David G. Ashbrook

dashbrook@uthsc.edu

Assistant Professor
University of Tennessee Health Science Center, Department of Genetics, Genomics and Informatics
Address: Translational Science Research Building, Room 410H, 71 S Manassas St, Memphis, Tennessee, USA, 38103
Website: https://davidashbrook.wordpress.com/ **Twitter:** @davidashbrook

Professional Identifiers:
ORCID ID: 0000-0002-7397-8910 **Scorpus ID:** 55652260000
ResearcherID: H-5702-2019 **Google scholar:** crVDM7MAAAAJ

Education & Qualifications

2011 – 2015, PhD Systems Biology, The University of Manchester, UK
Thesis title: '*A systems-genetics analysis of complex phenotypes'*
Supervisor: Dr. Reinmar Hager
External examiner: Dr. Darren Logan, Internal examiner Dr. Kathryn Hentges
Developed methods to investigate the genetics and epigenetics underlying complex traits. This involved extensive behavioral analysis of early life interactions in mice.

2007 – 2011, BSc (Hons) Neuroscience (Ind), 2:1, The University of Leeds, UK
Research project: Protein phosphorylation in Myshkin mice, a Na^+,K^+ ATPase α3 knockout strain, as a model of bipolar disorder.

Research Experience

2020 – Current, Assistant Professor, University of Tennessee Health Science Center, Memphis, Tennessee, USA
Carrying out genome-by-environment interactions in rodent models of human disease.

2017 – 2020, Postdoctoral Fellow, University of Tennessee Health Science Center, Memphis, Tennessee, USA
In Prof. Robert W. Williams' group, working on several bioinformatics and behavioral genetics projects, using mouse, rat, and human data.

2016 – 2017, Postdoctoral Fellow, University of Toronto, Canada
In the lab of Prof. Patrick O. McGowan, studying the epigenetics of a mouse model of Gulf War Illness, using next-generation sequencing technologies, e.g. RNA-seq, RRBS, and ChIP-seq.

2009 – 2010, Industrial placement, Molecular Toxicology, AstraZeneca, UK
Development and characterization of a primary rat kidney cell *in vitro* model.

Honours and awards

2020	Nominated for IMGS Nominations and Elections Committee
2020	Elected member of IBANGS Membership Committee
2019	International Mammalian Genome Society (IMGC) Scholarship
2018	International Behavioural and Neural Genetics Society (IBANGS) Travel Award
2018	Parental Brain Conference 2018 Invited Speaker, Toronto, Ontario, Canada
2016	Canadian Epigenetics, Environment and Health Research Consortium Travel Award
2015	Medical Research Council (MRC) and the National Institute for Social Care and Health

Research (NISCHR) Travel Award
2014 Manchester PhD Conference, prize for best talk

Grant support

Current support

U01DA047638-01A1 (Chen/Williams) 04/01/2019 - 3/31/2024 NIH/NIDA
Systems genetics of menthol and nicotine addiction
Role: Co-Investigator
Genetic studies of addiction using hybrid rat diversity panel (HRDP) genetic reference population. We are using the HRDP to identify sequence variants that control motivational effects of nicotine with a menthol cue.

R01AG070913-01 (Williams/Johnson) 02/01/2021 - 8/31/2026 NIH/NIA
Imaging genetics of brain structure and cognitive aging in murine models of Alzheimer's Disease
Role: Co-investigator
Genetic study of the physiological and behavioural features of Alzheimer's and their genetic modifiers, using the BXD recombinant inbred population and AD-BXD population.

R01ES031656-01 (Jones) 04/01/2021 - 6/30/2026 NIH/NIEHS
Genetics of epigenetic response to high circulating glucocorticoids and organophosphorous compounds
Role: Co-investigator
Genetic and epigenetic study of stress and organophosphorous compounds as a model of Gulf War Illness, using the BXD recombinant inbred population.

Pending support

R01 AG075813-01 (Ashbrook) 09/01/2021 - 08/31/2026 NIH/NIA
The interaction effects of genetic variants, age, diet, sex and mitochondrial copy number on Alzheimer's disease, aging-phenotypes and longevity
Role: Principal Investigator
Gene-by-environment study of the effects of age, sex and diet on mitochondrial DNA copy number, and its effects on longevity and Alzheimer's disease related traits.

