, S., Hong, N. A., Janssen, E., Rutschmann, S., Mudd, S., Sovath, S., Vivier, E., and Beutler, B. (2007). Jinx, an MCMV susceptibility phenotype caused by disruption of Unc13d: a mouse model of type 3 familial hemophagocytic lymphohistiocytosis. *The Journal of experimental medicine*, 204(4):853–63.
- D'Andrea, D., Grassi, L., Mazzapoda, M., and Tramontano, A. (2013). FIDEA: a server for the functional interpretation of differential expression analysis. *Nucleic acids research*, 41(Web Server issue):W84–8.
- Das, V., Nal, B., Dujeancourt, A., Thoulouze, M.-I., Galli, T., Roux, P., Dautry-Varsat, A., and Alcover, A. (2004). Activation-induced polarized recycling targets T cell antigen receptors to the immunological synapse; involvement of SNARE complexes. *Immunity*, 20(5):577–88.
- de la Roche, M., Asano, Y., and Griffiths, G. M. (2016). Origins of the cytolytic synapse. *Nature Reviews Immunology*, 16(7):421–432.
- de Saint Basile, G., Ménasché, G., and Fischer, A. (2010). Molecular mechanisms of biogenesis and exocytosis of cytotoxic granules. *Nature Reviews Immunology*, 10(8):568–579.

- Dell'Angelica, E. C., Shotelersuk, V., Aguilar, R. C., Gahl, W. A., and Bonifacino, J. S. (1999). Altered trafficking of lysosomal proteins in Hermansky-Pudlak syndrome due to mutations in the beta 3A subunit of the AP-3 adaptor. *Molecular cell*, 3(1):11–21.
- Delville, M., Soheili, T., Bellier, F., Durand, A., Denis, A., Lagresle-Peyrou, C., Cavazzana, M., Andre-Schmutz, I., and Six, E. (2018). A Nontoxic Transduction Enhancer Enables Highly Efficient Lentiviral Transduction of Primary Murine T Cells and Hematopoietic Stem Cells. *Molecular therapy. Methods & clinical development*, 10:341–347.
- Demaison, C., Parsley, K., Brouns, G., Scherr, M., Battmer, K., Kinnon, C., Grez, M., and Thrasher, A. J. (2002). High-Level Transduction and Gene Expression in Hematopoietic Repopulating Cells Using a Human Immunodeficiency Virus Type 1-Based Lentiviral Vector Containing an Internal Spleen Focus Forming Virus Promoter. *Human Gene Therapy*, 13(7):803–813.
- Dieckmann, N. M. G., Frazer, G. L., Asano, Y., Stinchcombe, J. C., and Griffiths, G. M. (2016). The cytotoxic T lymphocyte immune synapse at a glance. *Journal of Cell Science*, 129(15):2881–2886.
- Dobin, A., Davis, C. A., Schlesinger, F., Drenkow, J., Zaleski, C., Jha, S., Batut, P., Chaisson, M., and Gingeras, T. R. (2013). STAR: ultrafast universal RNA-seq aligner. *Bioinformatics*, 29(1):15–21.
- Doedens, A. L., Phan, A. T., Stradner, M. H., Fujimoto, J. K., Nguyen, J. V., Yang, E., Johnson, R. S., and Goldrath, A. W. (2013). Hypoxia-inducible factors enhance the effector responses of CD8+ T cells to persistent antigen. *Nature Immunology*, 14(11):1173–1182.
- Doench, J. G. (2017). Am I ready for CRISPR? A user's guide to genetic screens. *Nature Reviews Genetics*, 19(2):67–80.
- Doench, J. G., Hartenian, E., Graham, D. B., Tothova, Z., Hegde, M., Smith, I., Sullender, M., Ebert, B. L., Xavier, R. J., and Root, D. E. (2014). Rational design of highly active sgRNAs for CRISPR-Cas9-mediated gene inactivation. *Nature Biotechnology*, 32(12):1262–1267.
- D'Orlando, O., Zhao, F., Kasper, B., Orinska, Z., Müller, J., Hermans-Borgmeyer, I., Griffiths, G. M., Zur Stadt, U., and Bulfone-Paus, S. (2013). Syntaxin 11 is required for NK and CD8+ T-cell cytotoxicity and neutrophil degranulation. *European Journal of Immunology*, 43(1):194–208.
- Dorsett, Y. and Tuschl, T. (2004). siRNAs: applications in functional genomics and potential as therapeutics. *Nature Reviews Drug Discovery*, 3(4):318–329.
- Doudna, J. A. and Charpentier, E. (2014). The new frontier of genome engineering with CRISPR-Cas9. *Science*, 346(6213):1258096–1258096.
- Doyle, A., McGarry, M. P., Lee, N. A., and Lee, J. J. (2012). The construction of transgenic and gene knockout/knockin mouse models of human disease. *Transgenic research*, 21(2):327–49.

- Durchfort, N., Verhoef, S., Vaughn, M. B., Shrestha, R., Adam, D., Kaplan, J., and Ward, D. M. (2012). The Enlarged Lysosomes in beigej Cells Result From Decreased Lysosome Fission and Not Increased Lysosome Fusion. *Traffic*, 13(1):108–119.
- Ebert, O., Finke, S., Salahi, A., Herrmann, M., Trojaneck, B., Lefterova, P., Wagner, E., Kircheis, R., Huhn, D., Schriever, F., and Schmidt-Wolf, I. (1997). Lymphocyte apoptosis: induction by gene transfer techniques. *Gene Therapy*, 4(4):296–302.
- Elstak, E. D., Neeft, M., Nehme, N. T., Voortman, J., Cheung, M., Goodarzifard, M., Gerritsen, H. C., van Bergen en Henegouwen, P. M. P., Callebaut, I., de Saint Basile, G., and van der Sluijs, P. (2011). The munc13-4-rab27 complex is specifically required for tethering secretory lysosomes at the plasma membrane. *Blood*, 118(6):1570–1578.
- Feldmann, J., Callebaut, I., Raposo, G., Certain, S., Bacq, D., Dumont, C., Lambert, N., Ouachée-Chardin, M., Chedeville, G., Tamary, H., Minard-Colin, V., Vilmer, E., Blanche, S., Le Deist, F., Fischer, A., and de Saint Basile, G. (2003). Munc13-4 is essential for cytolytic granules fusion and is mutated in a form of familial hemophagocytic lymphohistiocytosis (FHL3). *Cell*, 115(4):461–73.
- Fesnak, A. D., June, C. H., and Levine, B. L. (2016). Engineered T cells: the promise and challenges of cancer immunotherapy. *Nature Reviews Cancer*, 16(9):566–581.
- Finlay, D. K., Rosenzweig, E., Sinclair, L. V., Feijoo-Carnero, C., Hukelmann, J. L., Rolf, J., Panteleyev, A. A., Okkenhaug, K., and Cantrell, D. A. (2012). PDK1 regulation of mTOR and hypoxia-inducible factor 1 integrate metabolism and migration of CD8+ T cells. *The Journal of experimental medicine*, 209(13):2441–53.
- Fox, C. J., Hammerman, P. S., and Thompson, C. B. (2005). Fuel feeds function: energy metabolism and the T-cell response. *Nature Reviews Immunology*, 5(11):844–852.
- Fukuda, M. (2013). Rab27 Effectors, Pleiotropic Regulators in Secretory Pathways. *Traffic*, 14(9):949–963.
- Fukuda, M., Kuroda, T. S., and Mikoshiba, K. (2002). Slac2-a/Melanophilin, the Missing Link between Rab27 and Myosin Va. *Journal of Biological Chemistry*, 277(14):12432–12436.
- Garber, M., Grabherr, M. G., Guttman, M., and Trapnell, C. (2011). Computational methods for transcriptome annotation and quantification using RNA-seq. *Nature Methods*, 8(6):469–477.
- Garcia-Pineres, A. J., Castro, V., Mora, G., Schmidt, T. J., Strunck, E., Pahl, H. L., and Merfort, I. (2001). Cysteine 38 in p65/NF-κB Plays a Crucial Role in DNA Binding Inhibition by Sesquiterpene Lactones. *Journal of Biological Chemistry*, 276(43):39713–39720.
- Gascoyne, D. M., Long, E., Veiga-Fernandes, H., de Boer, J., Williams, O., Seddon, B., Coles, M., Kioussis, D., and Brady, H. J. M. (2009). The basic leucine zipper transcription factor E4BP4 is essential for natural killer cell development. *Nature Immunology*, 10(10):1118–1124.

