

David Gate, Ph.D.

dgate@stanford.edu
www.linkedin.com/in/dgate



EDUCATION

University of Southern California

Degree: Ph.D., Integrative Biology of Disease
Los Angeles, CA

2013 – 2015

Cedars-Sinai Medical Center

Graduate Program in Biomedical Science & Translational Medicine
Los Angeles, CA

2010 – 2013

American Federation of Aging Research

Advanced School on Neuroscience and Aging
Venice, Italy

June 2013

University of California at Santa Barbara

Degree: Bachelor of Arts, Psychology
Santa Barbara, CA

2003 – 2007

RESEARCH EXPERIENCE

Stanford University – Palo Alto, CA

Irene Diamond/AFAR Postdoctoral Fellow
NIH/NIA National Research Service Award Fellow
Advisor: Dr. Tony Wyss-Coray

2015 –

- Project: Clonally expanded CD8 T cells patrol Alzheimer's cerebrospinal fluid
- Utilized mass cytometry to detect an adaptive immune signature in the blood of Alzheimer's patients, consisting of increased numbers of highly differentiated CD8 memory T cells.
- Provided the first evidence of clonally expanded CD8 memory T cells in the CSF of Alzheimer's and Parkinson's disease patients using single cell T cell receptor sequencing.
- Combined scRNAseq and scTCRseq to identify antigen-specific, cytotoxic CD8 T cells in Alzheimer's cerebrospinal fluid.

University of Southern California – Los Angeles, CA

NIH/NINDS National Research Service Award Fellow
Advisor: Dr. Terrence Town

2013 – 2015

- Project: Abrogation of T Cell TGF- β Signaling Restricts Medulloblastoma Progression
- Showed that blockade of the TGF- β signaling pathway promotes memory T cell development, conferring antitumor immunity to the *smoothened A1* mouse model of MB.
- These data lay the cellular immune mechanistic framework for blocking T cell TGF- β signaling in pediatric brain cancer.
- Co-authored a Neuron study modulating IL-10 signaling alters microglial activation and A β phagocytosis, suggesting that rebalancing cerebral innate immunity and promoting beneficial neuroinflammation may be therapeutically relevant for Alzheimer's

Cedars-Sinai Medical Center – Los Angeles, CA

2010 – 2013

Graduate Researcher

Advisor: Dr. Terrence Town

- Aided in the characterization of a novel transgenic rat model of Alzheimer's disease (TgF344-AD) by performing microscopy and oligomeric A β ELISA measurements.
- Utilized *in vivo* strategies to assess the role of immunosuppressive molecules in mouse models of neurologic disease, including pediatric brain cancer and Alzheimer's disease
- Designed and implemented *in vitro* strategies to assess immune cell populations in the brain, spleen, and thymus by immunofluorescence confocal microscopy, flow cytometry and Western blot methods.
- Developed a novel technique to target pial surface progenitor cells for rapid genetic manipulation via electroporation.

Research Associate II

2007 – 2010

Advisor: Dr. Terrence Town

- Established and maintained a tissue repository of human medulloblastoma and Alzheimer's disease tissue samples.
- Performed immunohistochemistry and confocal microscopy of immune cells in brains of mice infected with West Nile virus and herpes simplex virus.
- Authored multiple review articles on the role of the immune system in Alzheimer's disease.

University of California at Santa Barbara – Santa Barbara, CA

2004 – 2007

Undergraduate Researcher

Advisor: Dr. Benjamin Reese

- Tested the efficacy of naturally-occurring compounds for the treatment of the neurodegenerative disease glaucoma.
- Mastered techniques in animal surgery, intracardial perfusion and histology.
- Received an undergraduate research and creative activities grant for 3 consecutive years.

PUBLICATIONS

Book Chapters

1. **Gate D**, Town T. Cerebral innate immunity: a new conceptual framework for Alzheimer's. Genes, Environment and Alzheimer's Disease. Elsevier [chapter and book cover art].