R01NS124696-01 (Mulligan/Lu) 09/01/2021 - 8/31/2026 NIH/NINDS
Novel methods and models for efficient genomic dissection of cortical defect mutations.
Role: Co-investigator
Using deep genome sequencing of a pair of closely related strains, and targeted sequencing of their backcrossed offspring to identify variants underlying a cortical defect phenotype.

R01AG066625-01A1 (Mozhui) 09/01/2021 - 8/31/2026 NIH/NIA
Functional genetic analysis of epigenetic age acceleration and the regulatory landscape of the methylome
Role: Co-investigator
Investigating gene-by-environment (age, diet) effects on the methylome, and how these relate to longevity and aging.

R01CA262112-01 (Makowski) 07/01/2021 - 6/30/2026 NIH/NCI
Determining susceptibility loci in triple negative breast cancer using a novel pre-clinical model
Role: Co-investigator
Genetic study of modifiers of triple negative breast cancer phenotypes using a humanized mouse

model, the TNBC-BXD strains.

R21DK129883-01 (Bajwa) 07/01/2021 - 6/30/2023 NIH/NIDDK
Genetic factors underlying the pathogenesis of acute kidney injury
Role: Co-investigator
Gene-by-intervention study of acute kidney injury and its modifiers. We will be using the BXD to identify variants which lead to adverse sequelae.

Completed support

2011-2015 1088088 via Systems Biology Doctoral Training Centre BB/G530225/1. *A systems genetics analysis of complex traits in mouse and human model systems.* Role: Award Holder (100% effort).

Supervisory experience

Staff
2021 – Present, Main supervisor, Research Assistant (animal lab)
2020 – Present, Main supervisor, Senior Research Specialist (molecular lab)

PhD students
2021 – Present, Member of PhD Committee, Pamela M. Watson (UTHSC)
2020 – Present, Member of PhD Committee, Andrew B. Stiemke (UTHSC)
2020, Main supervisor, rotation project, Pamela M. Watson (UTHSC)

MD students
2021 – Present, Main supervisor, rotation project, Catherine L. Diethelm (UTHSC)

Undergraduate students
2021, Main Supervisor, Summer project, Alisha Chunduri (UTHSC)

Mentorship of more junior lab members in Manchester, Toronto, and Tennessee, including four undergraduates, two Masters students, and six PhD students.

Teaching experience

2020 – Present, University of Tennessee Health Sciences Center, Instructor, Medical Genetics
2020 – Present, University of Tennessee Health Sciences Center, Instructor, Bioinformatics I
2017 – Present, University of Tennessee Health Sciences Center, Instructor, Integrative Genetics
2016 – 2017, University of Toronto, Sessional Lecturer, Epigenetics in Health and Disease
2014, 2015, University of Manchester, Teaching Assistant, Africa field course on behaviour and ecology, lecturing and exam marking
2013 – 2015, University of Manchester, Teaching Assistant, Undergraduate practical sessions

Peer-reviewed publications

(21 peer-reviewed publications, Google Scholar > 1000 citations, h-index: 10, WoK > 650 citations, WoK h-index = 7)
(7 preprint deposits on BioRxiv; 5 peer-reviewed and published)

Peer-reviewed manuscripts

21. Lauby, S. C., Ashbrook, D. G., Malik, H. R., Chatterjee, D., Pan, P., Fleming, A. S., et al. (2021).

The role of interindividual licking received and dopamine genotype on later-life licking provisioning in female rat offspring. **Brain and Behavior**, e02069. doi:10.1002/brb3.2069.

