NA CAI

CONTACT INFORMATION

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EDUCATION

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

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 context and environmental modulators behind them.

PROFESSIONAL EXPERIENCE

Principal Investigator (Oct 2019 – present)
Helmholtz Pioneer Campus, Helmholtz Zentrum München, Germany

- Using large-scale biobank and disease specific cohorts, identify 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
- 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 utilizing new sequencing and single cell technologies
- 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
- The Cai lab currently consists of 5 PhD students and 2 Postdocs

EBI-Sanger Postdoctoral Fellowship (Mar 2016 – Sept 2019)
Wellcome Sanger Institute and 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, as well as modify nuclear DNA control of molecular traits and disease risks

DPhil Project (Oct 2011 – Mar 2016)
Wellcome Trust Centre for Human Genetics, 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

GRANTS

2023 **Lundbeckfonden Fellowship (10M DKK), Cai (PI)**
This is a personal grant awarded for a proposal NextStepDep, calling for the careful evaluation of Danish medical and prescription registry data for investigation of treatment response and disease comorbidity among psychiatric disorders.

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 Gordon Research Conference (GRC) on "Quantitative Genetics and Genomics", Lucca (Barga), Italy

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

2022 **Panelist** at Ernst Struengmann Forum on "Exploring and Exploiting Genetic Risk for Psychiatric Disorders", Frankfurt, Germany

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

2022-present **Program committee for** World Congress on Psychiatric Genetics

2022 – present **Member** of the Psychiatric Genomics Consortium Cross Disorder Working Group

2015 – present **Member** of the Psychiatric Genomics Consortium Major Depressive Disorder Working Group

SELECTED CONFERENCES AND SEMINARS

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 virtual seminar, USC Centre for Genetic Epidemiology, Los Angeles, USA**
Phenotype integration improves power and preserves specificity in biobank-based genetic studies of Major Depressive Disorder

2022 **Invited talk at Zangwill Club, University of Cambridge, UK**
Genetics of MDD: Lessons and challenges ahead

2022 **Neurogenetics seminar series, UCLA Center for Neurobehavioral Genetics, Los Angeles, USA**
Genetics of MDD: Lessons and challenges ahead

2022 **Bioengineering Solutions for Biology and Medicine 2022, Munich, Germany**

Integrative multi-trait approaches improve power and specificity for biobank-based genetic analyses of Major Depressive Disorder

2022 **Ernst Struengmann Forum, Frankfurt, Germany**
Exploring and Exploiting Genetic Risk for Psychiatric Disorders

2022 **Invited talk at Institute of Biological Psychiatry, Roskilde, Denmark**
Genetics of MDD: Lessons and challenges ahead

2022 **International Mouse Phenotyping Consortium Workshop, Virtual**
Molecular signatures of depression

2020 **World Laurates Forum (WLF), Shanghai/Virtual Conference**
Lessons from genetic studies of Major Depressive Disorder

2020 **World Congress in Psychiatric Genetics (WCPG), Virtual Conference**
Heterogeneity of depression in GWAS

2020 **Invited talk at Max Planck Institute of Psychiatry, Munich, Germany**
Using different definitions of depression to understand its heterogeneity

2019 **World Congress in Psychiatric Genetics (WCPG), Anaheim, USA**
Definitions of depression in GWAS

2019 **"Dissecting the Heterogeneity of Major Depression" Symposium, Kings College London, United Kingdom**
Definitions of depression in GWAS

TEACHING EXPERIENCE

2020 – present **PhD Supervision** – 5 PhD Students
Department of Medicine, Technical University of Munich; Munch Data Science Graduate School (MUDS)

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

AWARDS/ HONORS

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, Cambridge

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

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

REFEREES

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

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

SELECTED PUBLICATIONS

Dahl A.*, … **Cai N**.* (corresponding author). Phenotype integration improves power and preserves specificity in biobank-based genetic studies of MDD. bioRxiv (2022) *In press at Nature Genetics*

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

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

Huang L., … **Cai N.** (corresponding author). Polygenic analyses show important differences between MDD symptoms collected using PHQ9 and CIDI-SF. MedRxiv (2023)

An U., … **Cai N**. (contributing author), et al. Deep Learning-based Phenotype Imputation on Population-scale Biobank Data Increases Genetic Discoveries. bioRxiv (2022)

Meng X, … **Cai N.** (contributing author), et al. Multi-ancestry GWAS of major depression aids locus discovery, fine-mapping, gene prioritisation, and causal inference. bioRxiv (2022)

Walters RG., … **Cai N**. (contributing author)., et al.,Genotyping and population structure of the China Kadoorie Biobank, medRxiv (2022)

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