NA CAI

CONTACT INFORMATION

D-BSSE
Klingelbergstrasse 48
4056 Basel
Switzerland

Email: na.cai@bsse.ethz.ch
Twitter/Github: caina89
Website: www.nacailab.com

EDUCATION

DPhil in Clinical Medicine (Oct 2011 – Feb 2016)
Nuffield Department of Clinical Medicine, University of Oxford
Wellcome Trust Centre for Human Genetics, University of Oxford
Supervisor: Professor Jonathan Flint
Conferred: 1 Feb 2016

BA (Hons), MA in Natural Sciences Tripos (Oct 2008 – Jun 2011)
Gonville and Caius College, University of Cambridge
Final year in Department of Physiology, Development and Neuroscience

CAREER PROFILE

My research group focuses on investigating the genetic effects on neuropsychiatric diseases, acting either directly or in interaction with the physiological and external environments, with a specific focus on understanding the heterogeneous etiology of Major Depressive Disorder (MDD). We use computational and quantitative methods to interrogate large-scale genomic datasets for the effects of genetic variation on neuropsychiatric disease risk. In addition to finding statistical associations, we aim to identify the molecular pathways, physiological contexts, and environmental modulators behind them.

PROFESSIONAL EXPERIENCE

Assistant Professor of Computational Medical Genomics (Feb 2025 – current)
Department of Biosystems Science and Engineering, ETH Zürich, Switzerland

- Develop quantitative genetics and functional genomics integration methods and frameworks for investigating the genetic heterogeneity of Major Depressive Disorder (MDD)
- Develop methods for optimizing the utility of electronic health records and biobanks for psychiatric genetics research design and execution
- Investigate the genetic architecture and etiology underlying psychiatric disorder comorbidity and development trajectories
- Investigate the consequences of chronic stress on cellular gene expression and intercellular interactions using spatial and single-cell sequencing of brain tissue of chronically stressed mice; method development in single cell data analysis to identify genes and inter/intra-cellular gene interactions as a result of chronic stress

Principal Investigator (Oct 2019 – Jan 2025)
Helmholtz Pioneer Campus, Helmholtz Munich, Germany
School of Medicine and Health, Technical University of Munich, Germany

- Investigate the genetic, environmental and psychosocial factors that contribute to heterogeneity of Major Depressive Disorder (MDD), the interactions between them, and how they may be shared with other psychiatric or other comorbid conditions, using large-scale biobank and electronic health record data
- Investigate mitochondria's role in stress resilience through quantitative analysis on tissue-specific gene expression and function on multi-omic datasets, and experiments in cellular and animal models
- Spatial and single-cell sequencing of brain tissue of chronically stressed mice

EBI-Sanger Postdoctoral Fellow (Mar 2016 – Sept 2019)
Wellcome Sanger Institute, United Kingdom
European Bioinformatics Institute, United Kingdom

- Investigate the utility of MDD phenotypes derived from questionnaires in UKBiobank (500,000 individuals) in terms of genome-wide association studies (GWAS) findings, and analyse their genetic architectures and genetic overlap with other psychiatric conditions
- Using transcriptomics, proteomics, metabolomics and bulk organismal phenotypes, investigate how variation in the mtDNA direct human molecular phenotypes and modify nuclear DNA control of molecular traits and disease risks

DPhil (Oct 2011 – Mar 2016)
Wellcome Trust Centre for Human Genetics, University of Oxford, United Kingdom
Nuffield Department of Clinical Medicine, University of Oxford, United Kingdom

- Detecting sequence variants from low-coverage (1x) whole-genome sequencing and performing GWAS and analyses of genetic architecture on MDD and related phenotypes in 12,000 Han Chinese women
- Quantification of mitochondrial and telomeric DNA from NGS data and investigating their relationship with stress, metabolism and MDD; verifying the causal relationship between changes in mitochondrial and telomeric DNA and stress using hypothesis driven laboratory experiments on mice

AWARDS/ HONORS

2024 **Theodore Reich Early Career Award**
International Society of Psychiatric Genetics