Research Papers (Peer Reviewed) h-index=14

1. Bai F, Town T, Qian F, Wang P, Kamanaka M, Connolly T, **Gate D**, Montgomery R, Flavell R, Fikrig E. Il-10 signalling blockade controls murine West Nile virus infection (2009). PLoS Pathogens. 5(10):e1000610 (PMID: 19816558).
2. Mott K, **Gate D**, Zandian M, Allen SJ, Kumar RN, Rouse BT, van Rooijen N, Town T, Ghiasi H. Macrophage IL-12p70 signaling prevents HSV-1-induced CNS autoimmunity triggered by autoaggressive CD4⁺ Tregs (2010). Investigative Ophthalmology and Visual Science. 52(5):2321-33 (PMID: 21220560).
3. Allen SJ, Hamrah P, **Gate D**, Mott KR, Mantopoulos D, Zheng L, Town T, Jones C, von Andrian UH, Freeman GJ, Sharpe AH, BenMohamed L, Ahmed R, Wechsler SL, Ghiasi H. The role of LAT in increased CD8⁺ T cell exhaustion in trigeminal ganglia of mice latently infected with herpes simplex virus 1 (2011). Journal of Virology. 85(9):4184-97 (PMID: 21307196).
4. Breunig JJ*, **Gate D***, Levy R, Rodriguez J, Danielpour M, Svendsen C, Town T. Rapid genetic targeting of pial surface neural progenitors and immature neurons by neonatal electroporation (2012). Neural Development. 7(1):26 (PMID: 22776033). *first author equivalent contribution