- Gawden-Bone, C. M., Frazer, G. L., Richard, A. C., Ma, C. Y., Strege, K., and Griffiths, G. M. (2018). PIP5 Kinases Regulate Membrane Phosphoinositide and Actin Composition for Targeted Granule Secretion by Cytotoxic Lymphocytes. *Immunity*, 49(3):427–437.e4.
- Gene Ontology Consortium, Blake, J. A., Dolan, M., Drabkin, H., Hill, D. P., Li, N., Sitnikov, D., Bridges, S., Burgess, S., Buza, T., McCarthy, F., Peddinti, D., Pillai, L., Carbon, S., Dietze, H., Ireland, A., Lewis, S. E., Mungall, C. J., Gaudet, P., Chrisholm, R. L., Fey, P., Kibbe, W. A., Basu, S., Siegele, D. A., McIntosh, B. K., Renfro, D. P., Zweifel, A. E., Hu, J. C., Brown, N. H., Tweedie, S., Alam-Faruque, Y., Apweiler, R., Auchinchloss, A., Axelsen, K., Bely, B., Blatter, M. C., Bonilla, C., Bouguerleret, L., Boutet, E., Breuza, L., Bridge, A., Chan, W. M., Chavali, G., Coudert, E., Dimmer, E., Streicher, A., Famiglietti, L., Feuermaier, M., Gos, A., Gruaz-Gumowski, N., Hieta, R., Hinz, C., Hulo, C., Huntley, R., James, J., Jungo, F., Keller, G., Laiho, K., Legge, D., Lemercier, P., Lieberherr, D., Magrane, M., Martin, M. J., Masson, P., Mutowo-Muellenet, P., O'Donovan, C., Pedruzzi, I., Pichler, K., Poggioli, D., Porras Millán, P., Poux, S., Rivoire, C., Roechert, B., Sawford, T., Schneider, M., Stutz, A., Sundaram, S., Tognolli, M., Xenarios, I., Foulgar, R., Lomax, J., Roncaglia, P., Khodiyar, V. K., Lovering, R. C., Talmud, P. J., Chibucus, M., Giglio, M. G., Chang, H. Y., Hunter, S., McAnulla, C., Mitchell, A., Sangrador, A., Stephan, R., Harris, M. A., Oliver, S. G., Rutherford, K., Wood, V., Bahler, J., Lock, A., Kersey, P. J., McDowall, D. M., Staines, D. M., Dwinell, M., Shimoyama, M., Laulederkind, S., Hayman, T., Wang, S. J., Petri, V., Lowry, T., D'Eustachio, P., Matthews, L., Balakrishnan, R., Binkley, G., Cherry, J. M., Costanzo, M. C., Dwight, S. S., Engel, S. R., Fisk, D. G., Hitz, B. C., Hong, E. L., Karra, K., Miyasato, S. R., Nash, R. S., Park, J., Skrzypek, M. S., Weng, S., Wong, E. D., Berardini, T. Z., Huala, E., Mi, H., Thomas, P. D., Chan, J., Kishore, R., Sternberg, P., Van Auken, K., Howe, D., and Westerfield, M. (2012). Gene Ontology Annotations and Resources. *Nucleic Acids Research*, 41(D1):D530–D535.
- Gene Ontology Consortium, T. G. O. (2012). The Gene Ontology: enhancements for 2011. *Nucleic acids research*, 40(Database issue):D559–64.
- Ghantous, A., Sinjab, A., Herceg, Z., and Darwiche, N. (2013). Parthenolide: from plant shoots to cancer roots. *Drug Discovery Today*, 18(17–18):894–905.
- Gomes-Silva, D., Srinivasan, M., Sharma, S., Lee, C. M., Wagner, D. L., Davis, T. H., Rouce, R. H., Bao, G., Brenner, M. K., and Mamontkin, M. (2017). CD7-edited T cells expressing a CD7-specific CAR for the therapy of T-cell malignancies. *Blood*, 130(3):285–296.
- Gopal, Y. V., Arora, T. S., and Van Dyke, M. W. (2007). Parthenolide Specifically Depletes Histone Deacetylase 1 Protein and Induces Cell Death through Ataxia Telangiectasia Mutated. *Chemistry & Biology*, 14(7):813–823.
- Grakoui, A., Bromley, S. K., Sumen, C., Davis, M. M., Shaw, A. S., Allen, P. M., and Dustin, M. L. (1999). The immunological synapse: a molecular machine controlling T cell activation. *Science (New York, N.Y.)*, 285(5425):221–7.
- Griffin, G. E., Liu, Y., Li, C., Jin, W., Shattock, R. J., Wang, P., Wu, B., Guan, X., Hu, B., Du, T., and Hu, Q. (2015). Inhibition of HIV-1 infection of primary CD4+ T-cells by gene editing of CCR5 using adenovirus-delivered CRISPR/Cas9. *Journal of General Virology*, 96(8):2381–2393.

- Griscelli, C., Durandy, A., Guy-Grand, D., Daguillard, F., Herzog, C., and Prunieras, M. (1978). A syndrome associating partial albinism and immunodeficiency. *The American journal of medicine*, 65(4):691–702.
- Gundry, M., Brunetti, L., Lin, A., Mayle, A., Kitano, A., Wagner, D., Hsu, J., Hoegenauer, K., Rooney, C., Goodell, M., and Nakada, D. (2016). Highly Efficient Genome Editing of Murine and Human Hematopoietic Progenitor Cells by CRISPR/Cas9. *Cell Reports*, 17(5):1453–1461.
- Hackett, P. B., Largaespada, D. A., and Cooper, L. J. N. (2010). A transposon and transposase system for human application. *Molecular therapy : the journal of the American Society of Gene Therapy*, 18(4):674–83.
- Hackmann, Y., Graham, S. C., Ehl, S., Honing, S., Lehmberg, K., Arico, M., Owen, D. J., and Griffiths, G. M. (2013). Syntaxin binding mechanism and disease-causing mutations in Munc18-2. *Proceedings of the National Academy of Sciences*, 110(47):E4482–E4491.
- Haeryfar, S. M. M. and Hoskin, D. W. (2004). Thy-1: more than a mouse pan-T cell marker. *Journal of immunology (Baltimore, Md. : 1950)*, 173(6):3581–8.
- Hanson, D. A., Kaspar, A. A., Poulin, F. R., and Krensky, A. M. (1999). Biosynthesis of granulysin, a novel cytolytic molecule. *Molecular immunology*, 36(7):413–22.
- Harty, J. T. and Badovinac, V. P. (2008). Shaping and reshaping CD8+ T-cell memory. *Nature Reviews Immunology*, 8(2):107–119.
- He, S. and Wang, X. (2018). RIP kinases as modulators of inflammation and immunity. *Nature Immunology*, 19(9):912–922.
- Hehner, S. P., Hofmann, T. G., Dröge, W., and Schmitz, M. L. (1999). The antiinflammatory sesquiterpene lactone parthenolide inhibits NF-kappa B by targeting the I kappa B kinase complex. *Journal of immunology (Baltimore, Md. : 1950)*, 163(10):5617–23.
- Hendel, A., Bak, R. O., Clark, J. T., Kennedy, A. B., Ryan, D. E., Roy, S., Steinfeld, I., Lunstad, B. D., Kaiser, R. J., Wilkens, A. B., Bacchetta, R., Tselenko, A., Dellinger, D., Bruhn, L., and Porteus, M. H. (2015). Chemically modified guide RNAs enhance CRISPR-Cas genome editing in human primary cells. *Nature Biotechnology*, 33(9):985–989.
- Henriksson, J., Chen, X., Gomes, T., Ullah, U., Meyer, K. B., Miragaia, R., Duddy, G., Pramanik, J., Yusa, K., Lahesmaa, R., and Teichmann, S. A. (2019). Genome-wide CRISPR Screens in T Helper Cells Reveal Pervasive Crosstalk between Activation and Differentiation. *Cell*, 176(4):882–896.e18.
- Henter, J.-I., Horne, A., Aricó, M., Egeler, R. M., Filipovich, A. H., Imashuku, S., Ladisch, S., McClain, K., Webb, D., Winiarski, J., and Janka, G. (2007). HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatric Blood & Cancer*, 48(2):124–131.
- Hermansky, F. and Pudlak, P. (1959). Albinism associated with hemorrhagic diathesis and unusual pigmented reticular cells in the bone marrow: report of two cases with histochemical studies. *Blood*, 14(2):162–9.