20. Ashbrook, D. G., Arends, D., Prins, P., Mulligan, M. K., Roy, S., Williams, E. G., et al. (2021). A platform for experimental precision medicine: The extended BXD mouse family. **Cell Systems** doi:10.1016/j.cels.2020.12.002.
19. Xu, F., Gao, J., Bergman, S., Sims, A. C., Ashbrook, D. G., Baric, R. S., et al. (2020). Genetic dissection of the regulatory mechanisms of *Ace2* in the infected mouse lung. **Frontiers Immunology** doi:10.3389/fimmu.2020.607314.
18. Sandoval-Sierra, J. V., Helbing, A. H. B., Williams, E. G., Ashbrook, D. G., Roy, S., Williams, R. W., et al. (2020). Body weight and high-fat diet are associated with epigenetic aging in female members of the BXD murine family. ***Aging Cell***, e13207. doi:10.1111/acel.13207.
17. Wang, N., Anderson, R. J., Ashbrook, D. G., Gopalakrishnan, V., Park, Y., Priebe, C. E., et al. (2020). Variability and heritability of mouse brain structure: Microscopic MRI atlases and connectomes for diverse strains. ***Neuroimage*** 222, 117274. doi:10.1016/j.neuroimage.2020.117274.
16. Xu, F., Ashbrook, D. G., Gao, J., Starlard-Davenport, A., Zhao, W., Miller, D. B., et al. (2020). Genome-wide transcriptome architecture in a mouse model of Gulf War Illness. ***Brain, Behavior, and Immunity*** doi:10.1016/j.bbi.2020.06.018.
15. Jones, B. C., Miller, D. B., Lu, L., Zhao, W., Ashbrook, D. G., Xu, F., et al. (2020). Modeling the genetic basis of individual differences in susceptibility to Gulf War Illness. ***Brain sciences*** 10, 143. doi:10.3390/brainsci10030143.
14. Ashbrook, D. G., Cahill, S., and Hager, R. (2019). A cross-species systems genetics analysis links *APBB1IP* as a candidate for schizophrenia and prepulse inhibition. ***Frontiers in behavioral neuroscience*** 13. doi:10.3389/fnbeh.2019.00266.
13. Potter, H. G., Ashbrook, D. G., and Hager, R. (2018). Offspring genetic effects on maternal care. ***Frontiers in neuroendocrinology,*** doi:10.1016/j.yfrne.2018.12.004.
12. Herrera, S., de Vega, W. C., Ashbrook, D., Vernon, S. D., and McGowan, P. O. (2018). Genome-epigenome interactions associated with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. ***Epigenetics,*** 13, 1174–1190. doi:10.1080/15592294.2018.1549769.
11. Ashbrook, D. G., Roy, S., Clifford, B. G., Riede, T., Scattoni, M. L., Heck, D. H., et al. (2018). Born to cry: A genetic dissection of infant bocalization. ***Frontiers in behavioral neuroscience,*** 12, 250. doi:10.3389/fnbeh.2018.00250.
10. Ashbrook, D. G., Hing, B., Michalovicz, L. T., Kelly, K. A., Miller, J. V, de Vega, W. C., et al. (2018). Epigenetic impacts of stress priming of the neuroinflammatory response to sarin surrogate in mice: a model of Gulf War illness. ***Journal of neuroinflammation,*** 15, 86. doi:10.1186/s12974-018-1113-9.
9. Ashbrook, D. G., Mulligan, M. K., and Williams, R. W. (2017). Post-genomic behavioral genetics: From revolution to routine. ***Genes, brain, and behavior,*** e12441. doi:10.1111/gbb.12441.
8. Ashbrook, D.G., Sharmin, N., Hager, R., (2017). Offspring genes indirectly influence sibling and maternal behavioural strategies over resource share. ***Proceedings of the Royal Society. B, Biological sciences,*** 284, 20171059. doi:10.1098/rspb.2017.1059
7. Franke, B., Stein, J. L., Ripke, S., Anttila, V., Hibar, D. P., van Hulzen, K. J. E., .,…Ashbrook, D.G., Hager, R., et al. (2016). Genetic influences on schizophrenia and subcortical brain volumes: large-scale proof of concept. ***Nature Neuroscience*** 19, 420–431. doi:10.1038/nn.4228
6. Ashbrook, D. G., Gini, B., and Hager, R. (2015). Genetic variation in offspring indirectly influences the quality of maternal behaviour in mice. ***Elife,*** 4. doi:10.7554/eLife.11814.
    - Won the University of Manchester Faculty of Life sciences best publications competition
5. Ashbrook, D. G., Williams, R. W., Lu, L., and Hager, R. (2015). A cross-species genetic analysis identifies candidate genes for mouse anxiety and human bipolar disorder. ***Frontiers in***

behavioral neuroscience, 9, 171. doi:10.3389/fnbeh.2015.00171.

