Title

Commentary: The International Mouse Phenotyping Consortium: high-throughput in vivo functional annotation of the mammalian genome

Journal

Mammalian Genome, 35(4)

ISSN

0938-8990

Author

Lloyd, KC Kent

Publication Date

2024-12-01

DOI

10.1007/s00335-024-10068-x

Peer reviewed

Mammalian Genome (2024) 35:537–543
https://doi.org/10.1007/s00335-024-10068-x

Commentary: The International Mouse Phenotyping Consortium: high-throughput *in vivo* functional annotation of the mammalian genome

K. C. Kent Lloyd[1,2]

Received: 24 July 2024 / Accepted: 30 August 2024 / Published online: 10 September 2024

Abstract
The International Mouse Phenotyping Consortium (IMPC) is a worldwide effort producing and phenotyping knockout mouse lines to expose the pathophysiological roles of all genes in human diseases and make mice and data available and accessible to the global research community. It has created new knowledge on the function of thousands of genes for which little to anything was known. This new knowledge has informed the genetic basis of rare diseases, posited gene product influences on common diseases, influenced research on targeted therapies, revealed functional pleiotropy, essentiality, and sexual dimorphism, and many more insights into the role of genes in health and disease. Its scientific contributions have been many and widespread, however there remain thousands of "dark" genes yet to be illuminated. Nearing the end of its current funding cycle, IMPC is at a crossroads. The vision forward is clear, the path to proceed less so.

Every so often, a widening gap in knowledge, resources, and capabilities becomes so insurmountable for merely one group or even a single country to overcome, yet too critical for transformative innovation to disregard. Not long ago, the potential for genomics to resolve diagnostic odysseys, inform targeted therapies, and design prevention strategies for human diseases was hindered by the lack of holistic approaches to define the *in vivo* biological function of every gene in the mammalian genome (Hirschhorn and Daly 2005). Successfully overcoming this formidable obstacle to expeditiously translate the promise of genomic medicine into clinical practice would require an audacious plan to rapidly yet reliably uncover the pathophysiological roles of all genes in human diseases.

Conceived from a globally-shared vision (Austin et al. 2004; Auwerx et al. 2004), the International Mouse Phenotyping Consortium (IMPC) represents a groundbreaking, paradigm-shifting leap in the field of genetics and biomedical research. Self-assembled as a collectively-governed consortium of 21 academic research institutions across 15 countries on 5 continents, the IMPC aims to create a comprehensive catalog of mammalian gene function that is freely available and equally accessible to the global research community. Inspired by publications announcing the sequencing of the human (Lander et al. 2001; Venter et al. 2001) and then mouse (Mouse Genome Sequencing Consortium 2002) genomes, the IMPC emerged as the logical next step following the International Knockout Mouse Consortium (IKMC) which produced gene-targeted embryonic stem (ES) cells for nearly the entire mouse genome (International Mouse Knockout Consortium 2007). But more importantly, the IMPC was also motivated by the slow pace of progress resulting from limited and narrowly focused approaches to study gene function *in vivo* (Stoeger et al. 2018). Nearly all studies to that point were hypothesis-testing, focusing on incremental efforts that only partially annotated the function of a small number of well-characterized genes (Edwards et al. 2011) or "popular" gene sets (Eppig et al. 2011), typically in male mice only and often on ill-described genetic backgrounds (Perrin 2014). Within this rubric, grant applications posing hypotheses-generating experiments to unveil the function of understudied or overlooked genes were unlikely to pass peer review to successfully secure funding. To address the neglected "dark" coding genome and reveal new insights into heretofore unknown genetic associations and causes of disease, in 2011 the IMPC was established

✉ K. C. Kent Lloyd
kclloyd@ucdavis.edu

[1] Department of Surgery, School of Medicine, University of California, Davis, California, USA

[2] Mouse Biology Program, University of California, Davis, California, USA

to reveal the function of every human orthogonal gene in the mouse genome (Brown and Moore 2012). Its ambitious goal was simple yet daunting: take an unbiased, systematic, broad-based, disease-agnostic approach to phenotype cohorts of male and female mice on a single, inbred genetic background (C57BL/6N) and associate analytical findings to human biology and disease mechanisms (Brown et al. 2009).

Similar to the challenges posed by the human genome sequencing project, the scale, technology, and complexity of resources, knowledge, and expertise needed to achieve the IMPC goal made international collaboration essential. Participating IMPC institutions received substantial funding from government agencies, research institutions, and philanthropic organizations, including the United States National Institutes of Health (NIH), European Union Horizon 2020, the Medical Research Council (MRC) and Wellcome Sanger Institute United Kingdom, Helmholtz Munich and the German Center for Diabetes Research (DZD), the French National Centre for Scientific Research (CNRS), the National Institute of Health and Medical Research (INSERM), and the Agence Nationale de la Recherche (ANR), Canadian Institutes of Health Research (CIHR) and Genome Canada, the Czech Academy of Sciences and the Ministry of Education, Youth and Sports of the Czech Republic, the Japanese Institute of Physical and Chemical Research (RIKEN) Japan, the National Key R&D program of China, and others. To date, those investments have resulted in the production of 9594 unique knockout mouse lines, of which 8901 have been phenotyped, generating over 30 million data points and images that have revealed 106,511 statistically-significant adult and embryo phenotype calls. Even more importantly, 1311 knockout lines for mouse genes with a human ortholog exhibit phenotypes associated with human disease, with many more expected (Cacheiro et al. 2024).

Initially, mouse lines were derived from IKMC-produced embryonic stem (ES) cells expressing either a complete null (Valenzuela et al. 2003) or "knockout first" conditional, loxP-flanked allele (Pettitt et al. 2009; Skarnes et al. 2011; Birling et al. 2021) and a LacZ reporter. More recently, knockouts have been created using CRISPR/Cas9 in mouse embryos to delete critical exons essential to gene function (Peterson and Murray 2022). Once produced, mice undergo a standardized, high-throughput phenotyping pipeline of tests and procedures covering a wide range of biological systems, including neurological (e.g., open field), metabolic (e.g., glucose tolerance test, body fat), cardiovascular (e.g., ECG), hematological (e.g., complete blood count), renal (e.g., blood urea nitrogen), musculoskeletal (e.g., X-ray), immunological (e.g., cytokines), reproductive (e.g., fertility), special senses (e.g., auditory brainstem response), and more (Brown et al. 2009; Mallon et al. 2008). Data and images are gathered under standard operating procedures and rigorous quality control measures (e.g., contemporary wildtype control mice) that are strictly adhered to by all participating IMPC Centers, ensuring consistent and accurate experimental outcomes (Kurbatova et al. 2015).