- Heusel, J. W., Wesselschmidt, R. L., Shresta, S., Russell, J. H., and Ley, T. J. (1994). Cytotoxic lymphocytes require granzyme B for the rapid induction of DNA fragmentation and apoptosis in allogeneic target cells. *Cell*, 76(6):977–987.
- Hodi, F. S., O'Day, S. J., McDermott, D. F., Weber, R. W., Sosman, J. A., Haanen, J. B., Gonzalez, R., Robert, C., Schadendorf, D., Hassel, J. C., Akerley, W., van den Eertwegh, A. J., Lutzky, J., Lorigan, P., Vaubel, J. M., Linette, G. P., Hogg, D., Ottensmeier, C. H., Lebbé, C., Peschel, C., Quirt, I., Clark, J. I., Wolchok, J. D., Weber, J. S., Tian, J., Yellin, M. J., Nichol, G. M., Hoos, A., and Urba, W. J. (2010). Improved Survival with Ipilimumab in Patients with Metastatic Melanoma. *New England Journal of Medicine*, 363(8):711–723.
- Höfig, I., Atkinson, M. J., Mall, S., Krackhardt, A. M., Thirion, C., and Anastasov, N. (2012). Poloxamer syneronic F108 improves cellular transduction with lentiviral vectors. *The Journal of Gene Medicine*, 14(8):549–560.
- Hogan, P. G., Chen, L., Nardone, J., and Rao, A. (2003). Transcriptional regulation by calcium, calcineurin, and NFAT. *Genes & Development*, 17(18):2205–2232.
- Hogquist, K. A., Jameson, S. C., Heath, W. R., Howard, J. L., Bevan, M. J., and Carbone, F. R. (1994). T cell receptor antagonist peptides induce positive selection. *Cell*, 76(1):17–27.
- Holt, O., Kanno, E., Bossi, G., Booth, S., Daniele, T., Santoro, A., Arico, M., Saegusa, C., Fukuda, M., and Griffiths, G. M. (2008). Slp1 and Slp2-a Localize to the Plasma Membrane of CTL and Contribute to Secretion from the Immunological Synapse. *Traffic*, 9(4):446–457.
- Hsu, P., Lander, E., and Zhang, F. (2014). Development and Applications of CRISPR-Cas9 for Genome Engineering. *Cell*, 157(6):1262–1278.
- Huang, B., Johansen, K. H., and Schwartzberg, P. L. (2019). Efficient CRISPR/Cas9-Mediated Mutagenesis in Primary Murine T Lymphocytes. *Current Protocols in Immunology*, 124(1):e62.
- Huang, D. W., Sherman, B. T., and Lempicki, R. A. (2009a). Bioinformatics enrichment tools: paths toward the comprehensive functional analysis of large gene lists. *Nucleic Acids Research*, 37(1):1–13.
- Huang, D. W., Sherman, B. T., and Lempicki, R. A. (2009b). Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. *Nature Protocols*, 4(1):44–57.
- Hukelmann, J. L., Anderson, K. E., Sinclair, L. V., Grzes, K. M., Murillo, A. B., Hawkins, P. T., Stephens, L. R., Lamond, A. I., and Cantrell, D. A. (2016). The cytotoxic T cell proteome and its shaping by the kinase mTOR. *Nature Immunology*, 17(1):104–112.
- Hultquist, J., Schumann, K., Woo, J., Manganaro, L., McGregor, M., Doudna, J., Simon, V., Krogan, N., and Marson, A. (2016). A Cas9 Ribonucleoprotein Platform for Functional Genetic Studies of HIV-Host Interactions in Primary Human T Cells. *Cell Reports*, 17(5):1438–1452.

- Hume, A. N., Collinson, L. M., Hopkins, C. R., Strom, M., Barral, D. C., Bossi, G., Griffiths, G. M., and Seabra, M. C. (2002). The leaden gene product is required with Rab27a to recruit myosin Va to melanosomes in melanocytes. *Traffic (Copenhagen, Denmark)*, 3(3):193–202.
- Hume, A. N., Collinson, L. M., Rapak, A., Gomes, A. Q., Hopkins, C. R., and Seabra, M. C. (2001). Rab27a regulates the peripheral distribution of melanosomes in melanocytes. *The Journal of cell biology*, 152(4):795–808.
- Isaaz, S., Baetz, K., Olsen, K., Podack, E., and Griffiths, G. M. (1995). Serial killing by cytotoxic T lymphocytes: T cell receptor triggers degranulation, re-filling of the lytic granules and secretion of lytic proteins via a non-granule pathway. *European Journal of Immunology*, 25(4):1071–1079.
- James, J. R. and Vale, R. D. (2012). Biophysical mechanism of T-cell receptor triggering in a reconstituted system. *Nature*, 487(7405):64–69.
- Janka, G. E. and Lehmberg, K. (2014). Hemophagocytic syndromes — An update. *Blood Reviews*, 28(4):135–142.
- Jellison, E. R., Kim, S.-K., and Welsh, R. M. (2005). Cutting edge: MHC class II-restricted killing in vivo during viral infection. *Journal of immunology (Baltimore, Md. : 1950)*, 174(2):614–8.
- Jenkins, M. R., Rudd-Schmidt, J. A., Lopez, J. A., Ramsbottom, K. M., Mannerling, S. I., Andrews, D. M., Voskoboinik, I., and Trapani, J. A. (2015). Failed CTL/NK cell killing and cytokine hypersecretion are directly linked through prolonged synapse time. *The Journal of experimental medicine*, 212(3):307–17.
- Jinek, M., Chylinski, K., Fonfara, I., Hauer, M., Doudna, J. A., and Charpentier, E. (2012). A Programmable Dual-RNA-Guided DNA Endonuclease in Adaptive Bacterial Immunity. *Science*, 337(6096):816–821.
- Jinek, M., East, A., Cheng, A., Lin, S., Ma, E., and Doudna, J. (2013). RNA-programmed genome editing in human cells. *eLife*, 2:e00471.
- Joung, J., Konermann, S., Gootenberg, J. S., Abudayyeh, O. O., Platt, R. J., Brigham, M. D., Sanjana, N. E., and Zhang, F. (2017). Genome-scale CRISPR-Cas9 knockout and transcriptional activation screening. *Nature Protocols*, 12(4):828–863.
- Kabanova, A., Sanseviero, F., Candi, V., Gamberucci, A., Gozzetti, A., Campoccia, G., Bocchia, M., and Baldari, C. (2016). Human Cytotoxic T Lymphocytes Form Dysfunctional Immune Synapses with B Cells Characterized by Non-Polarized Lytic Granule Release. *Cell Reports*, 15(10):2313.
- Kägi, D., Ledermann, B., Bürki, K., Seiler, P., Odermatt, B., Olsen, K. J., Podack, E. R., Zinkernagel, R. M., and Hengartner, H. (1994a). Cytotoxicity mediated by T cells and natural killer cells is greatly impaired in perforin-deficient mice. *Nature*, 369(6475):31–37.
- Kägi, D., Vignaux, F., Ledermann, B., Bürki, K., Depraetere, V., Nagata, S., Hengartner, H., and Golstein, P. (1994b). Fas and perforin pathways as major mechanisms of T cell-mediated cytotoxicity. *Science (New York, N.Y.)*, 265(5171):528–30.

- Kanehisa, M., Goto, S., Sato, Y., Furumichi, M., and Tanabe, M. (2012). KEGG for integration and interpretation of large-scale molecular data sets. *Nucleic Acids Research*, 40(D1):D109–D114.
- Killeen, N. (1997). T-cell regulation: Thy-1 - hiding in full view. *Current biology : CB*, 7(12):R774–7.
- Kim, J. H., Lee, S.-R., Li, L.-H., Park, H.-J., Park, J.-H., Lee, K. Y., Kim, M.-K., Shin, B. A., and Choi, S.-Y. (2011). High Cleavage Efficiency of a 2A Peptide Derived from Porcine Teschovirus-1 in Human Cell Lines, Zebrafish and Mice. *PLoS ONE*, 6(4):e18556.
- Kim, S., Kim, D., Cho, S. W., Kim, J., and Kim, J.-S. (2014). Highly efficient RNA-guided genome editing in human cells via delivery of purified Cas9 ribonucleoproteins. *Genome research*, 24(6):1012–9.
- Kim, T. K. and Eberwine, J. H. (2010). Mammalian cell transfection: the present and the future. *Analytical and bioanalytical chemistry*, 397(8):3173–8.
- Kogawa, K., Lee, S. M., Villanueva, J., Marmer, D., Sumegi, J., and Filipovich, A. H. (2002). Perforin expression in cytotoxic lymphocytes from patients with hemophagocytic lymphohistiocytosis and their family members. *Blood*, 99(1):61–6.
- Komor, A. C., Badran, A. H., and Liu, D. R. (2017). CRISPR-Based Technologies for the Manipulation of Eukaryotic Genomes. *Cell*, 168(1-2):20–36.
- Kosicki, M., Tomberg, K., and Bradley, A. (2018). Repair of double-strand breaks induced by CRISPR–Cas9 leads to large deletions and complex rearrangements. *Nature Biotechnology*, 36(8):765.
- Krammer, P. H. (2000). CD95's deadly mission in the immune system. *Nature*, 407(6805):789–795.
- Krensky, A. M. and Clayberger, C. (2009). Biology and clinical relevance of granulysin. *Tissue antigens*, 73(3):193–8.
- Krummel, M. F. and Allison, J. P. (1995). CD28 and CTLA-4 have opposing effects on the response of T cells to stimulation. *The Journal of experimental medicine*, 182(2):459–65.
- Kuroda, T. S., Fukuda, M., Ariga, H., and Mikoshiba, K. (2002a). Synaptotagmin-like protein 5: a novel Rab27A effector with C-terminal tandem C2 domains. *Biochemical and Biophysical Research Communications*, 293(3):899–906.
- Kuroda, T. S., Fukuda, M., Ariga, H., and Mikoshiba, K. (2002b). The Slp Homology Domain of Synaptotagmin-like Proteins 1–4 and Slac2 Functions as a Novel Rab27A Binding Domain. *Journal of Biological Chemistry*, 277(11):9212–9218.
- Kurowska, M., Goudin, N., Nehme, N. T., Court, M., Garin, J., Fischer, A., de Saint Basile, G., and Menasche, G. (2012). Terminal transport of lytic granules to the immune synapse is mediated by the kinesin-1/Slp3/Rab27a complex. *Blood*, 119(17):3879–3889.
- Kuta, A. E., Reynolds, C. R., and Henkart, P. A. (1989). Mechanism of lysis by large granular lymphocyte granule cytolysin: generation of a stable cytolysin-RBC intermediate. *Journal of immunology (Baltimore, Md. : 1950)*, 142(12):4378–84.