4. Hibar, D. P., Stein, J. L., Renteria, M. E., Arias-Vasquez, A., Desrivières, S., Jahanshad, N., Toro, R., Wittfeld, K., Abramovic, L., Andersson, M.,…Ashbrook, D.G., Hager, R., et al. (2015). Common genetic variants influence human subcortical brain structures. ***Nature,*** 520, 224–229. doi:10.1038/nature14101.
3. Ashbrook, D. G., Delprato, A., Grellmann, C., Klein, M., Wetzel, R., Overall, R. W., and Badea, A. (2014). Transcript co-variance with Nestin in two mouse genetic reference populations identifies *Lef1* as a novel candidate regulator of neural precursor cell proliferation in the adult hippocampus. ***Frontiers in neuroscience,*** 8, 418. doi:10.3389/fnins.2014.00418.
2. Ashbrook, D. G., Williams, R. W., Lu, L., Stein, J. L., Hibar, D. P., Nichols, T. E., Medland, S. E., Thompson, P. M., and Hager, R. (2014). Joint genetic analysis of hippocampal size in mouse and human identifies a novel gene linked to neurodegenerative disease. ***BMC Genomics,*** 15, 850. doi:10.1186/1471-2164-15-850.
1. Ashbrook, D. G., and Hager, R. (2013). Empirical testing of hypotheses about the evolution of genomic imprinting in mammals. ***Frontiers in neuroanatomy,*** 7, 6. doi:10.3389/fnana.2013.00006.

In preparation or submission

1. Sasani, T. A., Ashbrook, D. G., Lu, L., Palmer, A. A., Williams, R. W., Pritchard, J. K., et al. (2021). A wild-derived antimutator drives germline mutation spectrum differences in a genetically diverse murine family. **bioRxiv**, 2021.03.12.435196. doi:10.1101/2021.03.12.435196.
2. Watson, P. M., and Ashbrook, D. G. (2020). GeneNetwork: a continuously updated tool for systems genetics analyses. **bioRxiv**, 2020.12.23.424047. doi:10.1101/2020.12.23.424047.
3. Ashbrook, D.G., Ren, Y., Palmer, A., Clark, A.G., Pritchard, J.K., Harris, K., Lu, L., Williams, R.W. (In preparation) Deep sequencing of the BXD family. ***In preparation***
4. Chunduri, A., Ashbrook, D.G. (In preparation) Old data and friends improve with age: Advancements with the updated tools of GeneNetwork. ***In preparation***

Book Chapters

1. Ashbrook, D. G., and Hager, R. (2017). "Social interactions and indirect genetic effects on complex juvenile and adult traits," in ***Methods in Molecular Biology*** (Clifton, N.J.), eds. K. Schughart and R. W. Williams (New York: Springer New York), 499–517. doi:10.1007/978-1-4939-6427-7_24.
    - Invited chapter

In preparation or submission

1. Ashbrook, D. G., and Lu, L (2021) "Recombinant inbred mice as models for medicine and biology" in **Animal Models in Medicine and Biology** (IntechOpen), ed. E Purevjav (London), ISBN 978-1-83968-805-8. *In Press*

Conferences and selected presentations

18. **International Behavioural & Neural Genetics Society Virtual Trainee Symposium**, 23 September 2020
    - Talk: 'The interaction effects of genetic variants, diet, and mitochondrial copy number on aging and longevity in the BXD family'
17. **Systems Genetics: From Genomes to Complex Traits, EMBL, Heidelberg, Germany,** 29 September – 2 October 2019

- Talk: 'Sequencing the BXD family, a cohort for experimental systems genetics and precision medicine'