All test results are analyzed, curated, and posted online at www.impc.org where they are freely available to view, explore, and download (Groza et al. 2023). The IMPC employs robust bioinformatic and statistical methods to ensure experimental reliability and reproducibility. Beyond revealing previously unknown gene function, this extensive, broad-based analytical platform has uncovered scientifically significant features, including sexual dimorphism (Karp et al. 2017), pleiotropy (Muñoz-Fuentes et al. 2022), embryo lethality and neonatal subviability (Dickinson et al. 2016), and aging effects (publication pending) among homozygous and heterozygous gene knockout lines. This robust dataset is an invaluable resource, offering researchers a growing wealth of information that can be used to explore gene function and its implications for human health (Birling et al., 2021; Meehan et al. 2017). Indeed, the IMPC project has led to significant new scientific knowledge and insight into "rare" human Mendelian diseases, comparative genomics, drug discovery, and target development (Cacheiro et al. 2020; Cacheiro et al. 2022). For example, the IMPC has uncovered new genetic pathways and potential drug targets for a variety of conditions, including cardiomyopathies (Spielmann et al. 2022), schizophrenia (Garrett et al. 2024), ciliopathies (Higgins et al. 2022), pain (Wotton et al. 2022), osteoporosis (Swam et al. 2020), sleep disorders (Zhang et al. 2020), metabolic diseases (Rozman et al. 2018), deafness (Bowl et al. 2017), developmental defects (Dickinson et al. 2016), ocular disorders (Chee et al. 2023), dermatopathology (Moore et al. 2019), and diseases in other animal species (Muñoz-Fuentes et al. 2018). Newer and intriguing insights are sure to come.

IMPC data, resources, and expertise have been utilized by the worldwide research community contributing to a growing base of knowledge on genes and disease. Over two decades, an estimated 47,797 researchers at 1815 institutions in 99 countries have used IKMC and/or IMPC generated ES cells, mice, and/or data to publish 7281 papers in 764 scientific journals.[1] Researchers have placed orders for more than 6000 IMPC mouse lines deposited in distribution repositories around the world, including the Mutant Mouse Resource and Research Center (MMRRC) in the United States (Amos-Landgraf et al. 2022), the European Mouse Mutant Archive (EMMA) in the European Union (Ali Khan et al. 2023), and the Asian Mouse Mutagenesis Resource Association

[1] data derived from Web of Science, InCites, and Scopus analysis of 7281 publications listed at www.mousephenotype.org/data/publications.

(AMMRA) in the Asia Pacific (Chin et al. 2022), all of which are further described in their own articles published in this *Special Issue*. Interest in the latest information on IMPC lines continues, with over 18,000 research scientists registered for accounts and expressing interest in mouse lines and data at the MMRRC alone. In addition, the IMPC has played a crucial role in training the next generation of research scientists. Through workshops, conferences, and collaborative projects, the IMPC has provided valuable training opportunities for young scientists from diverse backgrounds, helping to build dedicated capacity and unique capability in the field of genetics and biomedical research using live mouse models. Further, investment in the IMPC has created a collaborative, internationally-coordinated group of highly reputable centers filled with expert scientists, experienced staff, and rigorous pipelines ready and prepared to produce and phenotype mouse models of human disease for future *in vivo* studies of functional genomics.

By 2027 when the current round of funding expires, the IMPC will have produced and phenotyped 11,846 knockout mouse lines representing ~ 60% of the human orthologous genome in the mouse.[2] Although this progress over a short timeline has been phenomenal, 7328 orthologous genes will remain to be studied before IMPC can claim "mission accomplished". Yet as of today, a plan to complete this goal has not been articulated. Foundering so close to success would not only be a disappointment scientifically, but a disservice to the community. Imagine if the human genome project had called off its trailblazing efforts after sequencing just 14 of the 23 pairs of chromosomes, leaving ~ 40% of the human genome undone.

But the impact of failing to deliver a complete and comprehensive catalog of mammalian gene function goes far beyond just an accounting of missing genes. Not only would the consequences of an incomplete phenotyping dataset be gaps in our understanding of gene function, the potential roles of many unstudied "dark" genes impacting mammalian biology and human disease would remain undiscovered, development of enhanced diagnostic tools would be delayed, publicly available databases that rely on IMPC data for comprehensive gene function information would become obsolete, and discovery of new targeted drug therapies would be hindered.

These shortfalls are not inevitable as long as the momentum, expertise, and processes invested in to date are not allowed to fizzle out. The IMPC has proven its scientific value as an unmatched powerhouse discovering new and essential knowledge about the mammalian genome…its capability, capacity, and will to define *in vivo* gene function is indisputable and indispensable. Unfortunately, IMPCs path to complete its vision of a comprehensive understanding of the biological function of all human orthologous genes in mice is less clear. Nevertheless, there is a way forward. First, curating the remaining genes will determine those with little, no, or ambiguous phenotypic information to inform a rationale for high-throughput production and systematic phenotyping of knockout mice. Second, engaging the scientific community on next steps will be key to making informed decisions on genomic loci to target, alleles to produce, and testing strategies to pursue. Third, establishing a roadmap, business plan, and timeline for a production and phenotyping strategy that maximizes the scientific value and research benefit of annotating the remaining genes will facilitate enabling discussions amongst international funding sources to collaborate on a sustainable financial commitment.

Challenging yes, and yet I have hope. The IMPC has made remarkable contributions to our understanding of gene function and its implications for human health. Through its comprehensive, rigorous, and collaborative approach to illuminating the "dark genome", the IMPC has advanced translational research, shortened diagnostic odysseys for patients, facilitated drug discovery, and inspired new targeted therapeutics. Despite technical, financial, and logistical challenges inherent in a project of this vision and scale, the IMPC continues to probe the boundaries of biomedical research, offering new insights into the genetic basis of rare diseases.

The IMPC must continue to push beyond the protein coding genome and apply *in vivo* functional annotation to comprehensively decipher variation in function of enhancers, silencers, promoters, and insulators in the non-coding genome, systematically interrogate epigenomic regulation of gene expression, broadly incorporate large language models and artificial intelligence to find linkages between single-cell analyses and *in vivo* function, strategically explore polygenic effects on common diseases, and effectively translate functional biological knowledge of genetic variants to clinical knowledge and practice (Lloyd et al. 2020). If it does so, the IMPC will undoubtedly continue to shape the landscape of genetics and biomedicine, drive scientific discovery, and contribute to improvements in human health.