- Kwok, B. H., Koh, B., Ndubuisi, M. I., Elofsson, M., and Crews, C. M. (2001). The anti-inflammatory natural product parthenolide from the medicinal herb Feverfew directly binds to and inhibits IkappaB kinase. *Chemistry & biology*, 8(8):759–66.
- Larkin, J., Chiarion-Sileni, V., Gonzalez, R., Grob, J. J., Cowey, C. L., Lao, C. D., Schadendorf, D., Dummer, R., Smylie, M., Rutkowski, P., Ferrucci, P. F., Hill, A., Wagstaff, J., Carlino, M. S., Haanen, J. B., Maio, M., Marquez-Rodas, I., McArthur, G. A., Ascierto, P. A., Long, G. V., Callahan, M. K., Postow, M. A., Grossmann, K., Sznol, M., Dreno, B., Bastholt, L., Yang, A., Rollin, L. M., Horak, C., Hodi, F. S., and Wolchok, J. D. (2015). Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. *New England Journal of Medicine*, 373(1):23–34.
- Law, R. H. P., Lukyanova, N., Voskoboinik, I., Caradoc-Davies, T. T., Baran, K., Dunstone, M. A., D'Angelo, M. E., Orlova, E. V., Coulibaly, F., Verschoor, S., Browne, K. A., Ciccone, A., Kuiper, M. J., Bird, P. I., Trapani, J. A., Saibil, H. R., and Whisstock, J. C. (2010). The structural basis for membrane binding and pore formation by lymphocyte perforin. *Nature*, 468(7322):447–451.
- Leach, D. R., Krummel, M. F., and Allison, J. P. (1996). Enhancement of antitumor immunity by CTLA-4 blockade. *Science (New York, N.Y.)*, 271(5256):1734–6.
- Legut, M., Dolton, G., Mian, A. A., Ottmann, O. G., and Sewell, A. K. (2018). CRISPR-mediated TCR replacement generates superior anticancer transgenic T cells. *Blood*, 131(3):311–322.
- Letschka, T., Kollmann, V., Pfeifhofer-Obermair, C., Lutz-Nicoladoni, C., Obermair, G. J., Fresser, F., Leitges, M., Hermann-Kleiter, N., Kaminski, S., and Baier, G. (2008). PKC-selectively controls the adhesion-stimulating molecule Rap1. *Blood*, 112(12):4617–4627.
- Li, D., Qiu, Z., Shao, Y., Chen, Y., Guan, Y., Liu, M., Li, Y., Gao, N., Wang, L., Lu, X., Zhao, Y., and Liu, M. (2013). Heritable gene targeting in the mouse and rat using a CRISPR-Cas system. *Nature Biotechnology*, 31(8):681–683.
- Liu, H., Sidiropoulos, P., Song, G., Pagliari, L. J., Birrer, M. J., Stein, B., Anrather, J., and Pope, R. M. (2000). TNF-alpha gene expression in macrophages: regulation by NF-kappa B is independent of c-Jun or C/EBP beta. *Journal of immunology (Baltimore, Md. : 1950)*, 164(8):4277–85.
- Liu, X., Berry, C. T., Ruthel, G., Madara, J. J., MacGillivray, K., Gray, C. M., Madge, L. A., McCorkell, K. A., Beiting, D. P., Hershberg, U., May, M. J., and Freedman, B. D. (2016). T Cell Receptor-induced Nuclear Factor κ B (NF- κ B) Signaling and Transcriptional Activation Are Regulated by STIM1- and Orai1-mediated Calcium Entry. *Journal of Biological Chemistry*, 291(16):8440–8452.
- Liu, Z., Liu, S., Xie, Z., Pavlovic, R. E., Wu, J., Chen, P., Aimiwu, J., Pang, J., Bhasin, D., Neviani, P., Fuchs, J. R., Plass, C., Li, P.-K., Li, C., Huang, T. H.-M., Wu, L.-C., Rush, L., Wang, H., Perrotti, D., Marcucci, G., and Chan, K. K. (2009). Modulation of DNA Methylation by a Sesquiterpene Lactone Parthenolide. *Journal of Pharmacology and Experimental Therapeutics*, 329(2):505–514.

- Loo, L. S., Hwang, L.-A., Ong, Y. M., Tay, H. S., Wang, C.-C., and Hong, W. (2009). A role for endobrevin/VAMP8 in CTL lytic granule exocytosis. *European Journal of Immunology*, 39(12):3520–3528.
- Lopez, J. A., Jenkins, M. R., Rudd-Schmidt, J. A., Brennan, A. J., Danne, J. C., Mannerling, S. I., Trapani, J. A., and Voskoboinik, I. (2013a). Rapid and Unidirectional Perforin Pore Delivery at the Cytotoxic Immune Synapse. *The Journal of Immunology*, 191(5):2328–2334.
- Lopez, J. A., Susanto, O., Jenkins, M. R., Lukyanova, N., Sutton, V. R., Law, R. H. P., Johnston, A., Bird, C. H., Bird, P. I., Whisstock, J. C., Trapani, J. A., Saibil, H. R., and Voskoboinik, I. (2013b). Perforin forms transient pores on the target cell plasma membrane to facilitate rapid access of granzymes during killer cell attack. *Blood*, 121(14):2659–2668.
- Love, M. I., Huber, W., and Anders, S. (2014). Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. *Genome Biology*, 15(12):550.
- Lowry, L. E. and Zehring, W. A. (2017). Potentiation of Natural Killer Cells for Cancer Immunotherapy: A Review of Literature. *Frontiers in Immunology*, 8:1061.
- Macian, F. (2005). NFAT proteins: key regulators of T-cell development and function. *Nature Reviews Immunology*, 5(6):472–484.
- MacIver, N. J., Michalek, R. D., and Rathmell, J. C. (2013). Metabolic Regulation of T Lymphocytes. *Annual Review of Immunology*, 31(1):259–283.
- Maher, J., Brentjens, R. J., Gunset, G., Rivière, I., and Sadelain, M. (2002). Human T-lymphocyte cytotoxicity and proliferation directed by a single chimeric TCR ζ /CD28 receptor. *Nature Biotechnology*, 20(1):70–75.
- Mali, P., Yang, L., Esvelt, K. M., Aach, J., Guell, M., DiCarlo, J. E., Norville, J. E., and Church, G. M. (2013). RNA-guided human genome engineering via Cas9. *Science (New York, N.Y.)*, 339(6121):823–6.
- Mandal, A. and Viswanathan, C. (2015). Natural killer cells: In health and disease. *Hematology/Oncology and Stem Cell Therapy*, 8(2):47–55.
- Mandal, P., Ferreira, L. M., Collins, R., Meissner, T., Boutwell, C., Friesen, M., Vrbanac, V., Garrison, B., Stortchevoi, A., Bryder, D., Musunuru, K., Brand, H., Tager, A., Allen, T., Talkowski, M., Rossi, D., and Cowan, C. (2014). Efficient Ablation of Genes in Human Hematopoietic Stem and Effector Cells using CRISPR/Cas9. *Cell Stem Cell*, 15(5):643–652.
- Marcket-Palacios, M., Odemuyiwa, S. O., Coughlin, J. J., Garofoli, D., Ewen, C., Davidson, C. E., Ghaffari, M., Kane, K. P., Lacy, P., Logan, M. R., Befus, A. D., Bleackley, R. C., and Moqbel, R. (2008). Vesicle-associated membrane protein 7 (VAMP-7) is essential for target cell killing in a natural killer cell line. *Biochemical and Biophysical Research Communications*, 366(3):617–623.
- Masson, D. and Tschopp, J. (1987). A family of serine esterases in lytic granules of cytolytic T lymphocytes. *Cell*, 49(5):679–85.

