

References

- [1] 1000 Genomes Project Consortium (2015). A global reference for human genetic variation. *Nature*, 526(7571):68.
- [2] Abegunde, A. T., Muhammad, B. H., Bhatti, O., and Ali, T. (2016). Environmental risk factors for inflammatory bowel diseases: evidence based literature review. *World Journal of Gastroenterology*, 22(27):6296.
- [3] Allchin, W. H. (1909). A discussion on ‘ulcerative colitis’: introductory address. *Proceedings of the Royal Society of Medicine*, 2(Med Sect):59.
- [4] Aloisio, M., Nuti, F., Stronati, L., and Cucchiara, S. (2014). Advances in the medical management of paediatric IBD. *Nature Reviews Gastroenterology & Hepatology*, 11(2):99.
- [5] Ananthakrishnan, A. N., Khalili, H., Konijeti, G. G., Higuchi, L. M., de Silva, P., Fuchs, C. S., Willett, W. C., Richter, J. M., and Chan, A. T. (2014). Long-term intake of dietary fat and risk of ulcerative colitis and Crohn’s disease. *Gut*, 63(5):776–784.
- [6] Ananthakrishnan, A. N., Khalili, H., Konijeti, G. G., Higuchi, L. M., de Silva, P., Korzenik, J. R., Fuchs, C. S., Willett, W. C., Richter, J. M., and Chan, A. T. (2013). A prospective study of long-term intake of dietary fiber and risk of Crohn’s disease and ulcerative colitis. *Gastroenterology*, 145(5):970–977.
- [7] Anderson, C. A., Pettersson, F. H., Clarke, G. M., Cardon, L. R., Morris, A. P., and Zondervan, K. T. (2010). Data quality control in genetic case-control association studies. *Nature Protocols*, 5(9):1564.
- [8] Anselmo, A. C., Gokarn, Y., and Mitragotri, S. (2018). Non-invasive delivery strategies for biologics. *Nature Reviews Drug Discovery*.
- [9] Arthur, R., Schulz-Trieglaff, O., Cox, A. J., and O’Connell, J. (2016). AKT: ancestry and kinship toolkit. *Bioinformatics*, 33(1):142–144.
- [10] Astle, W. J., Elding, H., Jiang, T., Allen, D., Ruklisa, D., Mann, A. L., Mead, D., Bouman, H., Riveros-Mckay, F., Kostadima, M. A., et al. (2016). The allelic landscape of human blood cell trait variation and links to common complex disease. *Cell*, 167(5):1415–1429.
- [11] Aterido, A., Palau, N., Domènech, E., Mateu, P. N., Gutiérrez, A., Gomollón, F., Mendoza, J. L., Garcia-Planella, E., Barreiro-de Acosta, M., Muñoz, F., et al. (2019).

- Genetic association between *CD96* locus and immunogenicity to anti-TNF therapy in Crohn's disease. *The Pharmacogenomics Journal*, 19(6):547–555.
- [12] Avitzur, Y., Guo, C., Mastropaolo, L. A., Bahrami, E., Chen, H., Zhao, Z., Elkadri, A., Dhillon, S., Murchie, R., Fattouh, R., et al. (2014). Mutations in tetratricopeptide repeat domain 7A result in a severe form of very early onset inflammatory bowel disease. *Gastroenterology*, 146(4):1028–1039.
- [13] Axelrad, J. E., Roy, A., Lawlor, G., Korelitz, B., and Lichtiger, S. (2016). Thiopurines and inflammatory bowel disease: current evidence and a historical perspective. *World Journal of Gastroenterology*, 22(46):10103.
- [14] Barrett, J. C. and Cardon, L. R. (2006). Evaluating coverage of genome-wide association studies. *Nature Genetics*, 38(6):659.
- [15] Barrett, J. C., Hansoul, S., Nicolae, D. L., Cho, J. H., Duerr, R. H., Rioux, J. D., Brant, S. R., Silverberg, M. S., Taylor, K. D., Barmada, M. M., et al. (2008). Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. *Nature Genetics*, 40(8):955.
- [16] Bastida, G., Nos, P., Aguas, M., Beltrán, B., Rubín, A., Dasí, F., and Ponce, J. (2005). Incidence, risk factors and clinical course of thiopurine-induced liver injury in patients with inflammatory bowel disease. *Alimentary Pharmacology & Therapeutics*, 22(9):775–782.
- [17] Beigel, F., Deml, M., Schnitzler, F., Breiteneicher, S., Göke, B., Ochsenkühn, T., and Brand, S. (2014). Rate and predictors of mucosal healing in patients with inflammatory bowel disease treated with anti-TNF-alpha antibodies. *PLoS One*, 9(6):e99293.
- [18] Beissinger, T. M., Rosa, G. J., Kaepller, S. M., Gianola, D., and de Leon, N. (2015). Defining window-boundaries for genomic analyses using smoothing spline techniques. *Genetics Selection Evolution*, 47(1):30.
- [19] Benchimol, E. I., Mack, D. R., Guttmann, A., Nguyen, G. C., To, T., Mojaverian, N., Quach, P., and Manuel, D. G. (2015). Inflammatory bowel disease in immigrants to Canada and their children: a population-based cohort study. *The American Journal of Gastroenterology*, 110(4):553.
- [20] Benner, C., Havulinna, A. S., Järvelin, M.-R., Salomaa, V., Ripatti, S., and Pirinen, M. (2017). Prospects of fine-mapping trait-associated genomic regions by using summary statistics from genome-wide association studies. *The American Journal of Human Genetics*, 101(4):539–551.
- [21] Benner, C., Spencer, C. C., Havulinna, A. S., Salomaa, V., Ripatti, S., and Pirinen, M. (2016). FINEMAP: efficient variable selection using summary data from genome-wide association studies. *Bioinformatics*, 32(10):1493–1501.
- [22] Bernstein, B. E., Stamatoyannopoulos, J. A., Costello, J. F., Ren, B., Milosavljevic, A., Meissner, A., Kellis, M., Marra, M. A., Beaudet, A. L., Ecker, J. R., et al. (2010). The NIH Roadmap Epigenomics Mapping Consortium. *Nature Biotechnology*, 28(10):1045.