Acknowledgements The author would like to acknowledge all the scientists, staff, students, and technicians at the 21 research institutions in 15 countries that participate in the International Mouse Phenotyping Consortium. The author also acknowledges funding from the National Institutes of Health, Division of Program Coordination, Planning, and Strategic Initiatives, Office of Research Infrastructure Programs, Division of Comparative Medicine (UM1OD023221 and U42OD012210).

[2] unpublished analysis by Kevin Peterson (The Jackson Laboratory) of mouse-human orthologs at www.informatics.jax.org/mgihome/homepages/stats/all_stats.shtml) compared to mouse genes completed and projected to finish at IMPC by 2027 at https://www.gentar.org/tracker.

Author contributions The primary and corresponding author conceived of and wrote the manuscript.

Declarations

Conflict of interest The author is funded by an NIH grant (UM1OD023221) to the Davis-Toronto-Collaborative-Consortium (DTCC) which supports participation in the International Mouse Phenotyping Consortium (IMPC).

References

Ali Khan A, Valera Vazquez G, Gustems M, Matteoni R, Song F, Gormanns P, Fessele S, Raess M, Hrabě de Angelis M, INFRAFRONTIER Consortium (2023) INFRAFRONTIER: mouse model resources for modelling human diseases. Mamm Genome 34(3):408–417. https://doi.org/10.1007/s00335-023-10010-7

Amos-Landgraf J, Franklin C, Godfrey V, Grieder F, Grimsrud K, Korf I, Lutz C, Magnuson T, Mirochnitchenko O, Patel S, Reinholdt L, Lloyd KCK (2022) The Mutant Mouse Resource and Research Center (MMRRC): the NIH-supported National Public Repository and Distribution Archive of Mutant Mouse Models in the USA. Mamm Genome 33(1):203–212. https://doi.org/10.1007/s00335-021-09894-0

Austin CP, Battey JF, Bradley A, Bucan M, Capecchi M, Collins FS, Dove WF, Duyk G, Dymecki S, Eppig JT, Grieder FB, Heintz N, Hicks G, Insel TR, Joyner A, Koller BH, Lloyd KC, Magnuson T, Moore MW, Nagy A, Pollock JD, Roses AD, Sands AT, Seed B, Skarnes WC, Snoddy J, Soriano P, Stewart DJ, Stewart F, Stillman B, Varmus H, Varticovski L, Verma IM, Vogt TF, von Melchner H, Witkowski J, Woychik RP, Wurst W, Yancopoulos GD, Young SG, Zambrowicz B (2004) The knockout mouse project. Nat Genet 36(9):921–924. https://doi.org/10.1038/ng0904-921

Auwerx J, Avner P, Baldock R, Ballabio A, Balling R, Barbacid M, Berns A, Bradley A, Brown S, Carmeliet P, Chambon P, Cox R, Davidson D, Davies K, Duboule D, Forejt J, Granucci F, Hastie N, de Angelis MH, Jackson I, Kioussis D, Kollias G, Lathrop M, Lendahl U, Malumbres M, von Melchner H, Müller W, Partanen J, Ricciardi-Castagnoli P, Rigby P, Rosen B, Rosenthal N, Skarnes B, Stewart AF, Thornton J, Tocchini-Valentini G, Wagner E, Wahli W, Wurst W (2004) The European dimension for the mouse genome mutagenesis program. Nat Genet 36(9):925–927. https://doi.org/10.1038/ng0904-925

Birling MC, Yoshiki A, Adams DJ, Ayabe S, Beaudet AL, Bottomley J, Bradley A, Brown SDM, Bürger A, Bushell W, Chiani F, Chin HG, Christou S, Codner GF, DeMayo FJ, Dickinson ME, Doe B, Donahue LR, Fray MD, Gambadoro A, Gao X, Gertsenstein M, Gomez-Segura A, Goodwin LO, Heaney JD, Hérault Y, de Angelis MH, Jiang ST, Justice MJ, Kasparek P, King RE, Kühn R, Lee H, Lee YJ, Liu Z, Lloyd KCK, Lorenzo I, Mallon AM, McKerlie C, Meehan TF, Fuentes VM, Newman S, Nutter LMJ, Oh GT, Pavlovic G, Ramirez-Solis R, Rosen B, Ryder EJ, Santos LA, Schick J, Seavitt JR, Sedlacek R, Seisenberger C, Seong JK, Skarnes WC, Sorg T, Steel KP, Tamura M, Tocchini-Valentini GP, Wang CL, Wardle-Jones H, Wattenhofer-Donzé M, Wells S, Wiles MV, Willis BJ, Wood JA, Wurst W, XuB Y, International Mouse Phenotyping Consortium (IMPC), Teboul L, Murray SA (2021) A resource of targeted mutant mouse lines for 5061 genes. Nat Genet 53(4):416–419. https://doi.org/10.1038/s41588-021-00825-y

Bowl MR, Simon MM, Ingham NJ, Greenaway S, Santos L, Cater H, Taylor S, Mason J, Kurbatova N, Pearson S, Bower LR, Clary DA, Meziane H, Reilly P, Minowa O, Kelsey L, International Mouse Phenotyping Consortium, Tocchini-Valentini GP, Gao X, Bradley A, Skarnes WC, Moore M, Beaudet AL, Justice MJ, Seavitt J, Dickinson ME, Wurst W, de Angelis MH, Herault Y, Wakana S, Nutter LMJ, Flenniken AM, McKerlie C, Murray SA, Svenson KL, Braun RE, West DB, Lloyd KCK, Adams DJ, White J, Karp N, Flicek P, Smedley D, Meehan TF, Parkinson HE, Teboul LM, Wells S, Steel KP, Mallon AM, Brown SDM (2017) A large scale hearing loss screen reveals an extensive unexplored genetic landscape for auditory dysfunction. Nat Commun 8(1):886. https://doi.org/10.1038/s41467-017-00595-4

Brown SD, Moore MW (2012) The International Mouse Phenotyping Consortium: past and future perspectives on mouse phenotyping. Mamm Genome 23(9–10):632–40. https://doi.org/10.1007/s00335-012-9427-x

Brown SD, Wurst W, Kühn R, Hancock JM (2009) The functional annotation of mammalian genomes: the challenge of phenotyping. Annu Rev Genet 43:305–333. https://doi.org/10.1146/annurev-genet-102108-134143