- Masson, D., Zamai, M., and Tschopp, J. (1986). Identification of granzyme A isolated from cytotoxic T-lymphocyte-granules as one of the proteases encoded by CTL-specific genes. *FEBS letters*, 208(1):84–8.
- Matsumoto, R., Wang, D., Blonska, M., Li, H., Kobayashi, M., Pappu, B., Chen, Y., Wang, D., and Lin, X. (2005). Phosphorylation of CARMA1 Plays a Critical Role in T Cell Receptor-Mediated NF- κ B Activation. *Immunity*, 23(6):575–585.
- Matti, U., Pattu, V., Halimani, M., Schirra, C., Krause, E., Liu, Y., Weins, L., Fang Chang, H., Guzman, R., Olausson, J., Freichel, M., Schmitz, F., Pasche, M., Becherer, U., Bruns, D., and Rettig, J. (2013). Synaptobrevin2 is the v-SNARE required for cytotoxic T-lymphocyte lytic granule fusion. *Nature Communications*, 4(1):1439.
- Maude, S. L., Frey, N., Shaw, P. A., Aplenc, R., Barrett, D. M., Bunin, N. J., Chew, A., Gonzalez, V. E., Zheng, Z., Lacey, S. F., Mahnke, Y. D., Melenhorst, J. J., Rheingold, S. R., Shen, A., Teachey, D. T., Levine, B. L., June, C. H., Porter, D. L., and Grupp, S. A. (2014). Chimeric Antigen Receptor T Cells for Sustained Remissions in Leukemia. *New England Journal of Medicine*, 371(16):1507–1517.
- Meister, G. and Tuschl, T. (2004). Mechanisms of gene silencing by double-stranded RNA. *Nature*, 431(7006):343–349.
- Ménager, M. M., Ménasché, G., Romao, M., Knapnougel, P., Ho, C.-H., Garfa, M., Raposo, G., Feldmann, J., Fischer, A., and de Saint Basile, G. (2007). Secretory cytotoxic granule maturation and exocytosis require the effector protein hMunc13-4. *Nature Immunology*, 8(3):257–267.
- Menasche, G., Feldmann, J., Houdusse, A., Desaymard, C., Fischer, A., Goud, B., and de Saint Basile, G. (2003). Biochemical and functional characterization of Rab27a mutations occurring in Griscelli syndrome patients. *Blood*, 101(7):2736–2742.
- Ménasché, G., Ménager, M. M., Lefebvre, J. M., Deutsch, E., Athman, R., Lambert, N., Mahlaoui, N., Court, M., Garin, J., Fischer, A., and de Saint Basile, G. (2008). A newly identified isoform of Slp2a associates with Rab27a in cytotoxic T cells and participates to cytotoxic granule secretion. *Blood*, 112(13):5052–62.
- Ménasché, G., Pastural, E., Feldmann, J., Certain, S., Ersoy, F., Dupuis, S., Wulffraat, N., Bianchi, D., Fischer, A., Le Deist, F., and de Saint Basile, G. (2000). Mutations in RAB27A cause Griscelli syndrome associated with haemophagocytic syndrome. *Nature Genetics*, 25(2):173–176.
- Mescher, M. F., Curtsinger, J. M., Agarwal, P., Casey, K. A., Gerner, M., Hammerbeck, C. D., Popescu, F., and Xiao, Z. (2006). Signals required for programming effector and memory development by CD8+ T cells. *Immunological Reviews*, 211(1):81–92.
- Misura, K. M. S., Scheller, R. H., and Weis, W. I. (2000). Three-dimensional structure of the neuronal-Sec1-syntaxin 1a complex. *Nature*, 404(6776):355–362.
- Monks, C. R. F., Freiberg, B. A., Kupfer, H., Sciaky, N., and Kupfer, A. (1998). Three-dimensional segregation of supramolecular activation clusters in T cells. *Nature*, 395(6697):82–86.

- Morgan, R. A., Dudley, M. E., Wunderlich, J. R., Hughes, M. S., Yang, J. C., Sherry, R. M., Royal, R. E., Topalian, S. L., Kammula, U. S., Restifo, N. P., Zheng, Z., Nahvi, A., de Vries, C. R., Rogers-Freezer, L. J., Mavroukakis, S. A., and Rosenberg, S. A. (2006). Cancer Regression in Patients After Transfer of Genetically Engineered Lymphocytes. *Science*, 314(5796):126–129.
- Munafó, D., Johnson, J., Ellis, B., Rutschmann, S., Beutler, B., and Catz, S. (2007). Rab27a is a key component of the secretory machinery of azurophilic granules in granulocytes. *Biochemical Journal*, 402(2):229–239.
- Nagashima, K., Torii, S., Yi, Z., Igarashi, M., Okamoto, K., Takeuchi, T., and Izumi, T. (2002). Melanophilin directly links Rab27a and myosin Va through its distinct coiled-coil regions. *FEBS letters*, 517(1-3):233–8.
- Nagle, D. L., Karim, M. A., Woolf, E. A., Holmgren, L., Bork, P., Misumi, D. J., McGrail, S. H., Dussault, B. J., Perou, C. M., Boissy, R. E., Duyk, G. M., Spritz, R. A., and Moore, K. J. (1996). Identification and mutation analysis of the complete gene for Chediak–Higashi syndrome. *Nature Genetics*, 14(3):307–311.
- Nakamura, H., Makino, Y., Okamoto, K., Poellinger, L., Ohnuma, K., Morimoto, C., and Tanaka, H. (2005). TCR engagement increases hypoxia-inducible factor-1 alpha protein synthesis via rapamycin-sensitive pathway under hypoxic conditions in human peripheral T cells. *Journal of immunology (Baltimore, Md. : 1950)*, 174(12):7592–9.
- Navarro, M. N. and Cantrell, D. A. (2014). Serine-threonine kinases in TCR signaling. *Nature Immunology*, 15(9):808–814.
- Neefjes, J., Jongsma, M. L. M., Paul, P., and Bakke, O. (2011). Towards a systems understanding of MHC class I and MHC class II antigen presentation. *Nature Reviews Immunology*, 11(12):823–836.
- Neeft, M., Wieffer, M., de Jong, A. S., Negroiu, G., Metz, C. H., van Loon, A., Griffith, J., Krijgsveld, J., Wulffraat, N., Koch, H., Heck, A. J., Brose, N., Kleijmeer, M., and van der Sluijs, P. (2005). Munc13-4 Is an Effector of Rab27a and Controls Secretion of Lysosomes in Hematopoietic Cells. *Molecular Biology of the Cell*, 16(2):731–741.
- Ogino, S., Gulley, M. L., den Dunnen, J. T., Wilson, R. B., and Association for Molecular Pathology Training and Education Committee (2007). Standard Mutation Nomenclature in Molecular Diagnostics. *The Journal of Molecular Diagnostics*, 9(1):1–6.
- Oh, H. and Ghosh, S. (2013). NF-κB: roles and regulation in different CD4+ T-cell subsets. *Immunological Reviews*, 252(1):41–51.
- Ohadi, M., Laloz, M. R., Sham, P., Zhao, J., Dearlove, A. M., Shiach, C., Kinsey, S., Rhodes, M., and Layton, D. M. (1999). Localization of a Gene for Familial Hemophagocytic Lymphohistiocytosis at Chromosome 9q21.3-22 by Homozygosity Mapping. *The American Journal of Human Genetics*, 64(1):165–171.
- Okazaki, T., Chikuma, S., Iwai, Y., Fagarasan, S., and Honjo, T. (2013). A rheostat for immune responses: the unique properties of PD-1 and their advantages for clinical application. *Nature Immunology*, 14(12):1212–1218.

- Pahl, H. L. (1999). Activators and target genes of Rel/NF- κ B transcription factors. *Oncogene*, 18(49):6853–6866.
- Palazon, A., Tyrakis, P. A., Macias, D., Veliça, P., Rundqvist, H., Fitzpatrick, S., Vojnovic, N., Phan, A. T., Loman, N., Hedenfalk, I., Hatschek, T., Lövrot, J., Foukakis, T., Goldrath, A. W., Bergh, J., and Johnson, R. S. (2017). An HIF-1 α /VEGF-A Axis in Cytotoxic T Cells Regulates Tumor Progression. *Cancer cell*, 32(5):669–683.e5.
- Pan, D., Kobayashi, A., Jiang, P., Ferrari de Andrade, L., Tay, R. E., Luoma, A. M., Tsoucas, D., Qiu, X., Lim, K., Rao, P., Long, H. W., Yuan, G.-C., Doench, J., Brown, M., Liu, X. S., and Wucherpfennig, K. W. (2018). A major chromatin regulator determines resistance of tumor cells to T cell-mediated killing. *Science (New York, N.Y.)*, 359(6377):770–775.
- Parish, I. A. and Kaech, S. M. (2009). Diversity in CD8+ T cell differentiation. *Current Opinion in Immunology*, 21(3):291–297.
- Park, R. J., Wang, T., Koundakjian, D., Hultquist, J. F., Lamothe-Molina, P., Monel, B., Schumann, K., Yu, H., Krupczak, K. M., Garcia-Beltran, W., Piechocka-Trocha, A., Krogan, N. J., Marson, A., Sabatini, D. M., Lander, E. S., Hacohen, N., and Walker, B. D. (2017). A genome-wide CRISPR screen identifies a restricted set of HIV host dependency factors. *Nature Genetics*, 49(2):193–203.
- Patel, S. J., Sanjana, N. E., Kishton, R. J., Eidizadeh, A., Vodnala, S. K., Cam, M., Gartner, J. J., Jia, L., Steinberg, S. M., Yamamoto, T. N., Merchant, A. S., Mehta, G. U., Chichura, A., Shalem, O., Tran, E., Eil, R., Sukumar, M., Guijarro, E. P., Day, C.-P., Robbins, P., Feldman, S., Merlino, G., Zhang, F., and Restifo, N. P. (2017). Identification of essential genes for cancer immunotherapy. *Nature*, 548(7669):537–542.
- Paul, S. and Schaefer, B. C. (2013). A new look at T cell receptor signaling to nuclear factor- κ B. *Trends in immunology*, 34(6):269–81.
- Peña, S. V., Hanson, D. A., Carr, B. A., Goralski, T. J., and Krensky, A. M. (1997). Processing, subcellular localization, and function of 519 (granulysin), a human late T cell activation molecule with homology to small, lytic, granule proteins. *Journal of immunology (Baltimore, Md. : 1950)*, 158(6):2680–8.
- Peña, S. V. and Krensky, A. M. (1997). Granulysin, a new human cytolytic granule-associated protein with possible involvement in cell-mediated cytotoxicity. *Seminars in Immunology*, 9(2):117–125.
- Pennock, N. D., White, J. T., Cross, E. W., Cheney, E. E., Tamburini, B. A., and Kedl, R. M. (2013). T cell responses: naïve to memory and everything in between. *Advances in Physiology Education*, 37(4):273–283.
- Pereira-Leal, J. B., Hume, A. N., and Seabra, M. C. (2001). Prenylation of Rab GTPases: molecular mechanisms and involvement in genetic disease. *FEBS letters*, 498(2-3):197–200.
- Perou, C. M., Moore, K. J., Nagle, D. L., Misumi, D. J., Woolf, E. A., McGrail, S. H., Holmgren, L., Brody, T. H., Dussault, B. J., Monroe, C. A., Duyk, G. M., Pryor, R. J., Li, L., Justice, M. J., and Kaplan, J. (1996). Identification of the murine beige gene by YAC complementation and positional cloning. *Nature Genetics*, 13(3):303–308.