- [23] Billiet, T., Vande Castele, N., Van Stappen, T., Princen, F., Singh, S., Gils, A., Ferrante, M., Van Assche, G., Cleynen, I., and Vermeire, S. (2015). Immunogenicity to infliximab is associated with *HLA-DRB1*. *Gut*, 64(8):1344–5.
- [24] Björnsson, E. S., Bergmann, O. M., Björnsson, H. K., Kvaran, R. B., and Olafsson, S. (2013). Incidence, presentation, and outcomes in patients with drug-induced liver injury in the general population of Iceland. *Gastroenterology*, 144(7):1419–1425.
- [25] Blackstone, E. A. and Joseph, P. F. (2013). The economics of biosimilars. *American Health & Drug Benefits*, 6(8):469.
- [26] Bouameur, J.-E., Favre, B., and Borradori, L. (2014). Plakins, a versatile family of cytolinkers: roles in skin integrity and in human diseases. *Journal of Investigative Dermatology*, 134(4):885–894.
- [27] Boyle, E. A., Li, Y. I., and Pritchard, J. K. (2017). An expanded view of complex traits: from polygenic to omnigenic. *Cell*, 169(7):1177–1186.
- [28] Broad Institute Genomic Services (2019). Human whole exome sequencing. <http://genomics.broadinstitute.org/products/whole-exome-sequencing>. Accessed: 26.06.2019.
- [29] Brodie, A., Azaria, J. R., and Ofran, Y. (2016). How far from the SNP may the causative genes be? *Nucleic Acids Research*, 44(13):6046–6054.
- [30] Broekman, M. M., Coenen, M. J., Wanten, G. J., van Marrewijk, C. J., Klungel, O. H., Verbeek, A. L., Hooymans, P. M., Guchelaar, H.-J., Scheffer, H., Derijks, L. J., et al. (2017). Risk factors for thiopurine-induced myelosuppression and infections in inflammatory bowel disease patients with a normal *TPMT* genotype. *Alimentary Pharmacology & Therapeutics*, 46(10):953–963.
- [31] Browning, S. R. (2006). Multilocus association mapping using variable-length Markov chains. *The American Journal of Human Genetics*, 78(6):903–913.
- [32] Buenrostro, J. D., Giresi, P. G., Zaba, L. C., Chang, H. Y., and Greenleaf, W. J. (2013). Transposition of native chromatin for fast and sensitive epigenomic profiling of open chromatin, DNA-binding proteins and nucleosome position. *Nature Methods*, 10(12):1213.
- [33] Buniello, A., MacArthur, J. A. L., Cerezo, M., Harris, L. W., Hayhurst, J., Malangone, C., McMahon, A., Morales, J., Mountjoy, E., Sollis, E., et al. (2018). The NHGRI-EBI GWAS catalog of published genome-wide association studies, targeted arrays and summary statistics 2019. *Nucleic Acids Research*, 47(D1):D1005–D1012.
- [34] Burdett, T., Hall, P., Hastings, E., Hindorff, L., Junkins, H., Klemm, A., MacArthur, J., Manolio, T., Morales, J., Parkinson, H., et al. (2016). The NHGRI-EBI catalog of published genome-wide association studies. Available at: www.ebi.ac.uk/gwas.
- [35] Bycroft, C., Freeman, C., Petkova, D., Band, G., Elliott, L. T., Sharp, K., Motyer, A., Vukcevic, D., Delaneau, O., O'Connell, J., et al. (2018). The UK Biobank resource with deep phenotyping and genomic data. *Nature*, 562(7726):203.

- [36] Calkins, B. M. (1989). A meta-analysis of the role of smoking in inflammatory bowel disease. *Digestive Diseases and Sciences*, 34(12):1841–1854.
- [37] Chen, W., Larrabee, B. R., Ovsyannikova, I. G., Kennedy, R. B., Haralambieva, I. H., Poland, G. A., and Schaid, D. J. (2015). Fine mapping causal variants with an approximate Bayesian method using marginal test statistics. *Genetics*, 200(3):719–736.
- [38] Chun, S., Casparino, A., Patsopoulos, N. A., Croteau-Chonka, D. C., Raby, B. A., de Jager, P. L., Sunyaev, S. R., and Cotsapas, C. (2017). Limited statistical evidence for shared genetic effects of eQTLs and autoimmune-disease-associated loci in three major immune-cell types. *Nature Genetics*, 49(4):600.
- [39] Cirulli, E. T., Nicoletti, P., Abramson, K., Andrade, R. J., Bjornsson, E. S., Chalasani, N., Fontana, R. J., Hallberg, P., Li, Y. J., Lucena, M. I., et al. (2019). A missense variant in *PTPN22* is a risk factor for drug-induced liver injury. *Gastroenterology*, 156(6):1707–1716.
- [40] Cleynen, I., Boucher, G., Jostins, L., Schumm, L. P., Zeissig, S., Ahmad, T., Andersen, V., Andrews, J. M., Annese, V., Brand, S., et al. (2016). Inherited determinants of Crohn’s disease and ulcerative colitis phenotypes: a genetic association study. *The Lancet*, 387(10014):156–167.
- [41] Colombel, J. F., Sandborn, W. J., Reinisch, W., Mantzaris, G. J., Kornbluth, A., Rachmilewitz, D., Lichtiger, S., D’haens, G., Diamond, R. H., Broussard, D. L., et al. (2010). Infliximab, azathioprine, or combination therapy for Crohn’s disease. *New England Journal of Medicine*, 362(15):1383–1395.
- [42] Concannon, P., Rich, S. S., and Nepom, G. T. (2009). Genetics of type 1A diabetes. *New England Journal of Medicine*, 360(16):1646–1654.
- [43] Cooper, G. M. and Shendure, J. (2011). Needles in stacks of needles: finding disease-causal variants in a wealth of genomic data. *Nature Reviews Genetics*, 12(9):628.
- [44] Cornish, A. and Guda, C. (2015). A comparison of variant calling pipelines using genome in a bottle as a reference. *BioMed Research International*, 2015.
- [45] Daly, A. K., Donaldson, P. T., Bhatnagar, P., Shen, Y., Pe’er, I., Floratos, A., Daly, M. J., Goldstein, D. B., John, S., Nelson, M. R., et al. (2009). HLA-B*5701 genotype is a major determinant of drug-induced liver injury due to flucloxacillin. *Nature Genetics*, 41(7):816.
- [46] Dave, C. V., Hartzema, A., and Kesselheim, A. S. (2017). Prices of generic drugs associated with numbers of manufacturers. *New England Journal of Medicine*, 377(26):2597–2598.
- [47] de Bruyn, M. and Vermeire, S. (2017). *NOD2* and bacterial recognition as therapeutic targets for Crohn’s disease. *Expert Opinion on Therapeutic Targets*, 21(12):1123–1139.
- [48] de Groot, A. S., Knopp, P. M., and Martin, W. (2005). De-immunization of therapeutic proteins by T-cell epitope modification. *Developments in Biologicals*, 122:171–94.