Cacheiro P, Muñoz-Fuentes V, Murray SA, Dickinson ME, Bucan M, Nutter LMJ, Peterson KA, Haselimashhadi H, Flenniken AM, Morgan H, Westerberg H, Konopka T, Hsu CW, Christiansen A, Lanza DG, Beaudet AL, Heaney JD, Fuchs H, Gailus-Durner V, Sorg T, Prochazka J, Novosadova V, Lelliott CJ, Wardle-Jones H, Wells S, Teboul L, Cater H, Stewart M, Hough T, Wurst W, Sedlacek R, Adams DJ, Seavitt JR, Tocchini-Valentini G, Mammano F, Braun RE, McKerlie C, Herault Y, de Angelis MH, Mallon AM, Lloyd KCK, Brown SDM, Parkinson H, Meehan TF, Smedley D, Genomics England Research Consortium, International Mouse Phenotyping Consortium (2020) Human and mouse essentiality screens as a resource for disease gene discovery. Nat Commun 11(1):655. https://doi.org/10.1038/s41467-020-14284-2

Cacheiro P, Westerberg CH, Mager J, Dickinson ME, Nutter LMJ, Muñoz-Fuentes V, Hsu CW, Van den Veyver IB, Flenniken AM, McKerlie C, Murray SA, Teboul L, Heaney JD, Lloyd KCK, Lanoue L, Braun RE, White JK, Creighton AK, Laurin V, Guo R, Qu D, Wells S, Cleak J, Bunton-Stasyshyn R, Stewart M, Harrisson J, Mason J, Haseli Mashhadi H, Parkinson H, Mallon AM, International Mouse Phenotyping Consortium, Genomics England Research Consortium, Smedley D (2022) Mendelian gene identification through mouse embryo viability screening. Genome Med 14(1):119. https://doi.org/10.1186/s13073-022-01118-7

Cacheiro P, Pava D, Parkinson H, VanZanten M, Wilson R, Gunes O, The International Mouse Phenotyping Consortium, Smedley D (2024) Computational identification of disease models through cross-species phenotype comparison. Dis Model Mech. https://doi.org/10.1242/dmm.050604

Chee JM, Lanoue L, Clary D, Higgins K, Bower L, Flenniken A, Guo R, Adams DJ, Bosch F, Braun RE, Brown SDM, Chin HG, Dickinson ME, Hsu CW, Dobbie M, Gao X, Galande S, Grobler A, Heaney JD, Herault Y, de Angelis MH, Mammano F, Nutter LMJ, Parkinson H, Qin C, Shiroishi T, Sedlacek R, Seong JK, Xu Y,

International Mouse Phenotyping Consortium, Brooks B, McKerlie C, Lloyd KCK, Westerberg H, Moshiri A (2023) Genome-wide screening reveals the genetic basis of mammalian embryonic eye development. BMC Biol 21(1):22. https://doi.org/10.1186/s12915-022-01475-0

Chin HJ, Dobbie MS, Gao X, Hennessy JE, Nam KH, Seong JK, Shiroishi T, Takeo T, Yoshiki A, Zao J, Wang CL (2022) Asian Mouse Mutagenesis Resource Association (AMMRA): mouse genetics and laboratory animal resources in the Asia Pacific. Mamm Genome 33(1):192–202. https://doi.org/10.1007/s00335-021-09912-1

Dickinson ME, Flenniken AM, Ji X, Teboul L, Wong MD, White JK, Meehan TF, Weninger WJ, Westerberg H, Adissu H, Baker CN, Bower L, Brown JM, Caddle LB, Chiani F, Clary D, Cleak J, Daly MJ, Denegre JM, Doe B, Dolan ME, Edie SM, Fuchs H, Gailus-Durner V, Galli A, Gambadoro A, Gallegos J, Guo S, Horner NR, Hsu CW, Johnson SJ, Kalaga S, Keith LC, Lanoue L, Lawson TN, Lek M, Mark M, Marschall S, Mason J, McElwee ML, Newbigging S, Nutter LM, Peterson KA, Ramirez-Solis R, Rowland DJ, Ryder E, Samocha KE, Seavitt JR, Selloum M, Szoke-Kovacs Z, Tamura M, Trainor AG, Tudose I, Wakana S, Warren J, Wendling O, West DB, Wong L, Yoshiki A, International Mouse Phenotyping Consortium, Jackson Laboratory, Infrastructure Nationale PHENOMIN, Institut Clinique de la Souris (ICS), Charles River Laboratories, Harwell MRC, Toronto Centre for Phenogenomics, Wellcome Trust Sanger Institute, RIKEN BioResource Center, MacArthur DG, Tocchini-Valentini GP, Gao X, Flicek P, Bradley A, Skarnes WC, Justice MJ, Parkinson HE, Moore M, Wells S, Braun RE, Svenson KL, de Angelis MH, Herault Y, Mohun T, Mallon AM, Henkelman RM, Brown SD, Adams DJ, Lloyd KC, McKerlie C, Beaudet AL, Bućan M, Murray SA (2016) High-throughput discovery of novel developmental phenotypes. Nature 537(7621):508–514. https://doi.org/10.1038/nature19356

Edwards AM, Isserlin R, Bader GD, Frye SV, Willson TM, Yu FH (2011) Too many roads not taken. Nature 470:163–165. https://doi.org/10.1038/470163a

Eppig JT, Blake JA, Bult CJ, Kadin JA, Richardson JE, Mouse Genome Database Group (2011) The Mouse Genome Database (MGD): comprehensive resource for genetics and genomics of the laboratory mouse. Nucleic Acids Res. https://doi.org/10.1093/nar/gkr974

Garrett L, Trümbach D, Lee D, Mandillo S, Samaco R, Flenniken AM, Stewart M, IMPC Consortium, White JK, McKerlie C, Nutter LMJ, Vukobradovic I, Veeraragavan S, Yuva L, Heaney JD, Dickinson ME, Meziane H, Hérault Y, Wells S, Lloyd KCK, Bower L, Lanoue L, Clary D, Zimprich A, Gailus-Durner V, Fuchs H, Brown SDM, Chesler EJ, Wurst W, Hrabě de Angelis M, Hölter SM (2024) Co-expression of prepulse inhibition and schizophrenia genes in the mouse and human brain. Neurosci Appl. https://doi.org/10.1016/j.nsa.2024.104075