2024 **Early Excellence Science Award (Biology)**
Bayer Foundation

2024 **Preis in den Mathematisch-Naturwissenschaftlichen**
Niedersächsische Akademie der Wissenschaften zu Göttingen

2023 **Friedmund Neumann Preis**
Schering Stiftung

2017 – 2020 **Raymond and Beverly Sackler Research By-Fellowship**
Churchill College, University of Cambridge

2016 – 2019 **EBI-Sanger Postdoctoral Fellowship (ESPOD)**
European Bioinformatics Institute, Wellcome Trust Sanger Institute

2011 – 2015 **A*STAR Graduate Scholarship (Overseas)**
Agency of Science, Technology and Research, Singapore

2008 – 2011 **Honorary Scholar**
Cambridge Commonwealth Trust

2008 – 2011 **A*STAR National Science Scholarship (Overseas)**
Agency of Science, Technology and Research, Singapore

GRANTS/ FUNDING

2019 – 2025 **Core funding, Helmholtz Zentrum München (equivalent to 3.5M EUR)**
PI and 5 personnel salaries (3 PhD students and 2 postdocs) for 5 years, 500,000K EUR of investment to be spent across 5 years, and 50K EUR per year of consumables for 5 years

2022 **NIH R01: Co-applicant (300K EUR), Flint (PI), Role: Co-I**
This project aims to improve the interpretability of genetic studies of MDD using large-scale biobanks and electronic health records to identify risk genes.

2022 **BMBF German Mental Health Centre (300K EUR), Role: Co-I**
This consortium aims to build a nationwide research consortium across all research around mental health; I am part of the Munich site application, which is primarily leading the effort on bio-banking and big data analysis.

2021 **TUM Global Incentive Fund (10K EUR), Cai (PI)**
This project aims to use Mendelian Randomisation approaches to understand the causal environmental factors for Major Depressive Disorder.

SCIENTIFIC COMMUNITY AND LEADERSHIP

2025 **Co-chair** of RECOMB-Genetics (RECOMB Satellite), Seoul, South Korea

2025 **Program committee** for ECCB/ISMB, Liverpool, United Kingdom

2025 **Co-chair** of Gordon Research Conference (GRC) on “Quantitative Genetics and Genomics”, Lucca (Barga), Italy

2023 – present **Lead** of the heterogeneity subgroup of the Psychiatric Genomics Consortium Major Depressive Disorder Working Group (PGC-MDD)

2023 – present **Member** of the diagnostic committee of the Psychiatric Genomics Consortium Schizophrenia Working Group (PGC-SCZ)

2022 – present **Program committee** for World Congress on Psychiatric Genetics (WCPG), organized by International Society for Psychiatric Genetics (ISPG)

2022 – present **Member** of the Psychiatric Genomics Consortium Cross Disorder Working Group (PGC-CDG)

2023 **Vice-chair** of Gordon Research Conference (GRC) on “Quantitative Genetics and Genomics”, Los Angeles, USA

2019 **Co-chair** of Gordon Research Seminar (GRS) on “Quantitative Genetics and Genomics”, Lucca (Barga), Italy

	2015 – present	**Member** of the Psychiatric Genomics Consortium Major Depressive Disorder Working Group (PGC-MDD)

