**Supplementary References**

34    Tan, A., Abecasis, G. R. & Kang, H. M. Unified representation of genetic variants. *Bioinformatics* **31**, 2202-2204, doi:10.1093/bioinformatics/btv112 (2015).

35    McLaren, W., Gil, L., Hunt, S. E., Riat, H. S., Ritchie, G. R., Thormann, A., Flicek, P. & Cunningham, F. The Ensembl Variant Effect Predictor. *Genome Biol* **17**, 122, doi:10.1186/s13059-016-0974-4 (2016).

36    Rausch, T., Zichner, T., Schlattl, A., Stutz, A. M., Benes, V. & Korbel, J. O. DELLY: structural variant discovery by integrated paired-end and split-read analysis. *Bioinformatics* **28**, i333-i339, doi:10.1093/bioinformatics/bts378 (2012).

37    Wu, M. C., Lee, S., Cai, T., Li, Y., Boehnke, M. & Lin, X. Rare-variant association testing for sequencing data with the sequence kernel association test. *Am J Hum Genet* **89**, 82-93, doi:10.1016/j.ajhg.2011.05.029 (2011).

38    Mallick, S., Li, H., Lipson, M., Mathieson, I., Gymrek, M., Racimo, F., Zhao, M., Chennagiri, N., Nordenfelt, S., Tandon, A., Skoglund, P., Lazaridis, I., Sankararaman, S., Fu, Q., Rohland, N., Renaud, G., Erlich, Y., Willems, T., Gallo, C., Spence, J. P., Song, Y. S., Poletti, G., Balloux, F., van Driem, G., de Knijff, P., Romero, I. G., Jha, A. R., Behar, D. M., Bravi, C. M., Capelli, C., Hervig, T., Moreno-Estrada, A., Posukh, O. L., Balanovska, E., Balanovsky, O., Karachanak-Yankova, S., Sahakyan, H., Toncheva, D., Yepiskoposyan, L., Tyler-Smith, C., Xue, Y., Abdullah, M. S., Ruiz-Linares, A., Beall, C. M., Di Rienzo, A., Jeong, C., Starikovskaya, E. B., Metspalu, E., Parik, J., Villems, R., Henn, B. M., Hodoglugil, U., Mahley, R., Sajantila, A., Stamatoyannopoulos, G., Wee, J. T., Khusainova, R., Khusnutdinova, E., Litvinov, S., Ayodo, G., Comas, D., Hammer, M. F., Kivisild, T., Klitz, W., Winkler, C. A., Labuda, D., Bamshad, M., Jorde, L. B., Tishkoff, S. A., Watkins, W. S., Metspalu, M., Dryomov, S., Sukernik, R., Singh, L., Thangaraj, K., Paabo, S., Kelso, J., Patterson, N. & Reich, D. The Simons Genome Diversity Project: 300 genomes from 142 diverse populations. *Nature* **538**, 201-206, doi:10.1038/nature18964 (2016).

39    Waszak, S. M., Delaneau, O., Gschwind, A. R., Kilpinen, H., Raghav, S. K., Witwicki, R. M., Orioli, A., Wiederkehr, M., Panousis, N. I., Yurovsky, A., Romano-Palumbo, L., Planchon, A., Bielser, D., Padioleau, I., Udin, G., Thurnheer, S., Hacker, D., Hernandez, N., Reymond, A., Deplancke, B. & Dermitzakis, E. T. Population Variation and Genetic Control of Modular Chromatin Architecture in Humans. *Cell* **162**, 1039-1050, doi:10.1016/j.cell.2015.08.001 (2015).

40    Ainsworth, H. F., Shin, S. Y. & Cordell, H. J. A comparison of methods for inferring causal relationships between genotype and phenotype using additional biological measurements. *Genet Epidemiol* **41**, 577-586, doi:10.1002/gepi.22061 (2017).