Groza T, Gomez FL, Mashhadi HH, Munoz-Fuentes V, Gunes O, Wilson R, Cacheiro P, Frost A, Keskivali-Bond P, Vardal B, McCoy A, Cheng TK, Santos L, Wells S, Smedley D, Mallon AM, Parkinson H (2023) The International Mouse Phenotyping Consortium: comprehensive knockout phenotyping underpinning the study of human disease. Nucleic Acids Res 51(D1):D1038–D1045. https://doi.org/10.1093/nar/gkac972

Higgins K, Moore BA, Berberovic Z, Adissu HA, Eskandarian M, Flenniken AM, Shao A, Imai DM, Clary D, Lanoue L, Newbigging S, Nutter LMJ, Adams DJ, Bosch F, Braun RE, Brown SDM, Dickinson ME, Dobbie M, Flicek P, Gao X, Galande S, Grobler A, Heaney JD, Herault Y, de Angelis MH, Chin HG, Mammano F, Qin C, Shiroishi T, Sedlacek R, Seong JK, Xu Y, IMPC Consortium, Lloyd KCK, McKerlie C, Moshiri A (2022) Analysis of genome-wide knockout mouse database identifies candidate ciliopathy genes. Sci Rep 12(1):20791. https://doi.org/10.1038/s41598-022-19710-7

Hirschhorn JN, Daly MJ (2005) Genome-wide association studies for common diseases and complex traits. Nat Rev Genet 6(2):95–108. https://doi.org/10.1038/nrg1521

International Mouse Knockout Consortium, Collins FS, Rossant J, Wurst W (2007) A mouse for all reasons. Cell 128(1):9–13. https://doi.org/10.1016/j.cell.2006.12.018

Karp NA, Mason J, Beaudet AL, Benjamini Y, Bower L, Braun RE, Brown SDM, Chesler EJ, Dickinson ME, Flenniken AM, Fuchs H, Angelis MH, Gao X, Guo S, Greenaway S, Heller R, Herault Y, Justice MJ, Kurbatova N, Lelliott CJ, Lloyd KCK, Mallon AM, Mank JE, Masuya H, McKerlie C, Meehan TF, Mott RF, Murray SA, Parkinson H, Ramirez-Solis R, Santos L, Seavitt JR, Smedley D, Sorg T, Speak AO, Steel KP, Svenson KL, International Mouse Phenotyping Consortium, Wakana S, West D, Wells S, Westerberg H, Yaacoby S, White JK (2017) Prevalence of sexual dimorphism in mammalian phenotypic traits. Nat Commun 26(8):15475. https://doi.org/10.1038/ncomms15475

Kurbatova N, Mason JC, Morgan H, Meehan TF, Karp NA (2015) PhenStat: a tool kit for standardized analysis of high throughput phenotypic data. PLoS ONE 10(7):e0131274. https://doi.org/10.1371/journal.pone.0131274

Lander ES, Linton LM, Birren B, Nusbaum C, Zody MC, Baldwin J, Devon K, Dewar K, Doyle M, FitzHugh W, Funke R, Gage D, Harris K, Heaford A, Howland J, Kann L, Lehoczky J, LeVine R, McEwan P, McKernan K, Meldrim J, Mesirov JP, Miranda C, Morris W, Naylor J, Raymond C, Rosetti M, Santos R, Sheridan A, Sougnez C, Stange-Thomann Y, Stojanovic N, Subramanian A, Wyman D, Rogers J, Sulston J, Ainscough R, Beck S, Bentley D, Burton J, Clee C, Carter N, Coulson A, Deadman R, Deloukas P, Dunham A, Dunham I, Durbin R, French L, Grafham D, Gregory S, Hubbard T, Humphray S, Hunt A, Jones M, Lloyd C, McMurray A, Matthews L, Mercer S, Milne S, Mullikin JC, Mungall A, Plumb R, Ross M, Shownkeen R, Sims S, Waterston RH, Wilson RK, Hillier LW, McPherson JD, Marra MA, Mardis ER, Fulton LA, Chinwalla AT, Pepin KH, Gish WR, Chissoe SL, Wendl MC, Delehaunty KD, Miner TL, Delehaunty A, Kramer JB, Cook LL, Fulton RS, Johnson DL, Minx PJ, Clifton SW, Hawkins T, Branscomb E, Predki P, Richardson P, Wenning S, Slezak T, Doggett N, Cheng JF, Olsen A, Lucas S, Elkin C, Uberbacher E, Frazier M, Gibbs RA, Muzny DM, Scherer SE, Bouck JB, Sodergren EJ, Worley KC, Rives CM, Gorrell JH, Metzker ML, Naylor SL, Kucherlapati RS, Nelson DL, Weinstock GM, Sakaki Y, Fujiyama A, Hattori M, Yada T, Toyoda A, Itoh T, Kawagoe C, Watanabe H, Totoki Y, Taylor T, Weissenbach J, Heilig R, Saurin W, Artiguenave F, Brottier P, Bruls T, Pelletier E, Robert C, Wincker P, Smith DR, Doucette-Stamm L, Rubenfield M, Weinstock K, Lee HM, Dubois J, Rosenthal A, Platzer M, Nyakatura G, Taudien S, Rump A, Yang H, Yu J, Wang J, Huang G, Gu J, Hood L, Rowen L, Madan A, Qin S, Davis RW, Federspiel NA, Abola AP, Proctor MJ, Myers RM, Schmutz J, Dickson M, Grimwood J, Cox DR, Olson MV, Kaul R, Raymond C, Shimizu N, Kawasaki K, Minoshima S, Evans GA, Athanasiou M, Schultz R, Roe BA, Chen F, Pan H, Ramser J, Lehrach H, Reinhardt R, McCombie WR, de la Bastide M, Dedhia N, Blöcker H, Hornischer K, Nordsiek G, Agarwala R, Aravind L, Bailey JA, Bateman A, Batzoglou S, Birney E, Bork P, Brown DG, Burge CB, Cerutti L, Chen HC, Church D, Clamp M, Copley RR, Doerks T, Eddy SR, Eichler EE, Furey TS, Galagan J, Gilbert JG, Harmon C, Hayashizaki Y, Haussler D, Hermjakob H, Hokamp K, Jang W, Johnson LS, Jones TA, Kasif S, Kaspryzk A, Kennedy S, Kent WJ, Kitts P, Koonin EV, Korf I, Kulp D, Lancet D, Lowe TM, McLysaght A, Mikkelsen T, Moran JV, Mulder N, Pollara VJ, Ponting CP, Schuler G, Schultz J, Slater G, Smit AF, Stupka E, Szustakowki