- Peters, P. J., Borst, J., Oorschot, V., Fukuda, M., Krähenbühl, O., Tschopp, J., Slot, J. W., and Geuze, H. J. (1991). Cytotoxic T lymphocyte granules are secretory lysosomes, containing both perforin and granzymes. *The Journal of experimental medicine*, 173(5):1099–109.
- Platt, R., Chen, S., Zhou, Y., Yim, M., Swiech, L., Kempton, H., Dahlman, J., Parnas, O., Eisenhaure, T., Jovanovic, M., Graham, D., Jhunjhunwala, S., Heidenreich, M., Xavier, R., Langer, R., Anderson, D., Hacohen, N., Regev, A., Feng, G., Sharp, P., and Zhang, F. (2014). CRISPR-Cas9 Knockin Mice for Genome Editing and Cancer Modeling. *Cell*, 159(2):440–455.
- Postow, M. A., Chesney, J., Pavlick, A. C., Robert, C., Grossmann, K., McDermott, D., Linette, G. P., Meyer, N., Giguere, J. K., Agarwala, S. S., Shaheen, M., Ernstoff, M. S., Minor, D., Salama, A. K., Taylor, M., Ott, P. A., Rollin, L. M., Horak, C., Gagnier, P., Wolchok, J. D., and Hodi, F. S. (2015). Nivolumab and Ipilimumab versus Ipilimumab in Untreated Melanoma. *New England Journal of Medicine*, 372(21):2006–2017.
- Potter, T. A., Grebe, K., Freiberg, B., and Kupfer, A. (2001). Formation of supramolecular activation clusters on fresh ex vivo CD8+ T cells after engagement of the T cell antigen receptor and CD8 by antigen-presenting cells. *Proceedings of the National Academy of Sciences*, 98(22):12624–12629.
- Qasim, W., Zhan, H., Samarasinghe, S., Adams, S., Amrolia, P., Stafford, S., Butler, K., Rivat, C., Wright, G., Somana, K., Ghorashian, S., Pinner, D., Ahsan, G., Gilmour, K., Lucchini, G., Inglott, S., Mifsud, W., Chiesa, R., Peggs, K. S., Chan, L., Farzaneh, F., Thrasher, A. J., Vora, A., Pule, M., and Veys, P. (2017). Molecular remission of infant B-ALL after infusion of universal TALEN gene-edited CAR T cells. *Science Translational Medicine*, 9(374):eaaj2013.
- Quann, E. J., Merino, E., Furuta, T., and Huse, M. (2009). Localized diacylglycerol drives the polarization of the microtubule-organizing center in T cells. *Nature Immunology*, 10(6):627–635.
- Ramezani, A. and Hawley, R. G. (2002). Overview of the HIV-1 Lentiviral Vector System. In *Current Protocols in Molecular Biology*, volume Chapter 16, page Unit 16.21. John Wiley & Sons, Inc., Hoboken, NJ, USA.
- Ran, F. A., Hsu, P. D., Wright, J., Agarwala, V., Scott, D. A., and Zhang, F. (2013). Genome engineering using the CRISPR-Cas9 system. *Nature Protocols*, 8(11):2281–2308.
- Ren, J., Liu, X., Fang, C., Jiang, S., June, C. H., and Zhao, Y. (2017a). Multiplex Genome Editing to Generate Universal CAR T Cells Resistant to PD1 Inhibition. *Clinical Cancer Research*, 23(9):2255–2266.
- Ren, J., Zhang, X., Liu, X., Fang, C., Jiang, S., June, C. H., and Zhao, Y. (2017b). A versatile system for rapid multiplex genome-edited CAR T cell generation. *Oncotarget*, 8(10):17002–17011.
- Ricote, M. and Glass, C. K. (2007). PPARs and molecular mechanisms of transrepression. *Biochimica et biophysica acta*, 1771(8):926–35.

- Ritter, A. T., Asano, Y., Stinchcombe, J. C., Dieckmann, N. M. G., Chen, B.-C., Gawden-Bone, C., van Engelenburg, S., Legant, W., Gao, L., Davidson, M. W., Betzig, E., Lippincott-Schwartz, J., and Griffiths, G. M. (2015). Actin depletion initiates events leading to granule secretion at the immunological synapse. *Immunity*, 42(5):864–76.
- Ritter, A. T., Kapnick, S. M., Murugesan, S., Schwartzberg, P. L., Griffiths, G. M., and Lippincott-Schwartz, J. (2017). Cortical actin recovery at the immunological synapse leads to termination of lytic granule secretion in cytotoxic T lymphocytes. *Proceedings of the National Academy of Sciences*, 114(32):E6585–E6594.
- Robert, C., Thomas, L., Bondarenko, I., O'Day, S., Weber, J., Garbe, C., Lebbe, C., Baurain, J.-F., Testori, A., Grob, J.-J., Davidson, N., Richards, J., Maio, M., Hauschild, A., Miller, W. H., Gascon, P., Lotem, M., Harmankaya, K., Ibrahim, R., Francis, S., Chen, T.-T., Humphrey, R., Hoos, A., and Wolchok, J. D. (2011). Ipilimumab plus Dacarbazine for Previously Untreated Metastatic Melanoma. *New England Journal of Medicine*, 364(26):2517–2526.
- Rollings, C. M., Sinclair, L. V., Brady, H. J. M., Cantrell, D. A., and Ross, S. H. (2018). Interleukin-2 shapes the cytotoxic T cell proteome and immune environment-sensing programs. *Science signaling*, 11(526):eaap8112.
- Rosenberg, S. A., Restifo, N. P., Yang, J. C., Morgan, R. A., and Dudley, M. E. (2008). Adoptive cell transfer: a clinical path to effective cancer immunotherapy. *Nature Reviews Cancer*, 8(4):299–308.
- Rosenberg, S. A., Yang, J. C., Sherry, R. M., Kammula, U. S., Hughes, M. S., Phan, G. Q., Citrin, D. E., Restifo, N. P., Robbins, P. F., Wunderlich, J. R., Morton, K. E., Laurencot, C. M., Steinberg, S. M., White, D. E., and Dudley, M. E. (2011). Durable Complete Responses in Heavily Pretreated Patients with Metastatic Melanoma Using T-Cell Transfer Immunotherapy. *Clinical Cancer Research*, 17(13):4550–4557.
- Roth, T. L., Puig-Saus, C., Yu, R., Shifrut, E., Carnevale, J., Li, P. J., Hiatt, J., Saco, J., Krystofinski, P., Li, H., Tobin, V., Nguyen, D. N., Lee, M. R., Putnam, A. L., Ferris, A. L., Chen, J. W., Schickel, J.-N., Pellerin, L., Carmody, D., Alkorta-Aranburu, G., del Gaudio, D., Matsumoto, H., Morell, M., Mao, Y., Cho, M., Quadros, R. M., Gurumurthy, C. B., Smith, B., Haugwitz, M., Hughes, S. H., Weissman, J. S., Schumann, K., Esensten, J. H., May, A. P., Ashworth, A., Kupfer, G. M., Greeley, S. A. W., Bacchetta, R., Meffre, E., Roncarolo, M. G., Romberg, N., Herold, K. C., Ribas, A., Leonetti, M. D., and Marson, A. (2018). Reprogramming human T cell function and specificity with non-viral genome targeting. *Nature*, 559(7714):405–409.
- Rubio, V., Stuge, T. B., Singh, N., Betts, M. R., Weber, J. S., Roederer, M., and Lee, P. P. (2003). Ex vivo identification, isolation and analysis of tumor-cytolytic T cells. *Nature Medicine*, 9(11):1377–1382.
- Rupp, L. J., Schumann, K., Roybal, K. T., Gate, R. E., Ye, C. J., Lim, W. A., and Marson, A. (2017). CRISPR/Cas9-mediated PD-1 disruption enhances anti-tumor efficacy of human chimeric antigen receptor T cells. *Scientific Reports*, 7(1):737.