SELECT CONFERENCES AND SEMINARS

2025	**Invited speaker, European College of Neuropsychopharmacology (ECNP), Amsterdam, Netherlands** TBD
2025	**Invited speaker, European Society of Human Genetics, Milan, Italy** TBD
2025	**Invited speaker, Applied Machine Learning Days (AMLD), Lausanne, Switzerland** Use of AI in investigations into psychiatric disorders and their trajectories
2024	**Invited speaker, Ettore Majorana International school, Erice, Italy** Molecular markers of stress – from DNA sequencing to spatial transcriptomics
2024	**Invited speaker, Massachusetts General Hospital Center for Precision Psychiatry's Fourth Annual Conference on Precision Psychiatry, Boston, USA (virtual conference)** Investigating MDD heterogeneity using polygenic methods
2024	**Symposium Chair, World Congress in Psychiatric Genetics (WCPG), Singapore** Heterogeneity and comorbidity: Perspectives from biobanks, registries and EHRs
2024	**Invited speaker, EMBL Workshop on Profiling Environmental Exposures in Human Cohort Data, EMBL Heidelberg, Heidelberg, Germany** Molecular markers of stress – from DNA sequencing to spatial transcriptomics
2023	**Discussant, NHGRI's Advances in the Genetic Architecture of Complex Human Traits workshop, Bethesda, USA** Roundtable: What's missing from our understanding of genetic architecture across levels of biological organization
2023	**Symposium talk, World Congress in Psychiatric Genetics (WCPG), Montreal, Canada** Phenotype integration improves power and preserves specificity in biobank-based genetic studies of Major Depressive Disorder
2023	**Invited seminar, New York Genome Centre, New York City, USA** Genetics of depression: maximizing available data, informing epistemic iterations
2023	**Invited seminar, Centre for Precision Psychiatry, Massachusetts General Hospital, Boston, USA (virtual)** Polygenic means to investigate heterogeneity in Major Depressive Disorder
2023	**Invited keynote, RECOMB-Genetics (RECOMB satellite conference), Istanbul, Turkey** Epistemic iterations between genetic findings and phenotyping
2023	**Invited keynote, Gordon Research Seminar, Quantitative Genetics and Genomics, Ventura, USA** What we want in a phenotype – lessons from genetic studies on depression
2022	**Invited seminar, USC Centre for Genetic Epidemiology, Los Angeles, USA (virtual)** Phenotype integration improves power and preserves specificity in biobank-based genetic studies of Major Depressive Disorder
2022	**Invited seminar, Zangwill Club, University of Cambridge, UK** Genetics of MDD: Lessons and challenges ahead
2022	**Invited seminar, Neurogenetics seminar series, UCLA Center for Neurobehavioral Genetics, Los Angeles, USA** Genetics of MDD: Lessons and challenges ahead
2022	**Invited panelist, Ernst Struengmann Forum, Frankfurt, Germany** Exploring and Exploiting Genetic Risk for Psychiatric Disorders
2022	**Invited speaker, International Mouse Phenotyping Consortium Workshop (virtual)** Molecular signatures of depression
2020	**Invited speaker, World Laurates Forum (WLF), Shanghai, China (virtual)** Lessons from genetic studies of Major Depressive Disorder
2020	**Symposium talk, World Congress in Psychiatric Genetics (WCPG), Virtual Conference** Heterogeneity of depression in GWAS

TEACHING EXPERIENCE	2020 – present	**PhD Supervision** – 5 PhD Students (2 submitted) Department of Medicine, Technical University of Munich
	2020 – present	**Undergraduate Lecture -** Natural Sciences Tripos (Biological) Part II, Department of Psychology, Cambridge University
	2022	**Graduate Lecture** – IMPRS-TP graduate programme Max Planck Institute of Psychiatry
	2021 – 2022	**Graduate Lecture** – Masters in Genetic Epidemiology Ludwig Maximilian University of Munich
	2016 – 2018	**College Supervision –** Natural Sciences Tripos (Biological) Part IA and IB, Gonville and Caius College, Cambridge University

REFEREES

Professor Jonathan Flint (PhD advisor)
Center for Neurobehavioral Genetics, Semel Institute for Neuroscience and Human Behavior, Gonda Building, 695 Charles E. Young Drive South, Los Angeles, CA 90095, United States of America
JFlint@mednet.ucla.edu

Professor Kenneth S. Kendler (Close collaborator)
Bio-Technology Research Park, Building One, 800 E. Leigh Street, Suite 100, Box 980126, Richmond, VA 23298-0126, United States of America
kenneth.kendler@vcuhealth.org

Professor Oliver Stegle (Postdoc advisor)
Deutsches Krebsforschungszentrum (DKFZ), Im Neuenheimer Feld 280, 69120 Heidelberg, Germany
o.stegle@dkfz-heidelberg.de

Professor Nicole Soranzo (Postdoc advisor)
Fondazione Human Technopole - Viale Rita Levi-Montalcini, 1 - Area MIND - 20157 Milano, Italy
nicole.soranzo@fht.org

Professor John Mollon (Teaching reference)
Department of Psychology, Downing Street, Cambridge CB2 3EB, United Kingdom
jm123@cam.ac.uk

