HSING-CHEN TSAI, PH.D.
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Scientific and Biotech Leader - Drug Discovery, Preclinical & Translational Research

PROFILE

- Innovative, rigorous, and outcome-focused scientific leader with 15 years of industry experience in drug discovery and development and preclinical research, advancing 2 programs to IND filing and clinical development
- Extensive experience in scientific leadership and team management, research program development and management, strategic planning, risk mitigation, resource allocation, and cross-functional communication and coordination across biotechnology and pharmaceutical organizations ranging from startups to global enterprises
- Areas of expertise: neuroscience; cell and gene therapy; optogenetics; immunotherapy (antibody therapy, CAR-T therapy); hematopoietic/embryonic stem cell research; viral vector platform (AAV and LVV); translational animal models (mouse, rat, NHP); preclinical pharmacology (PK/PD, biomarker); IND-enabling studies

EDUCATION AND CERTIFICATIONS

- Google Project Management Professional Certificate – Anticipated Dec 2025
- Harvard Professional Certificate in Leadership and Communication – Anticipated Dec 2025
- Ph.D., Neuroscience, Stanford University – 2010
- M.S., Molecular Epidemiology, Harvard University – 2003

EXPERIENCE

Kelonia Therapeutics. Associate Director **2022–2025**

Head of *In Vivo* Pharmacology (IVP), Research Unit

- Key contributor to drug candidate nomination, selection, Pre-IND Meeting with FDA, and preclinical development of **KLN-1010 (inMMyCAR), an *in vivo* CAR-T therapy now in clinical trial for Refractory Multiple Myeloma**
- Mentored and developed a team of 6 *in vivo* scientists (3 direct reports) to establish new animal models, advance Kelonia's iGPS® platform, and **generate IND data package for KLN-1010**, including safety, efficacy, biodistribution, biomarker, and dose-finding studies using cell line-derived xenograft (CDX) models
- Oversaw the design and execution of 50+ *in vivo* studies by IVP team and CROs. Provided scientific guidance on data interpretation, presentation, and follow-up study design
- Planned and directed 18 IND-enabling studies to ensure full regulatory compliance, prepared documents for patent filling and regulatory submission, and served as **lead author of IND Module 4 Study Reports**
- Expanded IVP team by recruiting and onboarding 3 additional FTEs, doubling team size; implemented individualized training, streamlined workflows, and redefined roles to enhance productivity and adapt to company growth
- Served on a **4-person Research Leadership Team** meeting biweekly to develop scientific and operational strategies for generating proof-of-concept (POC) data to evaluate therapies, enabling candidate selection, understanding mechanism of action (MOA), and advancing projects while considering impact to FTEs, timelines, budgets, and risks

Cross-functional Study and CRO Manager, Research Unit and Non-clinical Development

- Directed resource allocation across multiple Research Programs and collaborated cross-functionally with Project Teams, CMC (Vector Core, Process Development, Analytical Development), Facilities, and CROs to ensure that projects are conducted timely and within budget with aligned project priorities, timelines, and quality deliverables
- Managed a 3-month **non-GLP toxicology and biodistribution nonhuman primate (NHP) study** from planning to completion in partnership with Non-clinical Development, CMC and Preclinical Research scientists, and external CROs
- Led cross-functional meetings with 12 stakeholders to finalize study design, developed study protocol with Head of Non-clinical Development and Charles River Laboratories, coordinated logistics and research activities spanning 6 months across 3 facilities
- Reviewed and analyzed data generated internally and externally for the NHP project to ensure data integrity; provided scientific feedback on data interpretation
- Managed 4 CROs, *all* in-house mouse studies, and 11 external *in vitro* and *in vivo* projects
- Collaborated with Facilities and external partners to design and establish an operational on-site vivarium, enhancing internal research capabilities

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Experience (continued 1)

bluebird bio, Inc. Senior Scientist / Senior Manager **2018–2022**
Senior Scientist / Senior Manager (2020–2022)
Scientist II / Manager (2018–2020)

Cross-functional Group Lead of bluebird bio's first *in vivo* gene therapy pipeline program