- [49] de Lange, K. M., Moutsianas, L., Lee, J. C., Lamb, C. A., Luo, Y., Kennedy, N. A., Jostins, L., Rice, D. L., Gutierrez-Achury, J., Ji, S.-G., et al. (2017). Genome-wide association study implicates immune activation of multiple integrin genes in inflammatory bowel disease. *Nature Genetics*, 49(2):256.
- [50] Dean, J. and Ghemawat, S. (2008). Mapreduce: simplified data processing on large clusters. *Communications of the ACM*, 51(1):107–113.
- [51] DeBoever, C., Li, H., Jakubosky, D., Benaglio, P., Reyna, J., Olson, K. M., Huang, H., Biggs, W., Sandoval, E., D’Antonio, M., et al. (2017). Large-scale profiling reveals the influence of genetic variation on gene expression in human induced pluripotent stem cells. *Cell Stem Cell*, 20(4):533–546.
- [52] del Val, J. H. (2011). Old-age inflammatory bowel disease onset: a different problem? *World Journal of Gastroenterology*, 17(22):2734.
- [53] D’Haens, G., Baert, F., van Assche, G., Caenepeel, P., Vergauwe, P., Tuynman, H., de Vos, M., van Deventer, S., Stitt, L., Donner, A., et al. (2008). Early combined immunosuppression or conventional management in patients with newly diagnosed Crohn’s disease: an open randomised trial. *The Lancet*, 371(9613):660–667.
- [54] D’Haens, G., Reinisch, W., Panaccione, R., Satsangi, J., Petersson, J., Bereswill, M., Arikian, D., Perotti, E., Robinson, A. M., Kalabic, J., Alperovich, G., Thakkar, R., and Loftus, E. V. (2018). Lymphoma risk and overall safety profile of adalimumab in patients with Crohn’s disease with up to 6 years of follow-up in the pyramid registry. *The American Journal of Gastroenterology*, 113(6):872–882.
- [55] Dilthey, A. T., Mentzer, A. J., Carapito, R., Cutland, C., Cereb, N., Madhi, S. A., Rhie, A., Koren, S., Bahram, S., McVean, G., et al. (2019). HLA*LA – HLA typing from linearly projected graph alignments. *Bioinformatics*, 35(21):4394–4396.
- [56] Drubay, D., Gautheret, D., and Michiels, S. (2018). A benchmark study of scoring methods for non-coding mutations. *Bioinformatics*, 34(10):1635–1641.
- [57] Duerr, R. H., Taylor, K. D., Brant, S. R., Rioux, J. D., Silverberg, M. S., Daly, M. J., Steinhart, A. H., Abraham, C., Regueiro, M., Griffiths, A., et al. (2006). A genome-wide association study identifies *IL23R* as an inflammatory bowel disease gene. *Science*, 314(5804):1461–1463.
- [58] Ek, W. E., D’Amato, M., and Halfvarson, J. (2014). The history of genetics in inflammatory bowel disease. *Annals of Gastroenterology*, 27(4):294.
- [59] ENCODE Project Consortium (2012). An integrated encyclopedia of DNA elements in the human genome. *Nature*, 489(7414):57.
- [60] Eu-ahsunthornwattana, J., Miller, E. N., Fakiola, M., Jeronimo, S. M., Blackwell, J. M., Cordell, H. J., Wellcome Trust Case Control Consortium 2, et al. (2014). Comparison of methods to account for relatedness in genome-wide association studies with family-based data. *PLoS Genetics*, 10(7).

- [61] Fevr, T., Robine, S., Louvard, D., and Huelsken, J. (2007). Wnt/ β -catenin is essential for intestinal homeostasis and maintenance of intestinal stem cells. *Molecular and Cellular Biology*, 27(21):7551–7559.
- [62] Fisher, S. A., Tremelling, M., Anderson, C. A., Gwilliam, R., Bumpstead, S., Prescott, N. J., Nimmo, E. R., Massey, D., Berzuini, C., Johnson, C., et al. (2008). Genetic determinants of ulcerative colitis include the *ECM1* locus and five loci implicated in Crohn's disease. *Nature Genetics*, 40(6):710.
- [63] Fuchsberger, C., Flannick, J., Teslovich, T. M., Mahajan, A., Agarwala, V., Gaulton, K. J., Ma, C., Fontanillas, P., Moutsianas, L., McCarthy, D. J., et al. (2016). The genetic architecture of type 2 diabetes. *Nature*, 536(7614):41.
- [64] Gamazon, E. R., Wheeler, H. E., Shah, K. P., Mozaffari, S. V., Aquino-Michaels, K., Carroll, R. J., Eyler, A. E., Denny, J. C., Nicolae, D. L., Cox, N. J., et al. (2015). A gene-based association method for mapping traits using reference transcriptome data. *Nature Genetics*, 47(9):1091–1098.
- [65] Gearry, R. B., Barclay, M. L., Burt, M. J., Collett, J. A., and Chapman, B. A. (2004). Thiopurine drug adverse effects in a population of New Zealand patients with inflammatory bowel disease. *Pharmacoepidemiology and Drug Safety*, 13(8):563–567.
- [66] Gevers, D., Kugathasan, S., Denson, L. A., Vázquez-Baeza, Y., van Treuren, W., Ren, B., Schwager, E., Knights, D., Song, S. J., Yassour, M., et al. (2014). The treatment-naïve microbiome in new-onset Crohn's disease. *Cell Host & Microbe*, 15(3):382–392.
- [67] Giambartolomei, C., Vukcevic, D., Schadt, E. E., Franke, L., Hingorani, A. D., Wallace, C., and Plagnol, V. (2014). Bayesian test for colocalisation between pairs of genetic association studies using summary statistics. *PLoS Genetics*, 10(5).
- [68] Gilly, A., Southam, L., Suveges, D., Kuchenbaecker, K., Moore, R., Melloni, G., Hatzikotoulas, K., Farmaki, A.-E., Ritchie, G., Schwartzentruber, J., et al. (2018). Very low depth whole genome sequencing in complex trait association studies. *bioRxiv*.
- [69] Gisbert, J. P., González-Lama, Y., and Maté, J. (2007). Thiopurine-induced liver injury in patients with inflammatory bowel disease: a systematic review. *The American Journal of Gastroenterology*, 102(7):1518.
- [70] Goldstein, D. B. et al. (2009). Common genetic variation and human traits. *New England Journal of Medicine*, 360(17):1696.
- [71] González-Galarza, F. F., Takeshita, L. Y., Santos, E. J., Kempson, F., Maia, M. H. T., da Silva, A. L. S., Silva, A. L. T. e., Ghattaoraya, G. S., Alfirevic, A., Jones, A. R., and Middleton, D. (2015). Allele frequency net 2015 update: new features for HLA epitopes, KIR and disease and HLA adverse drug reaction associations. *Nucleic Acids Research*, 43(D1):D784–D788.
- [72] Gordon, H., Trier Moller, F., Andersen, V., and Harbord, M. (2015). Heritability in inflammatory bowel disease: from the first twin study to genome-wide association studies. *Inflammatory Bowel Diseases*, 21(6):1428–1434.