5. Wang P, Bai F, Zenewicz L, Dai J, **Gate D**, Cheng G, Yang L, Qian F, Yuan X, Montgomery R, Flavell R, Town T, Fikrig E. IL-22 signaling contributes to West Nile encephalitis pathogenesis (2012). PLoS One. 7(8):e44153 (PMID: 22952908).
6. Cohen RM, Rezai-Zadeh K, Weitz T, Rentsendorj A, **Gate D**, Spivak I, Bholat Y, Vasilevko V, Glabe CG, Breunig JJ, Rakic P, Davtyan Y, Agadjanyan MG, Kepe V, Barrio J, Bannykh S, Szekely CA, Pechnick R, Town T. A transgenic Alzheimer rat model resource with plaques, tangles, behavioral impairment, intraneuronal A β and frank neuronal loss. (2013) Journal of Neuroscience, 10;33(15):6245-6256 (PMID: 23575824).
7. **Gate D**, Danielpour M, Rodriguez J, Kim G, Levy R, Bannykh S, Breunig JJ, Kaech S, Flavell R, Town T. T Cell TGF- β Signaling Abrogation Restricts Medulloblastoma Progression (2014). Proceedings of the National Academy of Sciences. 19;111(33):E3458-66 (PMID: 25082897).
Featured in: Berndt JD. Brain Cancer Uses TGF- β to Battle Immune Cells (2014). Science Signaling. 7, ec226.
8. Weitz TM, **Gate D**, Rezai-Zadeh K, and Town T. MyD88 is dispensable for cerebral amyloid pathology and neuroinflammation in APP/PS1 transgenic mice. (2014) American Journal of Pathology. 184(11):2855–2861 (PMID: 25174876).
9. Guillot-Sestier MV, Doty KR*, **Gate D***, Rodriguez J, Leung BP, Rezai-Zadeh K, Town T. Il10 deficiency re-balances innate immunity to mitigate Alzheimer-like pathology (2015). Neuron. 4;85(3):534-48. (PMID: 25619654). *second author equivalent contribution
10. **Gate D**, Danielpour M, Bannykh S, Town T. Characterization of cancer stem cells and primary cilia in medulloblastoma (2015). CNS & Neurological Disorders - Drug Targets. 14(5):600-11. (PMID: 25921740).
11. Tseng CW, Biancotti JC*, Berg B*, **Gate D***, Kolar SL, Muller S, Rodriguez MD, RezaiZadeh K, Fan X, Beenhouwer DO, Town T, Liu GY. Increased susceptibility of humanized NOD-SCID IL2r γ null mice to Panton-Valentine Leukocidin and Staphylococcus aureus skin infection (2015). PLoS Pathogens. 11(11):e1005292. (PMID: 26618545) *second author equivalent contribution.
12. Mott KR, **Gate D**, Matundan HH, Ghiasi YN, Town T, Ghiasi H. CD8+ T cells play a bystander role in HSV-1 latently infected mice (2016). J Virol. pii: JVI.00255-16. (PMID: 26962220).
13. Acharya D, Wang P, Paul AM, Dai J, **Gate D**, Lowery JE, Stokic DS, Leis AA, Flavell RA, Town T, Fikrig E, Bai F. Interleukin-17A promotes CD8+ T cell cytotoxicity to facilitate West Nile virus clearance (2016). Journal of Virology. pii: JVI.01529-16. (PMID: 27795421).
14. Yang AC, du Bois H, Olsson N, **Gate D**, Lehallier B, Berdnik D, Brewer KD, Bertozzi CR, Elias JE, Wyss-Coray T. Multiple Click-Selective tRNA Synthetases Expand Mammalian Cell-Specific Proteomics (2018). Journal of the American Chemical Society. 140(23):7046-7051. (PMID: 29775058).
15. Pluvinage JV, Haney MS, Smith BAH, Sun J, Iram T, Bonanno L, Li L, Lee DP, Morgens DW, Yang AC, Shuken SR, **Gate D**, Scott M, Khatri P, Luo J, Bertozzi CR, Bassik MC, Wyss-Coray T. CD22 blockade restores homeostatic microglial phagocytosis in aging brains (2019). Nature. 568(7751):187-192. (PMID: 30944478).
16. Lehallier B, **Gate D**, Schaum N, Nanasi T, Lee SE, Yousef H, Losada PM, Berdnik D, Keller A, Verghese J, Sathyan S, Franceschi C, Milman S, Barzilai N, Wyss-Coray T. Undulating changes in human plasma proteome profiles across the lifespan (2019) Nature Medicine. 25:1843–1850. (PMID: 31806903).
17. **Gate D**, Saligrama N, Leventhal O, Yang AC, Middeldorp J, Chen K, Lehallier B, Channappa D, De Los Santos MB, McBride A, Pluvinage J, Elahi F, Tam G K-Y, Greicius M, Wagner AD, Galasko D, Davis MM, Wyss-Coray T. Clonally expanded CD8 T cells patrol the cerebrospinal fluid in Alzheimer’s disease. (2020). Nature. (PMID: 31915375).
Featured in: Heneka MT. An immune-cell signature marks the brain in Alzheimer’s disease (2020). Nature.

Reviews (Peer Reviewed)

1. Rezai-Zadeh K, **Gate D**, Town T. CNS infiltration of peripheral immune cells: *D-Day* for neurodegenerative disease? (2009). Journal of Neuroimmune Pharmacology. 4(4):462-75 (PMID: 19669892).
2. Rezai-Zadeh K*, **Gate D***, Szekely CA, Town T. Can peripheral leukocytes be used as Alzheimer's disease biomarkers? (2009). Expert Review of Neurotherapeutics. 9(11):1623-33 (PMID: 19903022). *first author equivalent contribution
3. **Gate D**, Rezai-Zadeh K, Jodry D, Rentsendorj A, Town T. Macrophages in Alzheimer's disease: the blood-borne identity (2010). Journal of Neural Transmission. 117(8):961-70 (PMID: 20517700).
4. Rezai-Zadeh K*, **Gate D***, Gowing G, Town T. How to get from here to there: macrophage recruitment in Alzheimer's disease (2011). Current Alzheimer Research. 8(2):156-63 (PMID: 21345166). *first author equivalent contribution
5. **Gate D**, Danielpour M, Levy R, Breunig JJ, Town T. Basic biology and mechanisms of neural ciliogenesis and the B9 family (2012). Molecular Neurobiology. 45(3):564-70 (PMID: 22644387).