- Managed a cross-functional team of 8 Ph.D. and non-Ph.D. scientists to execute *in vitro* and *in vivo* studies to advance the pipeline program targeting an undisclosed ocular indication
- Developed research plan and program strategy from scratch, spearheaded program goals and a multi-year roadmap, assigned projects to team members, oversaw development of individual projects, and executed go/no-go decisions
- Assessed research platforms to screen and validate viral vector candidates; designed experiments using relevant *in vitro*, *ex vivo*, and *in vivo* models (e.g. mouse, canine, and NHP) for biodistribution, immunogenicity, and ocular tolerance studies
- Partnered with Business Development (BD) team to establish a program-specific Scientific Advisory Board (SAB) and conduct SAB meetings; refined research strategy and designed key decision-driving studies according to SAB feedback
- Led and coordinated research activities of external academic partners and CROs to generate supporting data for go/no-go decisions
- Worked closely with program manager and project stakeholders to develop timelines, communicate program objectives, determine resource allocation, prioritize project deliverables, track key milestones and inflection points, and develop risk mitigation strategies as program evolved

Set overall scientific strategy and research direction for Severe Genetic Disease Research Unit

- Conducted literature deep dives to identify key challenges and opportunities in developing disease-modifying gene therapies for 4 neurological indications. Evaluated external partnership opportunities and provided go/no-go recommendations to Research Leadership Team and Executive Team members
- Reviewed new research opportunities in 4 therapeutic areas (TAs)—neuroscience, autoimmune, ophthalmology, and hepatology—for BD partners. Collaborated with BD to compare across TAs to prioritize 9 disease indications and to develop a forward-looking research strategy leveraging lentiviral vector (LVV)-mediated gene therapy
- Results of these activities were key to launching **bluebird bio's first *in vivo* gene therapy pipeline program** targeting an undisclosed ocular indication in 2021

Program Lead for 2 distinct hematopoietic stem cell *ex vivo* gene therapy pipeline programs targeting rare diseases

- Supervised and trained 4 direct reports to perform *in vitro* and *ex vivo* experiments to characterize lentiviral drug products
- Led preclinical research effort to evaluate *in vivo* efficacy, safety, and efficiency of lentiviral gene therapy in alleviating enzyme deficiency, multi-organ abnormalities, and neurocognitive deficits in rodent models of lysosomal storage disorders
- Designed and executed 2 preclinical IND-enabling PharmTox studies in house. Directed 3 parallel preclinical research projects conducted by academic collaborators and CROs. (Published in Human Gene Therapy 2022)
- Analyzed, interpreted, and presented internal and external data to Research Leadership Team and authored 3 IND-enabling pharmacology study reports
- Collaborated with cross-functional teams to prepare documents for annual R&D portfolio reviews

Explored experimental approaches to better understand engraftment of bone marrow-derived cells into the CNS

- Identified and evaluated *in vitro* and *in vivo* assays to predict blood brain barrier (BBB) penetrance and appropriate mouse models for brain engraftment studies. Developed an exploratory research project to evaluate 3 endpoint technologies for analyzing donor cell engraftment in the CNS after experimental bone marrow transplantation

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Experience (continued 2)

Alector, Inc. Scientist II **2016–2018**
Scientist I (2016) | Scientist II (2017–2018)

Led AL002 antibody therapy evaluation in neurological disorders, advancing to clinical trials

- Led interdisciplinary team (5 Ph.D.-level scientists) to evaluate the therapeutic effect of lead antibodies in alleviating the cognitive deficits, brain pathology, and neuroinflammation observed in various rodent models of neurological conditions including traumatic brain injury (TBI), neurodegenerative disease, and neuroinflammatory disease
- Analyzed samples and experimental data/results collected by CROs and academic partners to evaluate the activities of antibodies, investigate their MOA and efficacy, and explore novel therapeutic hypotheses
- Results of these research contracts/projects were key to **Alector-AbbVie partnership** announced in October 2017 and **Clinical Trial INVOKE for Alzheimer's Disease** in November 2018

Oversaw *in vivo* translational work

- Designed and executed large and complex *in vivo* POC studies to support all pipeline programs
- Provided guidance on *in vivo* animal model selection, behavioral phenotyping, and CNS-targeted drug delivery
- Enabled drug target identification and validation by establishing a core neuroscience lab equipped with stereotaxic surgery suite, histopathology suite, cryostat, microtome, light and fluorescence/confocal microscopes, and automated slide scanner.
- Developed SOPs, wrote IACUC protocols, and provided company-wide workshops and individualized trainings
- Sought and implemented new technologies and research platforms suitable for antibody lead selection, biomarker assay development, and POC studies
- Designed and performed key *in vitro* and *in vivo* experiments and neurological behavioral analyses for all discovery programs to identify putative targets of Alector's proprietary immunomodulatory antibodies and enable go/no-go decisions

