BIOGRAPHICAL SKETCH

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NAME: Tianyu Cao

eRA COMMONS USER NAME: Tianyu

POSITION TITLE: Postdoctoral Fellow

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Beijing University of Chinese Medicine	BM	09/2013	06/2018	Medicine
Beijing University of Chinese Medicine	MD and residency	09/2018	06/2023	Clinical Science of Integrative Medicine
Johns Hopkins University	Trainee	05/2019	08/2021	Pathology
Johns Hopkins University	Postdoctoral Fellow	09/2023	Present	Pathology

A. Personal Statement

My academic and clinical training have shaped a unique path into the study of neurodegeneration. I received my medical degree from Beijing University of Chinese Medicine, where I trained as a neurologist with a focus on neurodegenerative diseases. Under the mentorship of Prof. Jinzhou Tian, I led meta-analyses evaluating the efficacy of Chinese medicine and acupuncture in dementia, and applied data mining to understand classical prescribing patterns[1-4]. My graduate research shifted toward amyotrophic lateral sclerosis (ALS), including a five-year prospective clinical cohort study under Prof. Dongsheng Fan, which revealed early non-motor features as potential predictors of disease progression. These experiences laid the foundation for my long-term commitment to developing disease-modifying therapies for ALS and frontotemporal dementia (FTD).

As a neurologist in training, I became acutely aware that most neurodegenerative diseases including ALS and FTD lack any mechanism based curative treatment. This recognition motivated me to pursue the molecular mechanisms underlying these diseases and to explore rational therapeutic strategies. During my postdoctoral training in Dr. Philip Wong's lab at Johns Hopkins University, I have pursued multiple lines of inquiry into the molecular pathology of neurodegeneration. My research has explored how TDP-43 loss of function leads to cryptic exon activation, how circlopriox olamine(CPO) exposure triggers cryptic exon inclusion, and how TDP-43 dysfunction activates caspase-3 and contributes to tau cleavage and aggregation[5]. In parallel, I have studied the bidirectional interactions between tau and α-synuclein, as well as their convergence with TDP-43 pathology in multi-proteinopathy models.

A major focus of my work is developing therapeutic strategies to restore TDP-43 function, using a chimeric therapeutic protein, CTR, that restores cryptic exon repression without the aggregation risk of full-length TDP-43. In a mouse model that lack TDP-43 in the forebrain neurons, I demonstrated that intracerebroventricular delivery of AAV-PHP.eB–CTR achieves ~40% hippocampal neuronal transduction and ~30% rescue of CA2/3 neurons at 12 months. CTR also restored social behavior and repressed cryptic exons such as *Unc13a,* while maintaining autoregulatory safety via the *TARDBP* 3′ UTR[6]. These results support CTR as a clinically promising therapeutic. To enable human-compatible delivery, I am now testing CTR with the BI-hTFR1 AAV capsid and TFRC knock-in mice, which allow transferrin receptor mediated systemic CNS biodistribution of CTR. This project represents a critical step in translating CTR from proof-of-concept to therapeutic candidate.

My long-term goal is to become an independent investigator developing splicing-based therapies for TDP-43–related neurodegeneration. I aim to translate TDP-43 repressor strategies into clinically viable treatments while uncovering how its dysfunction intersects with tau and α-synuclein pathology.

1. **Tianyu Cao**, Yuou Teng, Xuan Yao, Jing Shi, Jingnian Ni, Jinzhou Tian. Efficacy and safety of butylphthalide soft capsule in the treatment of vascular dementia: a meta-analysis. *Chin J Evid-Based Med*. 2020;20(04):444-452. doi:10.7507/1672-2531.201907060
2. Yuou Teng, Jing Shi, **Tianyu Cao**, Xuan Yao, Jingnian Ni, Jinzhou Tian. Efficacy and safety of butylphthalide soft capsule in the treatment of Alzheimer's disease: a meta-analysis. *Chin J Evid-Based Med*. 2019;19(12):1446-1452. doi:10.7507/1672-2531.201904115

3. **Tianyu Cao**, Yuou Teng, Yudi Zhuo, Junyi Ren, Ruijia Liu, Jinzhou Tian. Discussion on prescription and medication rules of Chinese medicine treating amyotrophic lateral sclerosis related atrophy disease in ancient books based on data mining. *Glob Tradit Chin Med*. 2020;13(06):986-992. doi:10.3969/j.issn.1674-1749.2020.06.008

4. Zhao C, **Cao T,** Zhou M, Tian J. Research on acupoint selection and prescription rules for acupuncture treatment of vascular cognitive impairment based on data mining. *Shanghai J Tradit Chin Med*. 2020;54(08):31-36. doi:10.16305/j.1007-1334.2020.08.000