16. **33rd International Mammalian Genome Society Conference, Strasbourg, France,** 25-28 September 2019
    - Talk: 'Sequencing the BXD family, a cohort for experimental systems genetics and precision medicine'
    - Received IMGS Scholarship to attend
15. **Complex Traits Consortium / Rat Genomics 17th Annual Meeting, La Jolla, CA, USA,** 8-11 June 2019
    - Talk: 'Sequencing the BXD family, a cohort for experimental systems genetics and precision medicine'
14. **21st Annual Genes, Brain & Behavior Meeting, Edinburgh, UK,** 10-14 May, 2019
    - Talk: 'Sequencing the BXD family, a cohort for experimental systems genetics and precision medicine'
13. **Parental Brain Conference 2018, Toronto, Ontario, Canada**, 13-14 July, 2018
    - Talk: 'Indirect genetic effects of, and on, maternal care'
    - Invited speaker
12. **16th Annual Meeting of the Complex Trait Community meeting, Glasgow, UK,** 20-22 June 2018
    - Talk: 'Sequencing the BXD family, a cohort for experimental systems genetics and precision medicine'
11. **20th Annual Genes, Brain & Behavior Meeting, Rochester, MN, USA**, 17-21 May 2018
    - Talk: 'Sequencing the BXD family, a cohort for experimental systems genetics and precision medicine'
    - Awarded IBANGS Young Investigator Travel Award to attend the conference
10. **15th Annual Meeting of The MidSouth Computational Biology and Bioinformatics Society, Starkville, MS, USA**, 29-31 March 2018
    - Talk: 'Sequencing the BXD family, a cohort for experimental systems genetics and precision medicine'
9. **11th Annual Canadian Neuroscience Meeting, Montreal**, **Québec, Canada**, 28-31 May 2017
    - Poster: 'Epigenetic impacts of stress priming of the neuroinflammatory response to sarin surrogate in mice: a model of Gulf War Illness'
8. **The Canadian Epigenetics, Environment and Health Research Consortium Network Annual Meeting, "Epigenomics in Development and Disease", Estérel, Québec, Canada**, 18-21 September 2016
    - Awarded a CEEHRC Travel Award to attend the conference
7. **MRC Centre for Neuropsychiatric Genetics and Genomics 6th Annual Summer School in Brain Disorder Research, Cardiff, UK**, 6th - 9th July 2015
    - Attendance award by MRC and NISCHR
6. **2015 Complex Trait Community 14th Annual Meeting, Portland, OR, USA**, 8th - 11th June 2015
    - Talk: 'Indirect genetic effects influence sibling and maternal behaviour in mice'
5. **From functional genomics to systems biology, EMBO Conference Series, Heidelberg, Germany**, 8th - 11th November 2014
    - Poster: 'Joint genetic analysis of hippocampal size in mouse and human identifies a novel gene linked to neurodegenerative disease'
4. **2014 PhD Conference, Manchester, UK**, 9th May 2014
    - Talk: 'Joint genetic analysis of hippocampal volume in mouse and human identifies novel genes linked to neurodegenerative disease'
    - Prize for Best Talk

3. **INCF Course on Neuroinformatics, Neurogenomics and Brain Disease, Fraueninsel, Germany**, 14th - 20th September 2013
    - Resulted in a paper (Ashbrook et al. 2014)
2. **Systems Biology Graduate Conference 2012, Oxford, UK**, 26th - 27th June 2012
    - Poster: 'Investigating parent of origin and imprinting effects in BXD using bioinformatics tools'
1. **The Dynamics of Disease - a Workshop in Medical Systems Biology, Manchester, UK**, 28th Nov - 2nd Dec 2011

Society Memberships

British Neuroscience Association, Complex Trait Community, The MidSouth Computational Biology and Bioinformatics Society, Federation of European Neuroscience Societies, International Mammalian Genome Society, International Behavioural and Neural Genetics Society (Member of The IBANGS Membership Committee)

Research Summary

My primary research interest is the interplay between genes and environment, and integrating levels of biology, from genes, to transcription, epigenetics, and finally complex behaviours and diseases. My previous work has involved extensive use of recombinant inbred rodent populations, both generating my own data, and reanalysing the broad phenome already available for these populations.

My work involved extensive use of the BXD mouse family, and I am currently leading a large sequencing project for this population. This sequencing project has generated ~38x, Chromium 10X linked-read sequencing for 152 BXD strains, plus deeper sequencing of the parental C57BL/6J and DBA/2J strains. This has allowed us to identify all segregating variants in the population (allowing unprecedented accuracy of QTL mapping in the BXD population), as well in private variants which explain 'outlier' strains, where the phenotype value for a particular strain is outside the normal distribution of values in the BXD family.

Current work in my group is particularly focused on age as an environmental effect, and gene-by-age effects on behaviours relating to normal cognitive aging and Alzheimer's disease. This has involved a large biobank of aged tissued from the BXD mouse population, and a new project currently underway involving behavioural characterization of ~40 strains of the AD-BXD family along with deep MRI imaging.

During my first postdoctoral fellowship in Toronto I investigated the transcriptomic and epigenomic effects of corticosterone combined with diisopropyl fluorophosphate, as a mouse model of Gulf War Illness. This gave me experience in analyzing the interactions between 'omics datasets and an experimental environmental perturbation.

Other aspects of my work include the examination of indirect genetic effects on early life behaviour as a specific subset of gene-by-environment interactions, and the joint-analysis of phenotypes collected across species.