Oral Presentations

1. "IRAK-M deletion activates microglia and restricts cerebral amyloid in PSAPP mice." **Gate D**, Rentsendorj A, Rezai-Zadeh K, Masliah E, Town T. *Alzheimer's Association International Conference*, Paris, France, July 16th – 21st, 2011.
2. "T Cell TGF- β Signaling Blockade Slows Medulloblastoma Progression." **Gate D**, Danielpour M, Rodriguez J, Levy R, Breunig JJ, Town, T. *ImmunologyLA*, Los Angeles, Ca, May 24th, 2012
3. "IRAK-M deletion promotes microglia-mediated cerebral amyloid clearance in PSAPP mice." **Gate D**, Masliah E, Rezai-Zadeh K, Town T. *Alzheimer's Association International Conference*, Vancouver, Canada, July 14th – 19th, 2012.
4. "IRAK-M deletion promotes microglia-mediated cerebral amyloid clearance in APP/PS1 mice." **Gate D**, Masliah E, Rezai-Zadeh K, Town T. *Advanced School on Neuroscience and Aging*, Venice, Italy, June 10th – 15th, 2013.
5. "IRAK-M deletion promotes microglia-mediated A β phagocytosis and improves cognition in PSAPP mice." **Gate D**, Rodriguez J, Leung B, Masliah E, Town T. *Alzheimer's Association International Conference*, Copenhagen, Denmark, July 12th – 17th, 2014.
6. "Immune involvement in Alzheimer's disease." **Gate D**. *Alzheimer's Association's Young Professionals Committee*, Los Angeles, Ca, January 14, 2015.
7. "IRAK-M removal endorses microglia-mediated amyloid phagocytosis and improves cognitive impairment in PSAPP mice." **Gate D**, Rodriguez J, Doty K, Leung B, Masliah E, Town T. *Alzheimer's Association International Conference*, Washington, D.C., USA, July 18th – 23rd, 2015.
8. "IRAK-M removal promotes microglia-mediated amyloid phagocytosis and improves cognitive impairment in PSAPP mice." **Gate D**, Rodriguez J, Doty K, Leung B, Masliah E, Town T. *12th International Conference AD/PD*, Nice, France, March 18th – 22nd, 2015.
9. "Microglial epigenetics in aging." **Gate D**. *14th Bay Area Aging Meeting*, Novato, Ca, March 30th, 2017.
10. "Clonally expanded CD8 T cells patrol Alzheimer's cerebrospinal fluid." **Gate D**. *Alzheimer's Researchers' Symposium (Young Investigator Award Presentation)*, Berkeley, Ca, September 17th, 2018.
11. "Clonally expanded CD8 T cells patrol Alzheimer's cerebrospinal fluid." **Gate D**, Saligrama N, Leventhal O, Yang AC, Middeldorp J, Chen K, Lehallier B, Channappa D, De Los Santos MB, McBride A, Pluvinage J, Elahi F, Tam G K-Y, Greicius M, Wagner AD, Galasko D, Davis MM, Wyss-Coray T. *14th International Conference AD/PD*, Lisbon, Portugal, March 26th – 31st, 2019.
12. "Clonally expanded CD8 T cells patrol Alzheimer's cerebrospinal fluid." **Gate D**, Saligrama N, Leventhal O, Yang AC, Middeldorp J, Chen K, Lehallier B, Channappa D, De Los Santos MB, McBride A, Pluvinage J, Elahi F, Tam G K-Y, Greicius M, Wagner AD, Galasko D, Davis MM, Wyss-Coray T. *14th International Conference AD/PD*, Lisbon, Portugal, March 26th – 31st, 2019. *Alzheimer's Association International Conference*, Los Angeles, Ca, USA, July 14th – 18th, 2019.