- [73] Goyette, P., Boucher, G., Mallon, D., Ellinghaus, E., Jostins, L., Huang, H., Ripke, S., Gusareva, E. S., Annese, V., Hauser, S. L., Oksenberg, J. R., Thomsen, I., Leslie, S., Daly, M. J., Van Steen, K., Duerr, R. H., Barrett, J. C., McGovern, D. P. B., Schumm, L. P., Traherne, J. A., Carrington, M. N., Kosmoliaptis, V., Karlsen, T. H., Franke, A., and Rioux, J. D. (2015). High-density mapping of the MHC identifies a shared role for HLA-DRB1*01:03 in inflammatory bowel diseases and heterozygous advantage in ulcerative colitis. *Nature Genetics*, 47(2):172–179.
- [74] Grob, S. and Cavalli, G. (2018). Technical review: a hitchhiker’s guide to chromosome conformation capture. In *Plant Chromatin Dynamics*, pages 233–246. Springer.
- [75] GTEx Consortium (2017). Genetic effects on gene expression across human tissues. *Nature*, 550(7675):204.
- [76] Gusev, A., Ko, A., Shi, H., Bhatia, G., Chung, W., Penninx, B. W., Jansen, R., de Geus, E. J., Boomsma, D. I., Wright, F. A., et al. (2016). Integrative approaches for large-scale transcriptome-wide association studies. *Nature Genetics*, 48(3):245–252.
- [77] Hail Team (2019). Hail. <https://github.com/hail-is/hail/releases/tag/0.2.20>. Accessed: 26.06.2019.
- [78] Han, F. and Pan, W. (2010). A data-adaptive sum test for disease association with multiple common or rare variants. *Human Heredity*, 70(1):42–54.
- [79] Hedin, C. and Halfvarson, J. (2018). Should we use vedolizumab as mono or combo therapy in ulcerative colitis? *Best Practice & Research Clinical Gastroenterology*, 32:27–34.
- [80] Hoofnagle, J. H. (2013). Livertox: a website on drug-induced liver injury. In *Drug-Induced Liver Disease*, pages 725–732. Elsevier.
- [81] Hooper, K. M., Casanova, V., Kemp, S., Staines, K. A., Satsangi, J., Barlow, P. G., Henderson, P., and Stevens, C. (2019). The inflammatory bowel disease drug azathioprine induces autophagy via mTORC1 and the unfolded protein response sensor PERK. *Inflammatory Bowel Diseases*, 25(9):1481–1496.
- [82] Huang, H., Fang, M., Jostins, L., Mirkov, M. U., Boucher, G., Anderson, C. A., Andersen, V., Cleynen, I., Cortes, A., Crins, F., et al. (2017). Fine-mapping inflammatory bowel disease loci to single-variant resolution. *Nature*, 547(7662):173.
- [83] Illumina (2017). Effects of index misassignment on multiplexing and downstream analysis. <https://emea.illumina.com/content/dam/illumina-marketing/documents/products/whitepapers/index-hopping-white-paper-770-2017-004.pdf>. Accessed: 26.06.2019.
- [84] International HapMap Consortium et al. (2005). A haplotype map of the human genome. *Nature*, 437(7063):1299.
- [85] International Human Genome Sequencing Consortium et al. (2001). Initial sequencing and analysis of the human genome. *Nature*, 409(6822):860.
- [86] IQVIA Institute (2019). The Global Use of Medicine in 2019 and Outlook to 2023.

- [87] Ji, S.-G., Juran, B. D., Mucha, S., Folseras, T., Jostins, L., Melum, E., Kumasaka, N., Atkinson, E. J., Schlicht, E. M., Liu, J. Z., et al. (2017). Genome-wide association study of primary sclerosing cholangitis identifies new risk loci and quantifies the genetic relationship with inflammatory bowel disease. *Nature Genetics*, 49(2):269.
- [88] Johnson, J. L. and Abecasis, G. R. (2017). Gas power calculator: web-based power calculator for genetic association studies. *bioRxiv*.
- [89] Johnston, R. D. and Logan, R. F. (2008). What is the peak age for onset of IBD? *Inflammatory Bowel Diseases*, 14(2):S4–S5.
- [90] Jones, G.-R., Lyons, M., Plevris, N., Jenkinson, P. W., Bisset, C., Burgess, C., Din, S., Fulforth, J., Henderson, P., Ho, G.-T., et al. (2019). IBD prevalence in Lothian, Scotland, derived by capture-recapture methodology. *Gut*, 68(11):1953–1960.
- [91] Jostins, L., Levine, A. P., and Barrett, J. C. (2013). Using genetic prediction from known complex disease loci to guide the design of next-generation sequencing experiments. *PLoS One*, 8(10).
- [92] Jostins, L., Ripke, S., Weersma, R. K., Duerr, R. H., McGovern, D. P., Hui, K. Y., Lee, J. C., Schumm, L. P., Sharma, Y., Anderson, C. A., et al. (2012). Host–microbe interactions have shaped the genetic architecture of inflammatory bowel disease. *Nature*, 491(7422):119.
- [93] Kaplan, G. G. (2015). The global burden of IBD: from 2015 to 2025. *Nature Reviews Gastroenterology & Hepatology*, 12(12):720.
- [94] Kaplan, G. G. and Ng, S. C. (2017). Understanding and preventing the global increase of inflammatory bowel disease. *Gastroenterology*, 152(2):313–321.
- [95] Karczewski, K. J., Francioli, L. C., Tiao, G., Cummings, B. B., Alföldi, J., Wang, Q., Collins, R. L., Laricchia, K. M., Ganna, A., Birnbaum, D. P., et al. (2019). Variation across 141,456 human exomes and genomes reveals the spectrum of loss-of-function intolerance across human protein-coding genes. *bioRxiv*.
- [96] Kennedy, N. A., Heap, G. A., Green, H. D., Hamilton, B., Bewshea, C., Walker, G. J., Thomas, A., Nice, R., Perry, M. H., Bouri, S., et al. (2019). Predictors of anti-TNF treatment failure in anti-TNF-naïve patients with active luminal Crohn's disease: a prospective, multicentre, cohort study. *The Lancet Gastroenterology & Hepatology*, 4(5):341–353.
- [97] Khera, A. V., Chaffin, M., Aragam, K. G., Haas, M. E., Roselli, C., Choi, S. H., Natarajan, P., Lander, E. S., Lubitz, S. A., Ellinor, P. T., et al. (2018). Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations. *Nature Genetics*, 50(9):1219.
- [98] King, E. A., Davis, J. W., and Degner, J. F. (2019). Are drug targets with genetic support twice as likely to be approved? Revised estimates of the impact of genetic support for drug mechanisms on the probability of drug approval. *bioRxiv*.