- Ruprecht, C. R., Gattorno, M., Ferlito, F., Gregorio, A., Martini, A., Lanzavecchia, A., and Sallusto, F. (2005). Coexpression of CD25 and CD27 identifies FoxP3⁺ regulatory T cells in inflamed synovia. *The Journal of Experimental Medicine*, 201(11):1793–1803.
- Russell, J. H. and Ley, T. J. (2002). Lymphocyte-mediated cytotoxicity. *Annual Review of Immunology*, 20(1):323–370.
- Sadelain, M. (2016). Chimeric antigen receptors: driving immunology towards synthetic biology. *Current Opinion in Immunology*, 41:68–76.
- Sadelain, M., Brentjens, R., and Rivière, I. (2013). The Basic Principles of Chimeric Antigen Receptor Design. *Cancer Discovery*, 3(4):388–398.
- Sanjana, N. E., Shalem, O., and Zhang, F. (2014). Improved vectors and genome-wide libraries for CRISPR screening. *Nature Methods*, 11(8):783–784.
- Schroeder, A., Mueller, O., Stocker, S., Salowsky, R., Leiber, M., Gassmann, M., Lightfoot, S., Menzel, W., Granzow, M., and Ragg, T. (2006). The RIN: an RNA integrity number for assigning integrity values to RNA measurements. *BMC Molecular Biology*, 7(1):3.
- Schulze-Luehrmann, J. and Ghosh, S. (2006). Antigen-Receptor Signaling to Nuclear Factor κB. *Immunity*, 25(5):701–715.
- Schumann, K., Lin, S., Boyer, E., Simeonov, D. R., Subramaniam, M., Gate, R. E., Haliburton, G. E., Ye, C. J., Bluestone, J. A., Doudna, J. A., and Marson, A. (2015). Generation of knock-in primary human T cells using Cas9 ribonucleoproteins. *Proceedings of the National Academy of Sciences*, 112(33):10437–10442.
- Seki, A. and Rutz, S. (2018). Optimized RNP transfection for highly efficient CRISPR/Cas9-mediated gene knockout in primary T cells. *The Journal of Experimental Medicine*, 215(3):985–997.
- Shalem, O., Sanjana, N. E., Hartenian, E., Shi, X., Scott, D. A., Mikkelsen, T. S., Heckl, D., Ebert, B. L., Root, D. E., Doench, J. G., and Zhang, F. (2014). Genome-Scale CRISPR-Cas9 Knockout Screening in Human Cells. *Science*, 343(6166):84–87.
- Shang, W., Jiang, Y., Boettcher, M., Ding, K., Mollenauer, M., Liu, Z., Wen, X., Liu, C., Hao, P., Zhao, S., McManus, M. T., Wei, L., Weiss, A., and Wang, H. (2018). Genome-wide CRISPR screen identifies FAM49B as a key regulator of actin dynamics and T cell activation. *Proceedings of the National Academy of Sciences*, 115(17):E4051–E4060.
- Sharma, P., Hu-Liesková, S., Wargo, J. A., and Ribas, A. (2017). Primary, Adaptive, and Acquired Resistance to Cancer Immunotherapy. *Cell*, 168(4):707–723.
- Shifrut, E., Carnevale, J., Tobin, V., Roth, T. L., Woo, J. M., Bui, C. T., Li, P. J., Diolaiti, M. E., Ashworth, A., and Marson, A. (2018). Genome-wide CRISPR Screens in Primary Human T Cells Reveal Key Regulators of Immune Function. *Cell*, 175(7):1958–1971.e15.
- Shirakawa, R., Higashi, T., Tabuchi, A., Yoshioka, A., Nishioka, H., Fukuda, M., Kita, T., and Horiuchi, H. (2004). Munc13-4 Is a GTP-Rab27-binding Protein Regulating Dense Core Granule Secretion in Platelets. *Journal of Biological Chemistry*, 279(11):10730–10737.

- Sinclair, L. V., Rolf, J., Emslie, E., Shi, Y.-B., Taylor, P. M., and Cantrell, D. A. (2013). Control of amino-acid transport by antigen receptors coordinates the metabolic reprogramming essential for T cell differentiation. *Nature Immunology*, 14(5):500–508.
- Smith-Garvin, J. E., Koretzky, G. A., and Jordan, M. S. (2009). T Cell Activation. *Annual Review of Immunology*, 27(1):591–619.
- Snow, K. and Judd, W. (1987). Heterogeneity of a human T-lymphoblastoid cell line. *Experimental cell research*, 171(2):389–403.
- Spessott, W. A., Sanmillan, M. L., McCormick, M. E., Kulkarni, V. V., and Giraudo, C. G. (2017). SM protein Munc18-2 facilitates transition of Syntaxin 11-mediated lipid mixing to complete fusion for T-lymphocyte cytotoxicity. *Proceedings of the National Academy of Sciences*, 114(11):E2176–E2185.
- Spessott, W. A., Sanmillan, M. L., McCormick, M. E., Patel, N., Villanueva, J., Zhang, K., Nichols, K. E., and Giraudo, C. G. (2015). Hemophagocytic lymphohistiocytosis caused by dominant-negative mutations in STXBP2 that inhibit SNARE-mediated membrane fusion. *Blood*, 125(10):1566–1577.
- Stepp, S. E., Dufourcq-Lagelouse, R., Le Deist, F., Bhawan, S., Certain, S., Mathew, P. A., Henter, J. I., Bennett, M., Fischer, A., de Saint Basile, G., and Kumar, V. (1999). Perforin gene defects in familial hemophagocytic lymphohistiocytosis. *Science (New York, N.Y.)*, 286(5446):1957–9.
- Sternberg, S. H., Redding, S., Jinek, M., Greene, E. C., and Doudna, J. A. (2014). DNA interrogation by the CRISPR RNA-guided endonuclease Cas9. *Nature*, 507(7490):62–67.
- Stinchcombe, J., Bossi, G., and Griffiths, G. M. (2004). Linking Albinism and Immunity: The Secrets of Secretory Lysosomes. *Science*, 305(5680):55–59.
- Stinchcombe, J. C., Barral, D. C., Mules, E. H., Booth, S., Hume, A. N., Machesky, L. M., Seabra, M. C., and Griffiths, G. M. (2001a). Rab27a is required for regulated secretion in cytotoxic T lymphocytes. *The Journal of cell biology*, 152(4):825–34.
- Stinchcombe, J. C., Bossi, G., Booth, S., and Griffiths, G. M. (2001b). The immunological synapse of CTL contains a secretory domain and membrane bridges. *Immunity*, 15(5):751–61.
- Stinchcombe, J. C. and Griffiths, G. M. (2003). The role of the secretory immunological synapse in killing by CD8+ CTL. *Seminars in Immunology*, 15(6):301–305.
- Stinchcombe, J. C. and Griffiths, G. M. (2007). Secretory Mechanisms in Cell-Mediated Cytotoxicity. *Annual Review of Cell and Developmental Biology*, 23(1):495–517.
- Stinchcombe, J. C., Majorovits, E., Bossi, G., Fuller, S., and Griffiths, G. M. (2006). Centrosome polarization delivers secretory granules to the immunological synapse. *Nature*, 443(7110):462–465.
- Stinchcombe, J. C., Randzavola, L. O., Angus, K. L., Mantell, J. M., Verkade, P., and Griffiths, G. M. (2015). Mother Centriole Distal Appendages Mediate Centrosome Docking at the Immunological Synapse and Reveal Mechanistic Parallels with Ciliogenesis. *Current Biology*, 25(24):3239–3244.