Liaison to internal and external stakeholders

- Identified, evaluated, and recommended CROs and academic labs to the CEO for exploratory research projects
- Represented Alector and served as the key technical contact on research contracts and projects requiring cross-functional coordination inside and outside of the company
- Established collaborations with 3 academic labs and designed 9 exploratory research projects to investigate Alector's novel biotherapeutic approaches against neurodegeneration and neuroinflammation
- Successfully managed a network of 6 CROs across US and Europe to design and implement 12 large and complex *in vivo* studies on Alector's proprietary antibodies

Pfizer, Inc. Postdoctoral Scientist, Neuroscience Research Unit (Mike Ehlers Lab) **2011–2015**

Subject matter expert in optogenetics

- Established and integrated an optogenetic research platform with Pfizer's preclinical platforms such as electrophysiology, pharmacology, and behavioral assays, enabling identification of novel therapeutic targets for CNS diseases
- Collaborated with academic partners at MIT to engineer and optimize novel opsins (i.e. optogenetic actuators) for dissecting clinically meaningful neural circuits involved in various neurological and psychiatric diseases
- Independently investigated dopaminergic (DA) modulation of brain cognition functions and its relevance to normal aging and schizophrenia by using a systemic and multidisciplinary optogenetic approach

Animal model development and characterization

- Developed and implemented various rodent behavioral paradigms for evaluating cognitive functions, motivation, locomotor activity and exploratory behavior to facilitate preclinical drug candidate selection and mouse disease model characterization

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Experience (continued 3)

Stanford University. Bio-X Neuroscience Fellow / Ph.D. Candidate (Karl Deisseroth Lab) 2005–2010

Optogenetic investigation of neural circuits underlying brain reward processing in animal models

- Designed and developed molecular optogenetic tools (i.e. genetically targetable optical neural activator and inhibitor) to identify and map the neural networks underlying brain functions. (Published by Cold Spring Harbor Laboratory Press 2011*) (* co-first author)
- Investigated the causal role of midbrain DA neuron activity in reward processing and learning in various rodent models of depression and drug addiction by using viral (AAV and LVV), optogenetic, biochemical, electrophysiological, pharmacological, and behavioral techniques
- Results of these research projects provided the first direct evidence to demonstrate the sufficiency of phasic DA neuron firing in shaping reward- and depression-related behaviors. (Published in Science 2009*; Journal of Neuroscience 2011*; Nature 2013; Nature 2013) (* co-first author)

Optogenetic modulation of neuronal differentiation of mouse embryonic stem cell (ESC)

- Developed a novel high-throughput system for the chronic optical stimulation and imaging of *in vitro* stem cell differentiation
- Created mouse ESC lines expressing light-sensitive protein, Channelrhodopsin-2 (ChR2). Optically stimulated ChR2-expressing ESCs using an automated microscope with laser paradigm system to induce neuronal differentiation. (Published in Stem Cells 2011*) (* co-first author)

Stanford Bio-X NeuroVentures Optogenetics Innovation Laboratory (OIL) instructor

- Taught and helped design a 3-week summer workshop on optogenetics for international visiting scholars
- Trained 4 Ph.D.-level scientists to perform optogenetic experiments, including virus production, survival stereotaxic surgery for cannula implantation and virus injection, confirmation of transgene expression, confocal microscopy, *in vivo* extracellular optrode recording in anesthetized rodents, and optical stimulation for behavioral testing

McLean Hospital. Research Associate in Psychiatry (Kwang-Soo Kim Lab) 2003–2005

Differentiation of ESCs into DA neurons for cell transplantation therapy in Parkinson's disease (PD)

- Optimized the protocol for differentiation of ESCs to the DA cell fate by combining genetic manipulation and *in vitro* cell culture conditions. Successfully transplanted differentiated DA cells into an *in vivo* mouse model of PD. (Published in Stem Cells 2006)

EARLIER EXPERIENCE

Chang Gung Memorial Hospital. Research Assistant (Jau-Song Yu Lab and Jeng-Shu Wei Lab)

- Identified an intracellular nitric oxide (NO) signal transduction pathway induced by the oncogene, latent membrane protein 1 (LMP1) of Epstein-Barr virus (EBV). Demonstrated a key role of this signaling pathway in LMP1-mediated *in vitro* cloning efficiency (in culture) and *in vivo* tumor growth (in nude mice). (Published in Oncogene 2002)
- Established an effective and reliable ELISA protocol for the detection of polyamines in human serum. Demonstrated the potential of polyamines as nonspecific, tissue-associated tumor biomarkers for clinical applications