- [99] Kirschner, B. S. (2016). Indeterminate colitis/inflammatory bowel disease unclassified (IBD-U). In *Textbook of Pediatric Gastroenterology, Hepatology and Nutrition*, pages 335–340. Springer.
- [100] Knox, N. C., Forbes, J. D., van Domselaar, G., and Bernstein, C. N. (2019). The gut microbiome as a target for IBD treatment: are we there yet? *Current Treatment Options in Gastroenterology*, 17(1):115–126.
- [101] Kondrashova, A., Mustalahti, K., Kaukinen, K., Viskari, H., Volodicheva, V., Haapala, A.-M., Ilonen, J., Knip, M., Mäki, M., Hyöty, H., et al. (2008). Lower economic status and inferior hygienic environment may protect against celiac disease. *Annals of Medicine*, 40(3):223–231.
- [102] Kosugi, S., Momozawa, Y., Liu, X., Terao, C., Kubo, M., and Kamatani, Y. (2019). Comprehensive evaluation of structural variation detection algorithms for whole genome sequencing. *Genome Biology*, 20(1):117.
- [103] Lamb, C. A., Kennedy, N. A., Raine, T., Hendy, P. A., Smith, P. J., Limdi, J. K., Hayee, B., Lomer, M. C., Parkes, G. C., Selinger, C., et al. (2019). British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut*, 68(Suppl 3):s1–s106.
- [104] Lee, P. H., Lee, C., Li, X., Wee, B., Dwivedi, T., and Daly, M. (2018). Principles and methods of in-silico prioritization of non-coding regulatory variants. *Human Genetics*, 137(1):15–30.
- [105] Levine, A. P., Pontikos, N., Schiff, E. R., Jostins, L., Speed, D., Lovat, L. B., Barrett, J. C., Grasberger, H., Plagnol, V., Segal, A. W., et al. (2016). Genetic complexity of Crohn’s disease in two large Ashkenazi Jewish families. *Gastroenterology*, 151(4):698–709.
- [106] Li, H. (2013). Aligning sequence reads, clone sequences and assembly contigs with BWA-MEM. *arXiv preprint arXiv:1303.3997*.
- [107] Li, H., Handsaker, B., Wysoker, A., Fennell, T., Ruan, J., Homer, N., Marth, G., Abecasis, G., and Durbin, R. (2009). The sequence alignment/map format and SAMtools. *Bioinformatics*, 25(16):2078–2079.
- [108] Li, Y., Sung, W.-K., and Liu, J. J. (2007). Association mapping via regularized regression analysis of single-nucleotide–polymorphism haplotypes in variable-sized sliding windows. *The American Journal of Human Genetics*, 80(4):705–715.
- [109] Lichtenstein, G. R., Feagan, B. G., Cohen, R. D., Salzberg, B. A., Diamond, R. H., Langholff, W., Londhe, A., and Sandborn, W. J. (2014). Drug therapies and the risk of malignancy in Crohn’s disease: results from the treat registry. *The American Journal of Gastroenterology*, 109(2):212–23.
- [110] Liu, J. Z. and Anderson, C. A. (2014). Genetic studies of Crohn’s disease: past, present and future. *Best Practice & Research Clinical Gastroenterology*, 28(3):373–386.

- [111] Liu, J. Z., van Sommeren, S., Huang, H., Ng, S. C., Alberts, R., Takahashi, A., Ripke, S., Lee, J. C., Jostins, L., Shah, T., et al. (2015). Association analyses identify 38 susceptibility loci for inflammatory bowel disease and highlight shared genetic risk across populations. *Nature Genetics*, 47(9):979–986.
- [112] Liu, M., Degner, J., Davis, J. W., Idler, K. B., Nader, A., Mostafa, N. M., and Waring, J. F. (2018). Identification of *HLA-DRB1* association to adalimumab immunogenicity. *PLoS One*, 13(4):e0195325.
- [113] Locke, A. E., Kahali, B., Berndt, S. I., Justice, A. E., Pers, T. H., Day, F. R., Powell, C., Vedantam, S., Buchkovich, M. L., Yang, J., et al. (2015). Genetic studies of body mass index yield new insights for obesity biology. *Nature*, 518(7538):197.
- [114] Lucena, M. I., Molokhia, M., Shen, Y., Urban, T. J., Aithal, G. P., Andrade, R. J., Day, C. P., Ruiz-Cabello, F., Donaldson, P. T., Stephens, C., et al. (2011). Susceptibility to amoxicillin-clavulanate-induced liver injury is influenced by multiple HLA class I and II alleles. *Gastroenterology*, 141(1):338–347.
- [115] Lund-Nielsen, J., Vedel-Krogh, S., Kobylecki, C. J., Brynskov, J., Afzal, S., and Nordestgaard, B. G. (2018). Vitamin D and inflammatory bowel disease: Mendelian randomization analyses in the Copenhagen studies and UK Biobank. *The Journal of Clinical Endocrinology & Metabolism*, 103(9):3267–3277.
- [116] Luo, Y., de Lange, K. M., Jostins, L., Moutsianas, L., Randall, J., Kennedy, N. A., Lamb, C. A., McCarthy, S., Ahmad, T., Edwards, C., et al. (2017). Exploring the genetic architecture of inflammatory bowel disease by whole-genome sequencing identifies association at ADCY7. *Nature Genetics*, 49(2):186.
- [117] Mägi, R., Horikoshi, M., Sofer, T., Mahajan, A., Kitajima, H., Franceschini, N., McCarthy, M. I., COGENT-Kidney Consortium, T.-G. C., and Morris, A. P. (2017). Trans-ethnic meta-regression of genome-wide association studies accounting for ancestry increases power for discovery and improves fine-mapping resolution. *Human Molecular Genetics*, 26(18):3639–3650.
- [118] Mahajan, A., Go, M. J., Zhang, W., Below, J. E., Gaulton, K. J., Ferreira, T., Horikoshi, M., Johnson, A. D., Ng, M. C., Prokopenko, I., et al. (2014). Genome-wide trans-ancestry meta-analysis provides insight into the genetic architecture of type 2 diabetes susceptibility. *Nature Genetics*, 46(3):234.
- [119] Maller, J. B., McVean, G., Byrnes, J., Vukcevic, D., Palin, K., Su, Z., Howson, J. M., Auton, A., Myers, S., Morris, A., et al. (2012). Bayesian refinement of association signals for 14 loci in 3 common diseases. *Nature Genetics*, 44(12):1294.
- [120] McCarthy, S., Das, S., Kretzschmar, W., Delaneau, O., Wood, A. R., Teumer, A., Kang, H. M., Fuchsberger, C., Danecek, P., Sharp, K., et al. (2016). A reference panel of 64,976 haplotypes for genotype imputation. *Nature Genetics*, 48(10):1279.
- [121] McKenna, A., Hanna, M., Banks, E., Sivachenko, A., Cibulskis, K., Kernytsky, A., Garimella, K., Altshuler, D., Gabriel, S., Daly, M., et al. (2010). The Genome Analysis Toolkit: a MapReduce framework for analyzing next-generation DNA sequencing data. *Genome Research*, 20(9):1297–1303.