- Strasser, A., Jost, P. J., and Nagata, S. (2009). The Many Roles of FAS Receptor Signaling in the Immune System. *Immunity*, 30(2):180–192.
- Sucker, A., Zhao, F., Real, B., Heeke, C., Bielefeld, N., Massen, S., Horn, S., Moll, I., Maltaner, R., Horn, P. A., Schilling, B., Sabbatino, F., Lennerz, V., Kloot, M., Ferrone, S., Schadendorf, D., Falk, C. S., Griewank, K., and Paschen, A. (2014). Genetic Evolution of T-cell Resistance in the Course of Melanoma Progression. *Clinical Cancer Research*, 20(24):6593–6604.
- Südhof, T. C. and Rothman, J. E. (2009). Membrane fusion: grappling with SNARE and SM proteins. *Science (New York, N.Y.)*, 323(5913):474–7.
- Tang, B. L., Low, D. Y., and Hong, W. (1998). Syntaxin 11: A Member of the Syntaxin Family without a Carboxyl Terminal Transmembrane Domain. *Biochemical and Biophysical Research Communications*, 245(2):627–632.
- Tanos, B. E., Yang, H.-J., Soni, R., Wang, W.-J., Macaluso, F. P., Asara, J. M., and Tsou, M.-F. B. (2013). Centriole distal appendages promote membrane docking, leading to cilia initiation. *Genes & development*, 27(2):163–8.
- Tebas, P., Stein, D., Tang, W. W., Frank, I., Wang, S. Q., Lee, G., Spratt, S. K., Surosky, R. T., Giedlin, M. A., Nichol, G., Holmes, M. C., Gregory, P. D., Ando, D. G., Kalos, M., Collman, R. G., Binder-Scholl, G., Plesa, G., Hwang, W.-T., Levine, B. L., and June, C. H. (2014). Gene Editing of CCR5 in Autologous CD4 T Cells of Persons Infected with HIV. *New England Journal of Medicine*, 370(10):901–910.
- Topalian, S., Drake, C., and Pardoll, D. (2015). Immune Checkpoint Blockade: A Common Denominator Approach to Cancer Therapy. *Cancer Cell*, 27(4):450–461.
- Topham, N. J. and Hewitt, E. W. (2009). Natural killer cell cytotoxicity: how do they pull the trigger? *Immunology*, 128(1):7–15.
- Trapani, J. A. (2001). Granzymes: a family of lymphocyte granule serine proteases. *Genome biology*, 2(12):REVIEWS3014.
- Trapani, J. A. and Sutton, V. R. (2003). Granzyme B: pro-apoptotic, antiviral and antitumor functions. *Current opinion in immunology*, 15(5):533–43.
- Tschopp, J. and Nabholz, M. (1990). Perforin-Mediated Target Cell Lysis by Cytolytic T Lymphocytes. *Annual Review of Immunology*, 8(1):279–302.
- Tzelepis, K., Koike-Yusa, H., De Braekeleer, E., Li, Y., Metzakopian, E., Dovey, O., Mupo, A., Grinkevich, V., Li, M., Mazan, M., Gozdecka, M., Ohnishi, S., Cooper, J., Patel, M., McKerrell, T., Chen, B., Domingues, A., Gallipoli, P., Teichmann, S., Ponstingl, H., McDermott, U., Saez-Rodriguez, J., Huntly, B., Iorio, F., Pina, C., Vassiliou, G., and Yusa, K. (2016). A CRISPR Dropout Screen Identifies Genetic Vulnerabilities and Therapeutic Targets in Acute Myeloid Leukemia. *Cell Reports*, 17(4):1193–1205.
- Uellner, R., Zvelebil, M. J., Hopkins, J., Jones, J., MacDougall, L. K., Morgan, B. P., Podack, E., Waterfield, M. D., and Griffiths, G. M. (1997). Perforin is activated by a proteolytic cleavage during biosynthesis which reveals a phospholipid-binding C2 domain. *The EMBO Journal*, 16(24):7287–7296.

- Valdez, A. C., Cabaniols, J. P., Brown, M. J., and Roche, P. A. (1999). Syntaxin 11 is associated with SNAP-23 on late endosomes and the trans-Golgi network. *Journal of cell science*, 112 (Pt 6):845–54.
- Vallabhapurapu, S. and Karin, M. (2009). Regulation and Function of NF- κ B Transcription Factors in the Immune System. *Annual Review of Immunology*, 27(1):693–733.
- Walsh, C. M., Matloubian, M., Liu, C. C., Ueda, R., Kurahara, C. G., Christensen, J. L., Huang, M. T., Young, J. D., Ahmed, R., and Clark, W. R. (1994). Immune function in mice lacking the perforin gene. *Proceedings of the National Academy of Sciences of the United States of America*, 91(23):10854–8.
- Wang, T., Wei, J. J., Sabatini, D. M., and Lander, E. S. (2014a). Genetic Screens in Human Cells Using the CRISPR-Cas9 System. *Science*, 343(6166):80–84.
- Wang, W., Ye, C., Liu, J., Zhang, D., Kimata, J. T., and Zhou, P. (2014b). CCR5 Gene Disruption via Lentiviral Vectors Expressing Cas9 and Single Guided RNA Renders Cells Resistant to HIV-1 Infection. *PLoS ONE*, 9(12):e115987.
- Wang, Z., Gerstein, M., and Snyder, M. (2009). RNA-Seq: a revolutionary tool for transcriptomics. *Nature Reviews Genetics*, 10(1):57–63.
- Ward, D. M., Griffiths, G. M., Stinchcombe, J. C., and Kaplan, J. (2000). Analysis of the lysosomal storage disease Chediak-Higashi syndrome. *Traffic (Copenhagen, Denmark)*, 1(11):816–22.
- Wardyn, J. D., Ponsford, A. H., and Sanderson, C. M. (2015). Dissecting molecular cross-talk between Nrf2 and NF- κ B response pathways. *Biochemical Society transactions*, 43(4):621–6.
- Wennerberg, K., Rossman, K. L., and Der, C. J. (2005). The Ras superfamily at a glance. *Journal of Cell Science*, 118(5):843–846.
- Williams, M. A. and Bevan, M. J. (2007). Effector and Memory CTL Differentiation. *Annual Review of Immunology*, 25(1):171–192.
- Wilson, S. M., Yip, R., Swing, D. A., O’Sullivan, T. N., Zhang, Y., Novak, E. K., Swank, R. T., Russell, L. B., Copeland, N. G., and Jenkins, N. A. (2000). A mutation in Rab27a causes the vesicle transport defects observed in ashen mice. *Proceedings of the National Academy of Sciences of the United States of America*, 97(14):7933–8.
- Wolchok, J. D., Kluger, H., Callahan, M. K., Postow, M. A., Rizvi, N. A., Lesokhin, A. M., Segal, N. H., Ariyan, C. E., Gordon, R.-A., Reed, K., Burke, M. M., Caldwell, A., Kronenberg, S. A., Agunwamba, B. U., Zhang, X., Lowy, I., Inzunza, H. D., Feely, W., Horak, C. E., Hong, Q., Korman, A. J., Wigginton, J. M., Gupta, A., and Sznol, M. (2013). Nivolumab plus Ipilimumab in Advanced Melanoma. *New England Journal of Medicine*, 369(2):122–133.
- Wu, X., Rao, K., Bowers, M. B., Copeland, N. G., Jenkins, N. A., and Hammer, J. A. (2001). Rab27a enables myosin Va-dependent melanosome capture by recruiting the myosin to the organelle. *Journal of cell science*, 114(Pt 6):1091–100.

- Wu, X. S., Rao, K., Zhang, H., Wang, F., Sellers, J. R., Matesic, L. E., Copeland, N. G., Jenkins, N. A., and Hammer, J. A. (2002). Identification of an organelle receptor for myosin-Va. *Nature Cell Biology*, 4(4):271–278.
- Wucherpfennig, K. W., Gagnon, E., Call, M. J., Huseby, E. S., and Call, M. E. (2010). Structural Biology of the T-cell Receptor: Insights into Receptor Assembly, Ligand Recognition, and Initiation of Signaling. *Cold Spring Harbor Perspectives in Biology*, 2(4):a005140–a005140.
- Ye, S., Karim, Z. A., Al Hawas, R., Pessin, J. E., Filipovich, A. H., and Whiteheart, S. W. (2012). Syntaxin-11, but not syntaxin-2 or syntaxin-4, is required for platelet secretion. *Blood*, 120(12):2484–2492.
- Young, J. D., Damiano, A., DiNome, M. A., Leong, L. G., and Cohn, Z. A. (1987). Dissociation of membrane binding and lytic activities of the lymphocyte pore-forming protein (perforin). *The Journal of experimental medicine*, 165(5):1371–82.
- Yu, H., Rathore, S. S., Lopez, J. A., Davis, E. M., James, D. E., Martin, J. L., and Shen, J. (2013). Comparative studies of Munc18c and Munc18-1 reveal conserved and divergent mechanisms of Sec1/Munc18 proteins. *Proceedings of the National Academy of Sciences*, 110(35):E3271–E3280.
- Yu, Z., Chen, Y., Wang, S., Li, P., Zhou, G., and Yuan, Y. (2018). Inhibition of NF- κ B results in anti-glioma activity and reduces temozolomide-induced chemoresistance by down-regulating MGMT gene expression. *Cancer Letters*, 428:77–89.
- Zhang, N. and Bevan, M. J. (2011). CD8(+) T cells: foot soldiers of the immune system. *Immunity*, 35(2):161–8.
- Zou, W., Wolchok, J. D., and Chen, L. (2016). PD-L1 (B7-H1) and PD-1 pathway blockade for cancer therapy: Mechanisms, response biomarkers, and combinations. *Science Translational Medicine*, 8(328):328rv4–328rv4.
- zur Stadt, U., Rohr, J., Seifert, W., Koch, F., Grieve, S., Pagel, J., Strauß, J., Kasper, B., Nürnberg, G., Becker, C., Maul-Pavicic, A., Beutel, K., Janka, G., Griffiths, G., Ehl, S., and Hennies, H. C. (2009). Familial Hemophagocytic Lymphohistiocytosis Type 5 (FHL-5) Is Caused by Mutations in Munc18-2 and Impaired Binding to Syntaxin 11. *The American Journal of Human Genetics*, 85(4):482–492.
- zur Stadt, U., Schmidt, S., Kasper, B., Beutel, K., Diler, A. S., Henter, J.-I., Kabisch, H., Schneppenheim, R., Nürnberg, P., Janka, G., and Hennies, H. C. (2005). Linkage of familial hemophagocytic lymphohistiocytosis (FHL) type-4 to chromosome 6q24 and identification of mutations in syntaxin 11. *Human Molecular Genetics*, 14(6):827–834.