J, Thierry-Mieg D, Thierry-Mieg J, Wagner L, Wallis J, Wheeler R, Williams A, Wolf YI, Wolfe KH, Yang SP, Yeh RF, Collins F, Guyer MS, Peterson J, Felsenfeld A, Wetterstrand KA, Patrinos A, Morgan MJ, de Jong P, Catanese JJ, Osoegawa K, Shizuya H, Choi S, Chen YJ, Szustakowki J, International Human Genome Sequencing Consortium (2001) Initial sequencing and analysis of the human genome. Nature 409(6822):860–921

Lloyd KCK, Adams DJ, Baynam G, Beaudet AL, Bosch F, Boycott KM, Braun RE, Caulfield M, Cohn R, Dickinson ME, Dobbie MS, Flenniken AM, Flicek P, Galande S, Gao X, Grobler A, Heaney JD, Herault Y, de Angelis MH, Lupski JR, Lyonnet S, Mallon AM, Mammano F, MacRae CA, McInnes R, McKerlie C, Meehan TF, Murray SA, Nutter LMJ, Obata Y, Parkinson H, Pepper MS, Sedlacek R, Seong JK, Shiroishi T, Smedley D, Tocchini-Valentini G, Valle D, Wang CL, Wells S, White J, Wurst W, Xu Y, Brown SDM (2020) The deep genome project. Genome Biol 21(1):18. https://doi.org/10.1186/s13059-020-1931-9

Mallon AM, Blake A, Hancock JM (2008) EuroPhenome and EMPReSS: online mouse phenotyping resource. Nucleic Acids Res. https://doi.org/10.1093/nar/gkm7284

Meehan TF, Conte N, West DB, Jacobsen JO, Mason J, Warren J, Chen CK, Tudose I, Relac M, Matthews P, Karp N, Santos L, Fiegel T, Ring N, Westerberg H, Greenaway S, Sneddon D, Morgan H, Codner GF, Stewart ME, Brown J, Horner N, International Mouse Phenotyping Consortium, Haendel M, Washington N, Mungall CJ, Reynolds CL, Gallegos J, Gailus-Durner V, Sorg T, Pavlovic G, Bower LR, Moore M, Morse I, Gao X, Tocchini-Valentini GP, Obata Y, Cho SY, Seong JK, Seavitt J, Beaudet AL, Dickinson ME, Herault Y, Wurst W, de Angelis MH, Lloyd KCK, Flenniken AM, Nutter LMJ, Newbigging S, McKerlie C, Justice MJ, Murray SA, Svenson KL, Braun RE, White JK, Bradley A, Flicek P, Wells S, Skarnes WC, Adams DJ, Parkinson H, Mallon AM, Brown SDM, Smedley D (2017) Disease model discovery from 3328 gene knockouts by The International Mouse Phenotyping Consortium. Nat Genet 49(8):1231–1238. https://doi.org/10.1038/ng.3901

Moore BA, Flenniken AM, Clary D, Moshiri AS, Nutter LMJ, Berberovic Z, Owen C, Newbigging S, Adissu H, Eskandarian M, McKerlie C, International Mouse Phenotyping Consortium, Thomasy SM, Lloyd KCK, Murphy CJ, Moshiri A (2019) Genome-wide screening of mouse knockouts reveals novel genes required for normal integumentary and oculocutaneous structure and function. Sci Rep 9(1):11211. https://doi.org/10.1038/s41598-019-47286-2

Mouse Genome Sequencing Consortium, Waterston RH, Lindblad-Toh K, Birney E, Rogers J, Abril JF, Agarwal P, Agarwala R, Ainscough R, Alexandersson M, An P, Antonarakis SE, Attwood J, Baertsch R, Bailey J, Barlow K, Beck S, Berry E, Birren B, Bloom T, Bork P, Botcherby M, Bray N, Brent MR, Brown DG, Brown SD, Bult C, Burton J, Butler J, Campbell RD, Carninci P, Cawley S, Chiaromonte F, Chinwalla AT, Church DM, Clamp M, Clee C, Collins FS, Cook LL, Copley RR, Coulson A, Couronne O, Cuff J, Curwen V, Cutts T, Daly M, David R, Davies J, Delehaunty KD, Deri J, Dermitzakis ET, Dewey C, Dickens NJ, Diekhans M, Dodge S, Dubchak I, Dunn DM, Eddy SR, Elnitski L, Emes RD, Eswara P, Eyras E, Felsenfeld A, Fewell GA, Flicek P, Foley K, Frankel WN, Fulton LA, Fulton RS, Furey TS, Gage D, Gibbs RA, Glusman G, Gnerre S, Goldman N, Goodstadt L, Grafham D, Graves TA, Green ED, Gregory S, Guigó R, Guyer M, Hardison RC, Haussler D, Hayashizaki Y, Hillier LW, Hinrichs A, Hlavina W, Holzer T, Hsu F, Hua A, Hubbard T, Hunt A, Jackson I, Jaffe DB, Johnson LS, Jones M, Jones TA, Joy A, Kamal M, Karlsson EK, Karolchik D, Kasprzyk A, Kawai J, Keibler E, Kells C, Kent WJ, Kirby A, Kolbe DL, Korf I, Kucherlapati RS, Kulbokas EJ, Kulp D, Landers T, Leger JP, Leonard S, Letunic I, Levine R, Li J, Li M, Lloyd C, Lucas S, Ma B, Maglott DR, Mardis ER, Matthews L, Mauceli E, Mayer JH, McCarthy M, McCombie WR, McLaren S, McLay K, McPherson JD, Meldrim J, Meredith B, Mesirov JP, Miller W, Miner TL, Mongin E, Montgomery KT, Morgan M, Mott R, Mullikin JC, Muzny DM, Nash WE, Nelson JO, Nhan MN, Nicol R, Ning Z, Nusbaum C, O'Connor MJ, Okazaki Y, Oliver K, Overton-Larty E, Pachter L, Parra G, Pepin KH, Peterson J, Pevzner P, Plumb R, Pohl CS, Poliakov A, Ponce TC, Ponting CP, Potter S, Quail M, Reymond A, Roe BA, Roskin KM, Rubin EM, Rust AG, Santos R, Sapojnikov V, Schultz B, Schultz J, Schwartz MS, Schwartz S, Scott C, Seaman S, Searle S, Sharpe T, Sheridan A, Shownkeen R, Sims S, Singer JB, Slater G, Smit A, Smith DR, Spencer B, Stabenau A, Stange-Thomann N, Sugnet C, Suyama M, Tesler G, Thompson J, Torrents D, Trevaskis E, Tromp J, Ucla C, Ureta-Vidal A, Vinson JP, Von Niederhausern AC, Wade CM, Wall M, Weber RJ, Weiss RB, Wendl MC, West AP, Wetterstrand K, Wheeler R, Whelan S, Wierzbowski J, Willey D, Williams S, Wilson RK, Winter E, Worley KC, Wyman D, Yang S, Yang SP, Zdobnov EM, Zody MC, Lander ES (2002) Initial sequencing and comparative analysis of the mouse genome. Nature 420(6915):520–62. https://doi.org/10.1038/nature01262