- [122] Megiorni, F. and Pizzuti, A. (2012). HLA-DQA1 and HLA-DQB1 in Celiac disease predisposition: practical implications of the HLA molecular typing. *Journal of Biomedical Science*, 19:88.
- [123] Mersha, T. B. and Abebe, T. (2015). Self-reported race/ethnicity in the age of genomic research: its potential impact on understanding health disparities. *Human Genomics*, 9(1):1.
- [124] Morris, A. P. (2011). Trans-ethnic meta-analysis of genome-wide association studies. *Genetic Epidemiology*, 35(8):809–822.
- [125] Natarajan, P., Peloso, G. M., Zekavat, S. M., Montasser, M., Ganna, A., Chaffin, M., Khera, A. V., Zhou, W., Bloom, J. M., Engreitz, J. M., et al. (2018). Deep-coverage whole genome sequences and blood lipids among 16,324 individuals. *Nature Communications*, 9(1):3391.
- [126] Neale, B. M., Rivas, M. A., Voight, B. F., Altshuler, D., Devlin, B., Orho-Melander, M., Kathiresan, S., Purcell, S. M., Roeder, K., and Daly, M. J. (2011). Testing for an unusual distribution of rare variants. *PLoS Genetics*, 7(3).
- [127] Neale Lab (2018). GWAS of the UK Biobank. <http://www.nealelab.is/uk-biobank/>. Accessed: 26.06.2019.
- [128] Nejentsev, S., Walker, N., Riches, D., Egholm, M., and Todd, J. A. (2009). Rare variants of *IFIH1*, a gene implicated in antiviral responses, protect against type 1 diabetes. *Science (New York, N.Y.)*, 324(5925):387–9.
- [129] Nelson, M. R., Tipney, H., Painter, J. L., Shen, J., Nicoletti, P., Shen, Y., Floratos, A., Sham, P. C., Li, M. J., Wang, J., et al. (2015). The support of human genetic evidence for approved drug indications. *Nature Genetics*, 47(8):856.
- [130] Ng, S. C., Shi, H. Y., Hamidi, N., Underwood, F. E., Tang, W., Benchimol, E. I., Panaccione, R., Ghosh, S., Wu, J. C., Chan, F. K., et al. (2017). Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: A systematic review of population-based studies. *The Lancet*, 390(10114):2769–2778.
- [131] Ng, S. C., Tang, W., Leong, R. W., Chen, M., Ko, Y., Studd, C., Niewiadowski, O., Bell, S., Kamm, M. A., de Silva, H., et al. (2015). Environmental risk factors in inflammatory bowel disease: a population-based case-control study in Asia-Pacific. *Gut*, 64(7):1063–1071.
- [132] Nica, A. C. and Dermitzakis, E. T. (2013). Expression quantitative trait loci: present and future. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 368(1620):20120362.
- [133] Nicoletti, P., Aithal, G. P., Bjornsson, E. S., Andrade, R. J., Sawle, A., Arrese, M., Barnhart, H. X., Bondon-Guitton, E., Hayashi, P. H., Bessone, F., et al. (2017). Association of liver injury from specific drugs, or groups of drugs, with polymorphisms in HLA and other genes in a genome-wide association study. *Gastroenterology*, 152(5):1078–1089.

- [134] Nielsen, D. S. G., Fredborg, M., Andersen, V., and Purup, S. (2017). Administration of protein kinase D1 induces a protective effect on lipopolysaccharide-induced intestinal inflammation in a co-culture model of intestinal epithelial Caco-2 cells and RAW264.7 macrophage cells. *International Journal of Inflammation*.
- [135] O'Connor, L. J., Schoech, A. P., Hormozdiari, F., Gazal, S., Patterson, N., and Price, A. L. (2019). Extreme polygenicity of complex traits is explained by negative selection. *The American Journal of Human Genetics*, 105(3):456–476.
- [136] Ogura, Y., Bonen, D. K., Inohara, N., Nicolae, D. L., Chen, F. F., Ramos, R., Britton, H., Moran, T., Karaliuskas, R., Duerr, R. H., et al. (2001). A frameshift mutation in *NOD2* associated with susceptibility to Crohn's disease. *Nature*, 411(6837):603.
- [137] Oliveira-Cortez, A., Melo, A. C., Chaves, V. E., Condino-Neto, A., and Camargos, P. (2016). Do HLA class II genes protect against pulmonary tuberculosis? A systematic review and meta-analysis. *European Journal of Clinical Microbiology & Infectious Diseases*, 35(10):1567–80.
- [138] Oo, C. and Kalbag, S. S. (2016). Leveraging the attributes of biologics and small molecules, and releasing the bottlenecks: a new wave of revolution in drug development. *Expert Review of Clinical Pharmacology*, 9(6):747–749.
- [139] Osterman, M. T., Sandborn, W. J., Colombel, J.-F., Robinson, A. M., Lau, W., Huang, B., Pollack, P. F., Thakkar, R. B., and Lewis, J. D. (2014). Increased risk of malignancy with adalimumab combination therapy, compared with monotherapy, for Crohn's disease. *Gastroenterology*, 146(4):941–9.
- [140] Panaccione, R., Ghosh, S., Middleton, S., Márquez, J. R., Scott, B. B., Flint, L., van Hoogstraten, H. J., Chen, A. C., Zheng, H., Danese, S., et al. (2014). Combination therapy with infliximab and azathioprine is superior to monotherapy with either agent in ulcerative colitis. *Gastroenterology*, 146(2):392–400.
- [141] Panaccione, R., Loftus, E. V., Binion, D., McHugh, K., Alam, S., Chen, N., Guerette, B., Mulani, P., and Chao, J. (2011). Efficacy and safety of adalimumab in Canadian patients with moderate to severe Crohn's disease: results of the adalimumab in Canadian subjects with moderate to severe Crohn's disease (ACCESS) trial. *Canadian Journal of Gastroenterology = Journal canadien de gastroenterologie*, 25(8):419–25.
- [142] Pardiñas, A. F., Holmans, P., Pocklington, A. J., Escott-Price, V., Ripke, S., Carrera, N., Legge, S. E., Bishop, S., Cameron, D., Hamshere, M. L., et al. (2018). Common schizophrenia alleles are enriched in mutation-intolerant genes and in regions under strong background selection. *Nature Genetics*, 50(3):381.
- [143] Parkes, M. (2019). IBD BioResource: an open-access platform of 25,000 patients to accelerate research in Crohn's and colitis. *Gut*, 68(9):1537–1540.
- [144] Pearson, D. C., May, G. R., Fick, G. H., and Sutherland, L. R. (1995). Azathioprine and 6-mercaptopurine in Crohn disease: a meta-analysis. *Annals of Internal Medicine*, 123(2):132–142.

- [145] Perry, M., Bewshea, C., Brown, R., So, K., Ahmad, T., and McDonald, T. (2015). Infliximab and adalimumab are stable in whole blood clotted samples for seven days at room temperature. *Annals of Clinical Biochemistry*, 52(6):672–674.
- [146] Pickrell, J. K. (2014). Joint analysis of functional genomic data and genome-wide association studies of 18 human traits. *The American Journal of Human Genetics*, 94(4):559–573.
- [147] Pollard, M. (2016). Variant discovery, accuracy and coverage on the Illumina HiSeq X. Unpublished presentation.
- [148] Poplin, R., Chang, P.-C., Alexander, D., Schwartz, S., Colthurst, T., Ku, A., Newburger, D., Dijamco, J., Nguyen, N., Afshar, P. T., et al. (2018). A universal SNP and small-indel variant caller using deep neural networks. *Nature Biotechnology*, 36(10):983.
- [149] Price, A. L., Weale, M. E., Patterson, N., Myers, S. R., Need, A. C., Shianna, K. V., Ge, D., Rotter, J. I., Torres, E., Taylor, K. D., et al. (2008). Long-range LD can confound genome scans in admixed populations. *The American Journal of Human Genetics*, 83(1):132–135.
- [150] Pilit, S. L., de With, S. A. J., and de Bakker, P. I. W. (2016). The multiple testing burden in sequencing-based disease studies of global populations. *bioRxiv*.
- [151] Purcell, S., Neale, B., Todd-Brown, K., Thomas, L., Ferreira, M. A., Bender, D., Maller, J., Sklar, P., de Bakker, P. I., Daly, M. J., et al. (2007). PLINK: a tool set for whole-genome association and population-based linkage analyses. *The American Journal of Human Genetics*, 81(3):559–575.
- [152] Rashkin, S., Jun, G., Chen, S., Abecasis, G. R., Genetics and Epidemiology of Colorectal Cancer Consortium, et al. (2017). Optimal sequencing strategies for identifying disease-associated singlettons. *PLoS Genetics*, 13(6).
- [153] Rimmer, A., Phan, H., Mathieson, I., Iqbal, Z., Twigg, S. R., Wilkie, A. O., McVean, G., Lunter, G., WGS500 Consortium, et al. (2014). Integrating mapping-, assembly- and haplotype-based approaches for calling variants in clinical sequencing applications. *Nature Genetics*, 46(8):912.
- [154] Rivas, M. A., Graham, D., Sulem, P., Stevens, C., Desch, A. N., Goyette, P., Gudbjartsson, D., Jonsdottir, I., Thorsteinsdottir, U., Degenhardt, F., et al. (2016). A protein-truncating R179X variant in *RNF186* confers protection against ulcerative colitis. *Nature Communications*, 7:12342.
- [155] Robinson, J., Halliwell, J. A., Hayhurst, J. D., Flicek, P., Parham, P., and Marsh, S. G. (2014). The IPD and IMGT/HLA database: allele variant databases. *Nucleic Acids Research*, 43(D1):D423–D431.
- [156] Roda, G., Jharap, B., Neeraj, N., and Colombel, J.-F. (2016). Loss of response to anti-TNFs: definition, epidemiology, and management. *Clinical and Translational Gastroenterology*, 7(1):e135.
- [157] Roe, D. and Kuang, R. (2019). Predicting KIR structural haplotypes with novel sequence signatures from short-read whole genome sequencing. *bioRxiv*.