5. Baghel MS, Burns GD, Tsapatsis M, et al. Depletion of TDP-43 exacerbates tauopathy-dependent brain atrophy by sensitizing vulnerable neurons to caspase 3-mediated endoproteolysis of tau in a mouse model of Multiple Etiology Dementia. *bioRxiv*. Published online June 29, 2024:2024.06.26.600814. doi:10.1101/2024.06.26.600814

6. **Cao T**, Thapa R, Liu R, et al. Broad brain biodistribution conferred by an AAV to restore TDP-43 function mitigates Frontotemporal Demenia-like deficits. *bioRxiv*. Preprint posted online September 2, 2025:2025.08.28.672900. doi:10.1101/2025.08.28.672900

B. Positions, Scientific Appointments and Honors

2023- Present Postdoctoral Researcher, Johns Hopkins University
2023- Present Member, Society for Neuroscience
2024- Present Member, American Society of Gene+Cell Therapy

Honors

2024 Baltimore Brain Series Award
2023 Excellent doctoral thesis, Beijing University of Chinese Medicine
2020 Winner in the Basic research category in Pathology Young Investigators' Day 2020 (poster and presentation), Johns Hopkins University
2020 The first prize of Data Analysis and Modeling Competition, Beijing University of Chinese Medicine
2019 The major award scholarship, Beijing University of Chinese Medicine
2019 Funding: Basic scientific research business expenses, Beijing University of Chinese Medicine

C. Contributions to Science

Early career: My undergraduate research was pioneering in integrating traditional Chinese medicine (TCM) with evidence-based medical practices. By conducting comprehensive meta-analyses, I assessed the efficacy and safety of TCM extracts and acupuncture in treating dementia and other neurological diseases. Taking advantage of these evidence, I also took part in writing the China's guidelines for dementia and pushed my findings to advice in the clinic. This work not only contributed to the scientific understanding of alternative treatments but also highlighted the potential of TCM as a complement to conventional medicine in neurology.

a. Yuou Teng, Jing Shi, **Tianyu Cao**, Xuan Yao, Jingnian Ni, Jinzhou Tian. Efficacy and safety of butylphthalide soft capsule in the treatment of Alzheimer's disease: a meta-analysis. *Chin J Evid-Based Med*. 2019;19(12):1446-1452. doi:10.7507/1672-2531.201904115

Graduate career: During my graduate studies, I led a longitudinal cohort study that provided invaluable insights into the clinical symptomatology of ALS. My findings revealed that ALS patients exhibit significant non-motor symptoms, some of which may serve as early indicators of rapid disease progression. This contribution is crucial for the early diagnosis and management of ALS, offering a new perspective on the disease's complexity and heterogeneity.

Postdoctoral career: My postdoctoral research at Johns Hopkins University focuses on developing a translational therapy for TDP-43 loss of function. I contributed to the design and validation of a chimeric splicing repressor (CTR), which restores cryptic exon repression in neurons lacking TDP-43. In CamKIIa-CreER;Tardbp$^{f/f}$ mice, I showed that AAV-CTR delivery rescues neuronal loss, restores behavior, and maintains autoregulatory safety. I am now extending this work by evaluating systemic, human-compatible CTR delivery using a transferrin receptor–targeted AAV in TFRC knock-in mice.

b. **Cao T**, Thapa R, Liu R, et al. Broad brain biodistribution conferred by an AAV to restore TDP-43 function mitigates Frontotemporal Demenia-like deficits. bioRxiv. Preprint posted online September 2, 2025:2025.08.28.672900. doi:10.1101/2025.08.28.672900

Complete List of Published Work in My Bibliography:
https://scholar.google.com/citations?view_op=list_works&hl=zh-CN&hl=zh-CN&user=JfIynKUAAAAJ

D. Scholastic Performance

YEAR	COURSE TITLE	GRADE
	BEIJING UNIVERSITY OF CHINESE MEDICINE	
2014	Medical Biology	P
2014	Anatomy of the Human Body	P
2014	Medical Genetics	P
2014	Cytobiology	P
2014	Histology and Embryology	P
2015	Developmental Biology	P
2015	Biochemistry	P
2015	Media Ethics	P
2015	Medical Statistics	P
2015	Genetics and Genomics	P
2015	Physiology	P
2015	Pharmacology	P
2015	Pathology	P
2015	Medical Psychology	P
2016	Fundamentals of Diagnostics	P
2016	Neurology	P
2017	Surgery	P
2017	Internal medicine (including infectious Diseases)	P
2018	Clinical epidemiology	P
2018	Clinical practice methodology	P
2018	Neuroanatomy	P
2018	Laboratory safety knowledge	P