41    Capper, D., Jones, D. T. W., Sill, M., Hovestadt, V., Schrimpf, D., Sturm, D., Koelsche, C., Sahm, F., Chavez, L., Reuss, D. E., Kratz, A., Wefers, A. K., Huang, K., Pajtler, K. W., Schweizer, L., Stichel, D., Olar, A., Engel, N. W., Lindenberg, K., Harter, P. N., Braczynski, A. K., Plate, K. H., Dohmen, H., Garvalov, B. K., Coras, R., Holsken, A., Hewer, E., Bewerunge-Hudler, M., Schick, M., Fischer, R., Beschorner, R., Schittenhelm, J., Staszewski, O., Wani, K., Varlet, P., Pages, M., Temming, P., Lohmann, D., Selt, F., Witt, H., Milde, T., Witt, O., Aronica, E., Giangaspero, F., Rushing, E., Scheurlen, W., Geisenberger, C., Rodriguez, F. J., Becker, A., Preusser, M., Haberler, C., Bjerkvig, R., Cryan, J., Farrell, M., Deckert, M., Hench, J., Frank, S., Serrano, J., Kannan, K., Tsirigos, A., Bruck, W., Hofer, S., Brehmer, S., Seiz-Rosenhagen, M., Hanggi, D., Hans, V., Rozsnoki, S., Hansford, J. R., Kohlhof, P., Kristensen, B. W., Lechner, M., Lopes, B., Mawrin, C., Ketter, R., Kulozik, A., Khatib, Z., Heppner, F., Koch, A., Jouvet, A., Keohane, C., Muhleisen, H., Mueller, W., Pohl, U., Prinz, M., Benner, A., Zapatka, M., Gottardo, N. G., Driever, P. H., Kramm, C. M., Muller, H. L., Rutkowski, S., von Hoff, K., Fruhwald, M. C., Gnekow, A., Fleischhack, G., Tippelt, S., Calaminus, G., Monoranu, C. M., Perry, A., Jones, C., Jacques, T. S., Radlwimmer, B., Gessi, M., Pietsch, T., Schramm, J., Schackert, G., Westphal, M., Reifenberger, G., Wesseling, P., Weller, M., Collins, V. P., Blumcke, I., Bendszus, M., Debus, J., Huang, A., Jabado, N., Northcott, P. A., Paulus, W., Gajjar, A., Robinson, G. W., Taylor, M. D., Jaunmuktane, Z., Ryzhova, M., Platten, M., Unterberg, A., Wick, W., Karajannis, M. A., Mittelbronn, M., Acker, T., Hartmann, C., Aldape, K., Schuller, U., Buslei, R., Lichter, P., Kool, M., Herold-Mende, C., Ellison, D. W., Hasselblatt, M., Snuderl, M., Brandner, S., Korshunov, A., von Deimling, A. & Pfister, S. M. DNA methylation-based classification of central nervous system tumours. *Nature* **555**, 469-474, doi:10.1038/nature26000 (2018).

42    Schubert, O. T., Gillet, L. C., Collins, B. C., Navarro, P., Rosenberger, G., Wolski, W. E., Lam, H., Amodei, D., Mallick, P., MacLean, B. & Aebersold, R. Building high-quality assay libraries for targeted analysis of SWATH MS data. *Nat Protoc* **10**, 426-441, doi:10.1038/nprot.2015.015 (2015).

43    Poullet, P., Carpentier, S. & Barillot, E. myProMS, a web server for management and validation of mass spectrometry-based proteomic data. *Proteomics* **7**, 2553-2556, doi:10.1002/pmic.200600784 (2007).

44      Rost, H. L., Rosenberger, G., Navarro, P., Gillet, L., Miladinovic, S. M., Schubert, O. T., Wolski, W., Collins, B. C., Malmstrom, J., Malmstrom, L. & Aebersold, R. OpenSWATH enables automated, targeted analysis of data-independent acquisition MS data. *Nat Biotechnol* **32**, 219-223, doi:10.1038/nbt.2841 (2014).

45      Shao, W., Guo, T., Toussaint, N. C., Xue, P., Wagner, U., Li, L., Charmpi, K., Zhu, Y., Wu, J., Buljan, M., Sun, R., Rutishauser, D., Hermanns, T., Fankhauser, C. D., Poyet, C., Ljubicic, J., Rupp, N., Ruschoff, J. H., Zhong, Q., Beyer, A., Ji, J., Collins, B. C., Liu, Y., Ratsch, G., Wild, P. J. & Aebersold, R. Comparative analysis of mRNA and protein degradation in prostate tissues indicates high stability of proteins. *Nat Commun* **10**, 2524, doi:10.1038/s41467-019-10513-5 (2019).

46      Choi, M., Chang, C. Y., Clough, T., Broudy, D., Killeen, T., MacLean, B. & Vitek, O. MSstats: an R package for statistical analysis of quantitative mass spectrometry-based proteomic experiments. *Bioinformatics* **30**, 2524-2526, doi:10.1093/bioinformatics/btu305 (2014).

47      Aken, B. L., Ayling, S., Barrell, D., Clarke, L., Curwen, V., Fairley, S., Fernandez Banet, J., Billis, K., Garcia Giron, C., Hourlier, T., Howe, K., Kahari, A., Kokocinski, F., Martin, F. J., Murphy, D. N., Nag, R., Ruffier, M., Schuster, M., Tang, Y. A., Vogel, J. H., White, S., Zadissa, A., Flicek, P. & Searle, S. M. The Ensembl gene annotation system. *Database (Oxford)* **2016**, doi:10.1093/database/baw093 (2016).

48      Dobin, A., Davis, C. A., Schlesinger, F., Drenkow, J., Zaleski, C., Jha, S., Batut, P., Chaisson, M. & Gingeras, T. R. STAR: ultrafast universal RNA-seq aligner. *Bioinformatics* **29**, 15-21, doi:10.1093/bioinformatics/bts635 (2013).

49      Love, M. I., Huber, W. & Anders, S. Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. *Genome Biol* **15**, 550, doi:10.1186/s13059-014-0550-8 (2014).