FUNDING

Diamond19023 (Gate)

Oct. 2019 – Sept. 2021

Irene Diamond Fund/AFAR Postdoctoral Transition Award in Aging

Antigen identification of clonally expanded T cells in aging cerebrospinal fluid

This highly competitive fellowship (given to only 7 postdoctoral fellows nationally) provides portable and flexible transitional funding for senior postdoctoral fellows as they develop and negotiate for junior faculty appointments and independent research programs. The aim of this study is to uncover a novel therapeutic target or biomarker for brain aging and/or Alzheimer's disease. In Specific Aim 1, T cell clonality and immunophenotyping of aged and AD CSF will be measured separately by sequencing TCRs and RNA of CSF immune cells. This approach will determine whether aged and/or AD CSF contains higher proportions of antigen-experienced, clonal T cells and will reveal their transcriptomic profile. In Specific Aim 2, antigen identification screens will be used to detect the antigen(s) driving T cell clonal expansion in aged/AD CSF.

1 F32 AG055255-01A1 (Gate)

Sept. 2018 – Sept. 2019

NIH/NINDS Ruth L. Kirchstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship

Reversing epigenetic changes in aged microglia via young circulatory factors

This work will determine whether epigenetic changes to the brain's immune cells (microglia) can be reversed in old mice exposed to young blood. Understanding the mechanism by which microglia undergo changes in gene expression with age will advance our knowledge of brain aging and may uncover novel therapeutic targets for neurodegeneration.

Mentor: Dr. Tony Wyss-Coray

Co-mentors: Dr. Thomas Rando, Dr. Anne Brunet (Stanford), Dr. Christopher Glass (UC San Diego)

PD15047 (Gate)

Nov. 2015 – Nov. 2016

Glenn/AFAR Postdoctoral Fellowship for Translational Research on Aging

Role of microglia in brain rejuvenation

This application will determine whether microglia contribute to the beneficial effects observed in old mice exposed to young rejuvenation factors. Understanding the mechanism by which the brain's immune cells contribute to brain rejuvenation will advance our knowledge of brain aging and may uncover novel therapeutic targets for neurodegeneration.

Mentor: Dr. Tony Wyss-Coray

1 F31 NS083339-01A1 (Gate)

Sept. 2013 – Sept. 2015

NIH/NINDS Ruth L. Kirchstein National Research Service Award (NRSA) Individual Predoctoral Fellowship

Targeting Abeta phagocytosis by blocking IRAK-M innate immunity in Alzheimer mice

The key goal of this project is to evaluate the role of genetic ablation of IRAK-M in innate immune cells in restricting the disease by phagocytic clearance of amyloid- β . These results could establish the importance of IRAK-M in Alzheimer's pathogenesis and further elucidate the role of innate immune cells in the disease.

Mentor: Dr. Terrence Town

Co-mentors: Dr. Eliezer Masliah (UC San Diego) and Dr. Greg Cole (UC Los Angeles)

HONORS AND AWARDS

Irene Diamond Fund/AFAR Postdoctoral Transition Award in Aging	2019 – 2021
Junior Faculty Award, AD/PD 2019 Congress	2019
ADRD Scholar, NIH NINDS/NIA ADRD Summit	2019
Ruth L. Kirchstein NRSA NIH/NIA Postdoctoral Fellowship	2018 – 2021
Young Investigator Award, Alzheimer's Association Bay Area	2018
Glenn/AFAR Postdoctoral Fellowship	2015
ISTAART Travel Award, Alzheimer's Association	2015
Harold M. Weintraub Graduate Student Award Nominee University of Southern California	2014
Young Investigator Award, Alzheimer's Association Los Angeles	2014
Zach Hall Travel Award – Zilkha Neurogenetic Institute University of Southern California, Los Angeles, CA	2014
Alzheimer's Association International Conference Travel Fellowship	2014
Spring Scholar Award University of Southern California, Los Angeles, CA	2014
Ruth L. Kirchstein NRSA NIH/NINDS Pre-doctoral Fellowship	2013 – 2015
Alzheimer's Association International Conference Travel Fellowship	2012
Excellence in Research Award, Department of Neurosurgery Cedars-Sinai Medical Center, Los Angeles, CA	2009
Undergraduate Research and Creative Activities Research Grant University of California at Santa Barbara, Santa Barbara, CA	2005 – 2007