PUBLICATION LIST *(NOTE: equal contribution is denoted with *)*

SELECTED PUBLICATIONS

Cai N.*, Verhulst B.*, et al. Assessment and Ascertainment in Psychiatric Molecular Genetics: Challenges and Opportunities for Cross-Disorder Research. Molecular Psychiatry (2024)

Dahl A.*, … **Cai N**.* (corresponding author). Phenotype integration improves power and preserves specificity in biobank-based genetic studies of MDD. Nature Genetics (2023)

Schork AJ.*, Peterson RE.*, Dahl A.*, **Cai N**.*, Kendler KS. Indirect paths from genetics to education, Nature Genetics (2022)

Cai N.*, Gomez-Duran A.*, et al. Mitochondrial DNA variants modulate N-formylmethionine, proteostasis and risk of late-onset human diseases. Nature Medicine (2021)

Cai N. (Corresponding author), et al., Minimal phenotyping yields GWAS hits of low specificity for major depression, Nature Genetics (2020)

Cai N. (Corresponding author), Choi, KW., Fried EI., Reviewing the genetics of heterogeneity in depression: Operationalizations, manifestations, and etiologies, Human Molecular Genetics (2020)

Peterson RE.*, **Cai N**.*, et al. Molecular genetic analysis subdivided by adversity exposure reveals etiologic heterogeneity in major depression, American Journal of Psychiatry (2018)

Peterson RE.*, **Cai N**.*, Bigdeli TB.*, et al., The genetic architecture of major depressive disorder in Han Chinese women, JAMA Psychiatry (2017)

Cai N. et al., Genetic control over mtDNA and its relationship to major depressive disorder, Current Biology (2015)

Cai N.*, Bigdeli TB.*, Kretzschmar WW.*, Li YH.*, et al., Sparse whole genome sequencing identifies two loci for major depressive disorder, Nature (2015)

Cai N.*, Li YH.*, Chang S.*, et al., Molecular Signatures of Major Depression, Current Biology (2015)

OTHER PUBLICATIONS

Adams M., … **Cai N**. (consortium member), et al. Genome-wide study of major depression in 685,808 diverse individuals identifies 698 independent associations, infers causal neuronal subtypes and biological targets for novel pharmacotherapies. Cell (2025)

Sadowski M., … **Cai N.** (contributing author), … et al. Characterizing the genetic architecture of drug response using gene-context interaction methods. Cell Genomics (2024)

Krebs MD., … **Cai N.** (contributing author) et al., PA-FGRS is a novel estimator of pedigree-based genetic liability that complements genotype-based inferences into the genetic architecture of major depressive disorder. AJHG (2024)

Meng X, … **Cai N.** (contributing author), et al. Multi-ancestry GWAS of major depression aids locus discovery, fine-mapping, gene prioritisation, and causal inference. Nature Genetics (2024)

Huang L., … **Cai N.** (corresponding author). Polygenic analyses show important differences between MDD symptoms collected using PHQ9 and CIDI-SF. Biological Psychiatry (2024)

An U., … **Cai N**. (contributing author), et al. Deep Learning-based Phenotype Imputation on Population-scale Biobank Data Increases Genetic Discoveries. Nature Genetics (2023)

Walters RG, … **Cai N** (contributing author), et al., Genotyping and population structure of the China Kadoorie Biobank, Cell Genomics (2023)

Chang S., … **Cai N.** (second last author), Duessing JM. Tripartite extended amygdala-basal ganglia CRH circuit drives arousal and avoidance behavior, Science Advances (2022)

Border R., … **Cai N.** (contributing author)., et al., Cross-trait assortative mating is widespread and inflates genetic correlation estimates, Science (2022)

Nyugen T-D., … **Cai N.** (contributing author), et al., Genetic heterogeneity and subtypes of major depression, Molecular Psychiatry (2022)

Zou J., … **Cai N.** (contributing author), et al., Analysis of independent cohorts of outbred CFW mice reveals novel loci for behavioral and physiological traits and identifies factors determining reproducibility, G3: Genes, Genomes, Genetics (2021)