- [158] Romero-Cara, P., Torres-Moreno, D., Pedregosa, J., Vílchez, J. A., García-Simón, M. S., Ruiz-Merino, G., Morán-Sánchez, S., and Conesa-Zamora, P. (2018). A *FCGR3A* polymorphism predicts anti-drug antibodies in chronic inflammatory bowel disease patients treated with anti-TNF. *International Journal of Medical Sciences*, 15(1):10.
- [159] Rozen, P., Zonis, J., Yekutiel, P., and Gilat, T. (1979). Crohn's disease in the Jewish population of Tel-Aviv-Yafo: epidemiologic and clinical aspects. *Gastroenterology*, 76(1):25–30.
- [160] Rozpedek, W., Pytel, D., Mucha, B., Leszczynska, H., Diehl, J. A., and Majsterek, I. (2016). The role of the PERK/eIF2 α /ATF4/CHOP signaling pathway in tumor progression during endoplasmic reticulum stress. *Current Molecular Medicine*, 16(6):533–544.
- [161] Sandborn, W. J., Rutgeerts, P., Enns, R., Hanauer, S. B., Colombel, J.-F., Panaccione, R., D'Haens, G., Li, J., Rosenfeld, M. R., Kent, J. D., and Pollack, P. F. (2007). Adalimumab induction therapy for Crohn disease previously treated with infliximab. *Annals of Internal Medicine*, 146(12):829.
- [162] Sanna, S., van Zuydam, N. R., Mahajan, A., Kurilshikov, A., Vila, A. V., Võsa, U., Mujagic, Z., Masclee, A. A., Jonkers, D. M., Oosting, M., et al. (2019). Causal relationships among the gut microbiome, short-chain fatty acids and metabolic diseases. *Nature Genetics*, 51(4):600.
- [163] Sathish, J. G., Sethu, S., Bielsky, M.-C., de Haan, L., French, N. S., Govindappa, K., Green, J., Griffiths, C. E. M., Holgate, S., Jones, D., Kimber, I., Moggs, J., Naisbitt, D. J., Pirmohamed, M., Reichmann, G., Sims, J., Subramanyam, M., Todd, M. D., van der Laan, J. W., Weaver, R. J., and Park, B. K. (2013). Challenges and approaches for the development of safer immunomodulatory biologics. *Nature Reviews Drug Discovery*, 12(4):306–24.
- [164] Sazonovs, A. and Barrett, J. (2018). Rare-variant studies to complement genome-wide association studies. *Annual Review of Genomics and Human Genetics*, 19:97–112.
- [165] Sazonovs, A., Kennedy, N. A., Moutsianas, L., Heap, G. A., Rice, D. L., Reppell, M., Bewshea, C. M., Chanchlani, N., Walker, G. J., Perry, M. H., et al. (2020). HLA-DQA1*05 carriage associated with development of anti-drug antibodies to infliximab and adalimumab in patients with Crohn's disease. *Gastroenterology*, 158(1):189–199.
- [166] Schröder, T., Schmidt, K. J., Olsen, V., Möller, S., Mackenroth, T., Sina, C., Lehnert, H., Fellermann, K., and Büning, J. (2015). Liver steatosis is a risk factor for hepatotoxicity in patients with inflammatory bowel disease under immunosuppressive treatment. *European journal of Gastroenterology & Hepatology*, 27(6):698–704.
- [167] Shah, T., Liu, J., Floyd, J., Morris, J. A., Wirth, N., Barrett, J. C., and Anderson, C. (2012). optiCall: a robust genotype-calling algorithm for rare, low-frequency and common variants. *Bioinformatics*, 28(12):1598–1603.
- [168] Shim, J. O. (2019). Recent advance in very early onset inflammatory bowel disease. *Pediatric Gastroenterology, Hepatology & Nutrition*, 22(1):41–49.

- [169] Singh, T., Kurki, M. I., Curtis, D., Purcell, S. M., Crooks, L., McRae, J., Suvisaari, J., Chheda, H., Blackwood, D., Breen, G., et al. (2016). Rare loss-of-function variants in *SETD1A* are associated with schizophrenia and developmental disorders. *Nature Neuroscience*, 19(4):571–577.
- [170] Singh, T., Walters, J. T., Johnstone, M., Curtis, D., Suvisaari, J., Torniainen, M., Rees, E., Iyegbe, C., Blackwood, D., McIntosh, A. M., et al. (2017). The contribution of rare variants to risk of schizophrenia in individuals with and without intellectual disability. *Nature Genetics*, 49(8):1167–1173.
- [171] Soon, S., Molodecky, N. A., Rabi, D. M., Ghali, W. A., Barkema, H. W., and Kaplan, G. G. (2012). The relationship between urban environment and the inflammatory bowel diseases: a systematic review and meta-analysis. *BMC Gastroenterology*, 12(1):51.
- [172] Soranzo, N. (2018). Whole genome sequencing in the UK Biobank. <http://www.ukbiobank.ac.uk/wp-content/uploads/2018/07/1145-Soranzo-UPDATED-1.pdf>. Accessed: 26.06.2019.
- [173] Southam, L., Gilly, A., Süveges, D., Farmaki, A.-E., Schwartzentruber, J., Tachmazidou, I., Matchan, A., Rayner, N. W., Tsafantakis, E., Karaleftheri, M., et al. (2017). Whole genome sequencing and imputation in isolated populations identify genetic associations with medically-relevant complex traits. *Nature Communications*, 8(1):1–11.
- [174] Spain, S. L. and Barrett, J. C. (2015). Strategies for fine-mapping complex traits. *Human Molecular Genetics*, 24(R1):R111–R119.
- [175] Stone, M. A., Mayberry, J. F., and Baker, R. (2003). Prevalence and management of inflammatory bowel disease: a cross-sectional study from central England. *European Journal of Gastroenterology & Hepatology*, 15(12):1275–1280.
- [176] Sveinbjornsson, G., Albrechtsen, A., Zink, F., Gudjonsson, S. A., Oddson, A., Másson, G., Holm, H., Kong, A., Thorsteinsdottir, U., Sulem, P., et al. (2016). Weighting sequence variants based on their annotation increases power of whole-genome association studies. *Nature Genetics*, 48(3):314.
- [177] Tachmazidou, I., Dedoussis, G., Southam, L., Farmaki, A.-E., Ritchie, G. R., Xifara, D. K., Matchan, A., Hatzikotoulas, K., Rayner, N. W., Chen, Y., et al. (2013). A rare functional cardioprotective *APOC3* variant has risen in frequency in distinct population isolates. *Nature Communications*, 4:2872.
- [178] Tang, R., Feng, T., Sha, Q., and Zhang, S. (2009). A variable-sized sliding-window approach for genetic association studies via principal component analysis. *Annals of Human Genetics*, 73(6):631–637.
- [179] Tran-Minh, M.-L., Sousa, P., Maillet, M., Allez, M., and Gornet, J.-M. (2017). Hepatic complications induced by immunosuppressants and biologics in inflammatory bowel disease. *World Journal of Hepatology*, 9(13):613.
- [180] UK10K consortium et al. (2015). The UK10K project identifies rare variants in health and disease. *Nature*, 526(7571):82.