Muñoz-Fuentes V, Cacheiro P, Meehan TF, Aguilar-Pimentel JA, Brown SDM, Flenniken AM, Flicek P, Galli A, Mashhadi HH, Hrabě de Angelis M, Kim JK, Lloyd KCK, McKerlie C, Morgan H, Murray SA, Nutter LMJ, Reilly PT, Seavitt JR, Seong JK, Simon M, Wardle-Jones H, Mallon AM, Smedley D, Parkinson HE, IMPC consortium (2018) The International Mouse Phenotyping Consortium (IMPC): a functional catalogue of the mammalian genome that informs conservation. Conserv Genet 19(4):995–1005. https://doi.org/10.1007/s10592-018-1072-9

Muñoz-Fuentes V, Haselimashhadi H, Santos L, Westerberg H, Parkinson H, Mason J (2022) Pleiotropy data resource as a primer for investigating co-morbidities/multi-morbidities and their role in disease. Mamm Genome 33(1):135–142. https://doi.org/10.1007/s00335-021-09917-w

Perrin S (2014) Preclinical research: make mouse studies work. Nature 507(7493):423–425. https://doi.org/10.1038/507423a

Peterson KA, Murray SA (2022) Progress towards completing the mutant mouse null resource. Mamm Genome 33(1):123–134. https://doi.org/10.1007/s00335-021-09905-0

Pettitt SJ, Liang Q, Rairdan XY, Moran JL, Prosser HM, Beier DR, Lloyd KC, Bradley A, Skarnes WC (2009) Agouti C57BL/6N embryonic stem cells for mouse genetic resources. Nat Method 6(7):493–5. https://doi.org/10.1038/nmeth.1342

Rozman J, Rathkolb B, Oestereicher MA, Schütt C, Ravindranath AC, Leuchtenberger S, Sharma S, Kistler M, Willershäuser M, Brommage R, Meehan TF, Mason J, Haselimashhadi H, IMPC Consortium, Hough T, Mallon AM, Wells S, Santos L, Lelliott CJ, White JK, Sorg T, Champy MF, Bower LR, Reynolds CL, Flenniken AM, Murray SA, Nutter LMJ, Svenson KL, West D, Tocchini-Valentini GP, Beaudet AL, Bosch F, Braun RB, Dobbie MS, Gao X, Herault Y, Moshiri A, Moore BA, Kent Lloyd KC, McKerlie C, Masuya H, Tanaka N, Flicek P, Parkinson HE, Sedlacek R, Seong JK, Wang CL, Moore M, Brown SD, Tschöp MH, Wurst W, Klingenspor M, Wolf E, Beckers J, Machicao F, Peter A, Staiger H, Häring HU, Grallert H, Campillos M, Maier H, Fuchs H, Gailus-Durner V, Werner T, Hrabe de Angelis M (2018) Identification of genetic elements in metabolism by high-throughput mouse phenotyping. Nat Commun 9(1):288. https://doi.org/10.1038/s41467-017-01995-2

Skarnes WC, Rosen B, West AP, Koutsourakis M, Bushell W, Iyer V, Mujica AO, Thomas M, Harrow J, Cox T, Jackson D, Severin J, Biggs P, Fu J, Nefedov M, de Jong PJ, Stewart AF, Bradley A (2011) A conditional knockout resource for the genome-wide study of mouse gene function. Nature 474(7351):337–342. https://doi.org/10.1038/nature10163

Spielmann N, Miller G, Oprea TI et al (2022) Publisher correction: extensive identification of genes involved in congenital and

structural heart disorders and cardiomyopathy. Nat Cardiovasc Res 1:529–531. https://doi.org/10.1038/s44161-022-00072-2

Stoeger T, Gerlach M, Morimoto RI, Nunes Amaral LA (2018) Large-scale investigation of the reasons why potentially important genes are ignored. PLoS Biol 16(9):e2006643. https://doi.org/10.1371/journal.pbio.2006643

Swan AL, Schütt C, Rozman J, del Mar MMM, Brandmaier S, Simon M, Leuchtenberger S, Griffiths M, Brommage R, Keskivali-Bond P, Grallert H, Werner T, Teperino R, Becker L, Miller G, Moshiri A, Seavitt JR, Cissell DD, Meehan TF, Acar EF, Lelliott CJ, Flenniken AM, Champy MF, Sorg T, Ayadi A, Braun RE, Cater H, Dickinson ME, Flicek P, Gallegos J, Ghirardello EJ, Heaney JD, Jacquot S, Lally C, Logan JG, Teboul L, Mason J, Spielmann N, McKerlie C, Murray SA, Nutter LMJ, Odfalk KF, Parkinson H, Prochazka J, Reynolds CL, Selloum M, Spoutil F, Svenson KL, Vales TS, Wells SE, White JK, Sedlacek R, Wurst W, Lloyd KCK, Croucher PI, Fuchs H, Williams GR, Bassett JHD, Gailus-Durner V, Herault Y, Mallon AM, Brown SDM, Mayer-Kuckuk P, Hrabe de Angelis M, IMPC Consortium (2020) Mouse mutant phenotyping at scale reveals novel genes controlling bone mineral density. PLoS Genet 16(12):e1009190. https://doi.org/10.1371/journal.pgen.1009190

Valenzuela DM, Murphy AJ, Frendewey D, Gale NW, Economides AN, Auerbach W, Poueymirou WT, Adams NC, Rojas J, Yasenchak J, Chernomorsky R, Boucher M, Elsasser AL, Esau L, Zheng J, Griffiths JA, Wang X, Su H, Xue Y, Dominguez MG, Noguera I, Torres R, Macdonald LE, Stewart AF, DeChiara TM, Yancopoulos GD (2003) High-throughput engineering of the mouse genome coupled with high-resolution expression analysis. Nat Biotechnol 21(6):652–659. https://doi.org/10.1038/nbt822