TECHNICAL SKILLS

Molecular cloning, qRT-PCR, western blot, plate-based immunoassays (ELISA, MSD), flow cytometry, histology, immunohistochemistry (IHC), light and fluorescence/confocal microscopy, quantitative image analysis, cell and tissue culture, adeno-associated virus (AAV) and lentivirus vector (LVV) transduction, mouse handling/dosing/necropsy techniques, stereotaxic surgery, behavioral phenotyping, small and large animal models, optogenetic and pharmacological modulation of neural circuits, *ex vivo* and *in vivo* lentiviral gene therapy

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PUBLICATIONS

Smith MC, Belur LR, Karlen AD, Erlanson O, Podetz-Pedersen KM, McKenzie J, Detellis J, Gagnidze K, Parsons G, Robinson N, Labarre S, Shah S, Furcich J, Lund TC, **Tsai HC**, McIvor RS, Bonner M. Phenotypic correction of murine mucopolysaccharidosis type II by engraftment of ex vivo lentiviral vector transduced hematopoietic stem and progenitor cells. **Human Gene Therapy**, Oct 13; 24(33):23-24. 2022 (**19 citations**)

Tye KM, Mirzabekov JJ, Warden MR, Ferenczi EA, **Tsai HC**, Finkelstein J, Kim SY, Adhikari A, Thompson KR, Andalman A, Gunaydin LA, Witten IB, Deisseroth K. Dopamine neurons modulate neural encoding and expression of depression-related behavior. **Nature**, Jan 24; 493(7433):537-41, 2013 (**1217 citations**)

Chaudhury D, Walsh JJ, Friedman AK, Juarez B, Ku SM, Koo JW, Ferguson D, **Tsai HC**, Pomeranz L, Christoffel DJ, Nectow AR, Ekstrand M, Domingos A, Mazie-Robison M, Mouzon E, Lobo MK, Neve RL, Friedman JM, Russo SJ, Deisseroth K, Nestler EJ, Han MH. Rapid regulation of depression-related behaviors by control of midbrain dopamine neurons. **Nature**, Jan 24; 493(7433):532-6, 2013 *Faculty 1000 "Exceptional" Article* (**1338 citations**)

*Stroh A, ***Tsai HC**, *Wang LP, Zhang F, Kressel J, Aravanis A, Santhanam N, Deisseroth K, Konnerth A, Schneider MB. Tracking stem cell differentiation in the setting of automated optogenetic stimulation. (* co-first authors) **Stem Cells**, Jan; 29(1):78-88, 2011 *Faculty 1000 "Recommended" Article* (**123 citations**)

*Zhang F, ***Tsai HC**, Airan RD, Stuber G, Adamantidis A, de Lecea L, Bonci A, Deisseroth K. Optogenetics in freely moving mammals: dopamine and reward. (* co-first authors) In: **Imaging in Neuroscience: A Laboratory Manual (1st ed.)**, New York: Cold Spring Harbor Laboratory Press 2011 (**Invited book chapter**) (**25 citations**)

*Adamantidis A, ***Tsai HC**, Boutrel B, Zhang F, Stuber G, Budygin E, Tourino C, Bonci A, Deisseroth K, de Lecea L. Optogenetic interrogation of dopaminergic modulation of the multiple phases of reward-seeking behavior. (* co-first authors) **Journal of Neuroscience**, Jul 27; 31(30):10829-35, 2011 *Faculty 1000 "Must Read" Article* (**478 citations**)

***Tsai HC**, *Zhang F, Adamantidis A, Stuber G, Bonci A, de Lecea L, Deisseroth K. Phasic firing in dopaminergic neurons is sufficient for behavioral conditioning. (* co-first authors) **Science**, Apr 23; 324(5930):1080-84, 2009 *Faculty 1000 "Exceptional" Article* (**1611 citations**)

Kim DW, Chung S, Hwang M, Ferree A, **Tsai HC**, Park JJ, Chung S, Nam TS, Kang UJ, Isacson O, Kim KS. Stromal cell-derived inducing activity (SDIA), Nurr1, and signaling molecules synergistically induce dopaminergic neurons from mouse embryonic stem cells. **Stem Cells**, Mar 24(3):557-67, 2006 (**120 citations**)

Yu JS, **Tsai HC**, Wu CC, Weng LP, Chung PJ, Chang YS. Induction of inducible nitric oxide synthase by Epstein-Barr virus B95-8-derived LMP1 in Balb/3T3 cells promotes stress-induced cell death and impairs LMP1-mediated transformation. **Oncogene**, Nov 14; 21(52):8047-61, 2002 (**33 citations**)