- [181] Urban, T. J., Nicoletti, P., Chalasani, N., Serrano, J., Stoltz, A., Daly, A. K., Aithal, G. P., Dillon, J., Navarro, V., Odin, J., et al. (2017). Minocycline hepatotoxicity: clinical characterization and identification of HLA-B*35:02 as a risk factor. *Journal of Hepatology*, 67(1):137–144.
- [182] Ursum, J., van der Weijden, M. A. C., van Schaardenburg, D., Prins, A. P. A., Dijkmans, B. A. C., Twisk, J. W. R., Crusius, J. B. A., and van der Horst-Bruinsma, I. E. (2010). IL10 GGC haplotype is positively and HLA-DQA1*05-DQB1*02 is negatively associated with radiographic progression in undifferentiated arthritis. *The Journal of Rheumatology*, 37(7):1431–8.
- [183] Vermeire, S., Gils, A., Accossato, P., Lula, S., and Marren, A. (2018). Immunogenicity of biologics in inflammatory bowel disease. *Therapeutic Advances in Gastroenterology*, 11.
- [184] Wainschtein, P., Jain, D. P., Yengo, L., Zheng, Z., Cupples, L. A., Shadyab, A. H., McKnight, B., Shoemaker, B. M., Mitchell, B. D., Psaty, B. M., et al. (2019). Recovery of trait heritability from whole genome sequence data. *bioRxiv*.
- [185] Walker, G. and Ahmad, T. (2019). Drug toxicity: personalising IBD therapeutics – the use of genetic biomarkers to reduce drug toxicity. In *Biomarkers in Inflammatory Bowel Diseases*, pages 257–269. Springer.
- [186] Walker, G. J., Harrison, J. W., Heap, G. A., Voskuil, M. D., Andersen, V., Anderson, C. A., Ananthakrishnan, A. N., Barrett, J. C., Beaugerie, L., Bewshea, C. M., et al. (2019). Association of genetic variants in *NUDT15* with thiopurine-induced myelosuppression in patients with inflammatory bowel disease. *JAMA*, 321(8):773–785.
- [187] Wan, Y. (2009). TPMT testing before azathioprine therapy? *Drug and Therapeutics Bulletin*, 47(1):9.
- [188] Wang, X. and Teo, Y.-Y. (2015). Trans-ethnic fine-mapping of rare causal variants. In *Assessing Rare Variation in Complex Traits*, pages 253–261. Springer.
- [189] Watanabe, K., Stringer, S., Frei, O., Mirkov, M. U., de Leeuw, C., Polderman, T. J., van der Sluis, S., Andreassen, O. A., Neale, B. M., and Posthuma, D. (2019). A global overview of pleiotropy and genetic architecture in complex traits. *Nature Genetics*, 51(9):1339–1348.
- [190] Wellcome Trust Case Control Consortium et al. (2007). Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. *Nature*, 447(7145):661.
- [191] Wu, M. C., Lee, S., Cai, T., Li, Y., Boehnke, M., and Lin, X. (2011). Rare-variant association testing for sequencing data with the sequence kernel association test. *The American Journal of Human Genetics*, 89(1):82–93.
- [192] Yamazaki, K., McGovern, D., Ragoussis, J., Paolucci, M., Butler, H., Jewell, D., Cardon, L., Takazoe, M., Tanaka, T., Ichimori, T., et al. (2005). Single nucleotide polymorphisms in *TNFSF15* confer susceptibility to Crohn's disease. *Human Molecular Genetics*, 14(22):3499–3506.

- [193] Yang, J., Weedon, M. N., Purcell, S., Lettre, G., Estrada, K., Willer, C. J., Smith, A. V., Ingelsson, E., O'Connell, J. R., Mangino, M., et al. (2011). Genomic inflation factors under polygenic inheritance. *European Journal of Human Genetics*, 19(7):807.
- [194] Yang, S.-K., Hong, M., Baek, J., Choi, H., Zhao, W., Jung, Y., Haritunians, T., Ye, B. D., Kim, K.-J., Park, S. H., et al. (2014). A common missense variant in *NUDT15* confers susceptibility to thiopurine-induced leukopenia. *Nature Genetics*, 46(9):1017.
- [195] Zhang, F., Flickinger, M., Taliun, S. A. G., Abecasis, G. R., Scott, L. J., McCaroll, S. A., Pato, C. N., Boehnke, M., Kang, H. M., InSYght Psychiatric Genetics Consortium, et al. (2020). Ancestry-agnostic estimation of DNA sample contamination from sequence reads. *Genome Research*, 30(2):185–194.
- [196] Zhang, Z., Reinikainen, J., Adeleke, K. A., Pieterse, M. E., and Groothuis-Oudshoorn, C. G. (2018). Time-varying covariates and coefficients in Cox regression models. *Annals of Translational Medicine*, 6(7).
- [197] Zhao, J., Akinsanmi, I., Arafat, D., Cradick, T., Lee, C. M., Banskota, S., Marigorta, U. M., Bao, G., and Gibson, G. (2016). A burden of rare variants associated with extremes of gene expression in human peripheral blood. *The American Journal of Human Genetics*, 98(2):299–309.
- [198] Zheng, X., Shen, J., Cox, C., Wakefield, J. C., Ehm, M. G., Nelson, M. R., and Weir, B. S. (2014). HIBAG—HLA genotype imputation with attribute bagging. *The Pharmacogenomics Journal*, 14(2):192.
- [199] Zimmermann, M., Zimmermann-Kogadeeva, M., Wegmann, R., and Goodman, A. L. (2019). Mapping human microbiome drug metabolism by gut bacteria and their genes. *Nature*, 570(7762):462.