Venter JC, Adams MD, Myers EW, Li PW, Mural RJ, Sutton GG, Smith HO, Yandell M, Evans CA, Holt RA, Gocayne JD, Amanatides P, Ballew RM, Huson DH, Wortman JR, Zhang Q, Kodira CD, Zheng XH, Chen L, Skupski M, Subramanian G, Thomas PD, Zhang J, Gabor Miklos GL, Nelson C, Broder S, Clark AG, Nadeau J, McKusick VA, Zinder N, Levine AJ, Roberts RJ, Simon M, Slayman C, Hunkapiller M, Bolanos R, Delcher A, Dew I, Fasulo D, Flanigan M, Florea L, Halpern A, Hannenhalli S, Kravitz S, Levy S, Mobarry C, Reinert K, Remington K, Abu-Threideh J, Beasley E, Biddick K, Bonazzi V, Brandon R, Cargill M, Chandramouliswaran I, Charlab R, Chaturvedi K, Deng Z, Di Francesco V, Dunn P, Eilbeck K, Evangelista C, Gabrielian AE, Gan W, Ge W, Gong F, Gu Z, Guan P, Heiman TJ, Higgins ME, Ji RR, Ke Z, Ketchum KA, Lai Z, Lei Y, Li Z, Li J, Liang Y, Lin X, Lu F, Merkulov GV, Milshina N, Moore HM, Naik AK, Narayan VA, Neelam B, Nusskern D, Rusch DB, Salzberg S, Shao W, Shue B, Sun J, Wang Z, Wang A, Wang X, Wang J, Wei M, Wides R, Xiao C, Yan C, Yao A, Ye J, Zhan M, Zhang W, Zhang H, Zhao Q, Zheng L, Zhong F, Zhong W, Zhu S, Zhao S, Gilbert D, Baumhueter S, Spier G, Carter C, Cravchik A, Woodage T, Ali F, An H, Awe A, Baldwin D, Baden H, Barnstead M, Barrow I, Beeson K, Busam D, Carver A, Center A, Cheng ML, Curry L, Danaher S, Davenport L, Desilets R, Dietz S, Dodson K, Doup L, Ferriera S, Garg N, Gluecksmann A, Hart B, Haynes J, Haynes C, Heiner C, Hladun S, Hostin D, Houck J, Howland T, Ibegwam C, Johnson J, Kalush F, Kline L, Koduru S, Love A, Mann F, May D, McCawley S, McIntosh T, McMullen I, Moy M, Moy L, Murphy B, Nelson K, Pfannkoch C, Pratts E, Puri V, Qureshi H, Reardon M, Rodriguez R, Rogers YH, Romblad D, Ruhfel B, Scott R, Sitter C, Smallwood M, Stewart E, Strong R, Suh E, Thomas R, Tint NN, Tse S, Vech C, Wang G, Wetter J, Williams S, Williams M, Windsor S, Winn-Deen E, Wolfe K, Zaveri J, Zaveri K, Abril JF, Guigó R, Campbell MJ, Sjolander KV, Karlak B, Kejariwal A, Mi H, Lazareva B, Hatton T, Narechania A, Diemer K, Muruganujan A, Guo N, Sato S, Bafna V, Istrail S, Lippert R, Schwartz R, Walenz B, Yooseph S, Allen D, Basu A, Baxendale J, Blick L, Caminha M, Carnes-Stine J, Caulk P, Chiang YH, Coyne M, Dahlke C, Deslattes Mays A, Dombroski M, Donnelly M, Ely D, Esparham S, Fosler C, Gire H, Glanowski S, Glasser K, Glodek A, Gorokhov M, Graham K, Gropman B, Harris M, Heil J, Henderson S, Hoover J, Jennings D, Jordan C, Jordan J, Kasha J, Kagan L, Kraft C, Levitsky A, Lewis M, Liu X, Lopez J, Ma D, Majoros W, McDaniel J, Murphy S, Newman M, Nguyen T, Nguyen N, Nodell M, Pan S, Peck J, Peterson M, Rowe W, Sanders R, Scott J, Simpson M, Smith T, Sprague A, Stockwell T, Turner R, Venter E, Wang M, Wen M, Wu D, Wu M, Xia A, Zandieh A, Zhu X (2001) The sequence of the human genome. Science 291(5507):1304–1351. https://doi.org/10.1126/science.1058040

Wotton JM, Peterson E, Flenniken AM, Bains RS, Veeraragavan S, Bower LR, Bubier JA, Parisien M, Bezginov A, Haselimashhadi H, Mason J, Moore MA, Stewart ME, Clary DA, Delbarre DJ, Anderson LC, D'Souza A, Goodwin LO, Harrison ME, Huang Z, Mckay M, Qu D, Santos L, Srinivasan S, Urban R, Vukobradovic I, Ward CS, Willett AM, Braun RE, Brown SDM, Dickinson ME, Heaney JD, Kumar V, Lloyd KCK, Mallon AM, McKerlie C, Murray SA, Nutter LMJ, Parkinson H, Seavitt JR, Wells S, Samaco RC, Chesler EJ, Smedley D, Diatchenko L, Baumbauer KM, Young EE, Bonin RP, Mandillo S, White JK, International Mouse Phenotyping Consortium (2022) Identifying genetic determinants of inflammatory pain in mice using a large-scale gene-targeted screen. Pain 163(6):1139–1157. https://doi.org/10.1097/j.pain.0000000000002481

Zhang T, Xie P, Dong Y, Liu Z, Zhou F, Pan D, Huang Z, Zhai Q, Gu Y, Wu Q, Tanaka N, Obata Y, Bradley A, Lelliott CJ, Sanger Institute Mouse Genetics Project, Nutter LMJ, McKerlie C, Flenniken AM, Champy MF, Sorg T, Herault Y, Angelis MH, Durner VG, Mallon AM, Brown SDM, Meehan T, Parkinson HE, Smedley D, Lloyd KCK, Yan J, Gao X, Seong JK, Wang CL, Sedlacek R, Liu Y, Rozman J, Yang L, Xu Y (2020) High-throughput discovery of genetic determinants of circadian misalignment. PLoS Genet. 16(1):e1008577. https://doi.org/10.1371/journal.pgen.1008577