Majumdar A., Giambartolomei C., **Cai N.** (3rd author), et al. Leveraging eQTLs to identify individual-level tissue of interest for a complex trait, PLoS Comp Bio (2021)

Bonder MJ., … **Cai N.** (contributing author)**,** et al. Identification of rare and common regulatory variants in pluripotent cells using population-scale transcriptomics, Nature Genetics (2021)

Chatzinakos C., Lee D., **Cai N.** (3rd author), et al, Increasing the resolution and precision of psychiatric genome-wide association studies by re-imputing summary statistics using a large, diverse reference panel, American Journal of Medical Genetics Part B: Neuropsychiatric Genetic (2021)

Vuckovic D, … **Cai N**. (contributing author), et al., The Polygenic and Monogenic Basis of Blood Traits and Diseases, Cell (2020)

Chatzinakos C., …, **Cai N.** (contributing author), et al, TWAS pathway method greatly enhances the number of leads for uncovering the molecular underpinnings of psychiatric disorders, American Journal of Medical Genetics Part B: Neuropsychiatric Genetic (2021)

Cai N. et al, No evidence of persistence or inheritance of mitochondrial DNA copy number in Holocaust survivors and their descendants, Frontiers in Genetics (2020)

Dahl A., Khiem Nguyen, **Cai N.** (3rd author), et al., A Robust Method Uncovers Significant Context-Specific Heritability in Diverse Complex Traits, AJHG (2020)

Dahl A., **Cai N**. (2nd author), et al., Reverse GWAS: Using Genetics to Identify and Model Phenotypic Subtypes, PloS Genetics (2019)

Peyrout W., … **Cai N**. (consortium member), et al., Does childhood trauma moderate polygenic risk for depression? A meta-analysis of 5765 subjects from the psychiatric genomics consortium, Biological Psychiatry (2018)

Wray N., … **Cai N**. (consortium member), et al., Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression, Nature Genetics (2018)

Speed D., **Cai N.** (2nd author), et al., Re-evaluation of SNP heritability in complex human traits, Nature Genetics (2017)

Nicod J., Davies RW., **Cai N.** (3rd author), et al., Genome-wide association of multiple complex traits in outbred mice by ultra low-coverage sequencing, Nature Genetics (2016)

Edwards AC., Aggen SH., **Cai N.** (3rd author), et al., Chronicity of depression and molecular markers in a large sample of Han Chinese women, Depression and anxiety (2016)

McIntyre RE., … **Cai N.** (5th author)., et al., A genome-wide association study for regulators of micronucleus formation in mice, G3: Genes, Genomes, Genetics (2016)

PREPRINTS

Wengert S., … Heinig M.*, **Cai N.*** (corresponding author). Tissue-specific apparent mtDNA heteroplasmy and its relationship with ageing and mtDNA gene expression. BioRxiv (2024)

Giannoulis X., … **Cai N**. (corresponding author). Interplay between mitochondrial and nuclear DNA in gene expression regulation. BioRxiv (2024)

Davis K.A.S., … **Cai N.** (contributing author), et al. The UK Biobank Mental Health Enhancement 2022: Methods and Results. medRxiv (2024)

Zuber V., Cronjé H.T., **Cai N.** (contributing author), Gill D., & Bottolo L. Mendelian randomization for multiple exposures and outcomes with Bayesian Directed Acyclic Graphs exploration and causal effects estimation. BioRxiv (2024)

Chang S., Fermani F., … Deussing J.*, **Cai N.*** (corresponding author). Molecular and neural mechanisms of behavioural integration in the extended-amygdala. BioRxiv (2024)

Han S., … **Cai N.** (contributing author), et al. LEOPARD: missing view completion for multi-timepoint omics data via representation disentanglement and temporal knowledge transfer. BioRxiv (2024)

Lam M, … **Cai N.** (contributing author), et al. Elucidating the Joint Genetic Architecture of Mood Disorder and Schizophrenia. MedRxiv (2020)

SUBMITTED

Grotzinger A.D., … **Cai N.** (contributing author), … et al. The Landscape of Shared and Divergent Genetic Influences across 14 Psychiatric Disorders. – *In review at Nature*