50      Sergushichev, A. An algorithm for fast preranked gene set enrichment. *bioRxiv*, doi:10.1101/060012 (2016).

51      Subramanian, A., Tamayo, P., Mootha, V. K., Mukherjee, S., Ebert, B. L., Gillette, M. A., Paulovich, A., Pomeroy, S. L., Golub, T. R., Lander, E. S. & Mesirov, J. P. Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proc Natl Acad Sci U S A* **102**, 15545-15550, doi:10.1073/pnas.0506580102 (2005).

52      Doerks, T., Copley, R. R., Schultz, J., Ponting, C. P. & Bork, P. Systematic identification of novel protein domain families associated with nuclear functions. *Genome Res* **12**, 47-56, doi:10.1101/ (2002).

53      Lek, M., Karczewski, K. J., Minikel, E. V., Samocha, K. E., Banks, E., Fennell, T., O'Donnell-Luria, A. H., Ware, J. S., Hill, A. J., Cummings, B. B., Tukiainen, T., Birnbaum, D. P., Kosmicki, J. A., Duncan, L. E., Estrada, K., Zhao, F., Zou, J., Pierce-Hoffman, E., Berghout, J., Cooper, D. N., Deflaux, N., DePristo, M., Do, R., Flannick, J., Fromer, M., Gauthier, L., Goldstein, J., Gupta, N., Howrigan, D., Kiezun, A., Kurki, M. I., Moonshine, A. L., Natarajan, P., Orozco, L., Peloso, G. M., Poplin, R., Rivas, M. A., Ruano-Rubio, V., Rose, S. A., Ruderfer, D. M., Shakir, K., Stenson, P. D., Stevens, C., Thomas, B. P., Tiao, G., Tusie-Luna, M. T., Weisburd, B., Won, H. H., Yu, D., Altshuler, D. M., Ardissino, D., Boehnke, M., Danesh, J., Donnelly, S., Elosua, R., Florez, J. C., Gabriel, S. B., Getz, G., Glatt, S. J., Hultman, C. M., Kathiresan, S., Laakso, M., McCarroll, S., McCarthy, M. I., McGovern, D., McPherson, R., Neale, B. M., Palotie, A., Purcell, S. M., Saleheen, D., Scharf, J. M., Sklar, P., Sullivan, P. F., Tuomilehto, J., Tsuang, M. T., Watkins, H. C., Wilson, J. G., Daly, M. J., MacArthur, D. G. & Exome Aggregation, C. Analysis of protein-coding genetic variation in 60,706 humans. *Nature* **536**, 285-291, doi:10.1038/nature19057 (2016).

54      Van der Auwera, G. A., Carneiro, M. O., Hartl, C., Poplin, R., Del Angel, G., Levy-Moonshine, A., Jordan, T., Shakir, K., Roazen, D., Thibault, J., Banks, E., Garimella, K. V., Altshuler, D., Gabriel, S. & DePristo, M. A. From FastQ data to high confidence variant calls: the Genome Analysis Toolkit best practices pipeline. *Curr Protoc Bioinformatics* **43**, 11 10 11-33, doi:10.1002/0471250953.bi1110s43 (2013).

55      Wang, K., Li, M. & Hakonarson, H. ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Res* **38**, e164, doi:10.1093/nar/gkq603 (2010).

56      Cardoso-Moreira, M., Halbert, J., Valloton, D., Velten, B., Chen, C., Shao, Y., Liechti, A., Ascencao, K., Rummel, C., Ovchinnikova, S., Mazin, P. V., Xenarios, I., Harshman, K., Mort, M., Cooper, D. N., Sandi, C., Soares, M. J., Ferreira, P. G., Afonso, S., Carneiro, M., Turner, J. M. A., VandeBerg, J. L., Fallahshahroudi, A., Jensen, P., Behr, R., Lisgo, S., Lindsay, S., Khaitovich, P., Huber, W., Baker, J., Anders, S., Zhang, Y. E. & Kaessmann, H. Gene expression across mammalian organ development. *Nature* **571**, 505-509, doi:10.1038/s41586-019-1338-5 (2019).

57      Su, D., Chan, C. T., Gu, C., Lim, K. S., Chionh, Y. H., McBee, M. E., Russell, B. S., Babu, I. R., Begley, T. J. & Dedon, P. C. Quantitative analysis of ribonucleoside modifications in tRNA by HPLC-coupled mass spectrometry. *Nature protocols* **9**, 828-841 (2014).

58      Machnicka, M. A., Milanowska, K., Osman Oglou, O., Purta, E., Kurkowska, M., Olchowik, A., Januszewski, W., Kalinowski, S., Dunin-Horkawicz, S., Rother, K. M., Helm, M., Bujnicki, J. M. &

Grosjean, H. MODOMICS: a database of RNA modification pathways--2013 update. *Nucleic Acids Res* **41**, D262-267, doi:10.1093/nar/gks1007 (2013).