Stanford

# Heng Zhao

Professor (Research) of Neurosurgery

Curriculum Vitae available Online  Resume available Online

## Bio

### ACADEMIC APPOINTMENTS

- Professor (Research), Neurosurgery
- Member, Bio-X
- Member, Wu Tsai Neurosciences Institute

### PROFESSIONAL EDUCATION

- PhD, Nihon University, Japan , Pharmacology (1999)
- MS, West China Univ. Med. Sci. , Pharmacognosy (1990)
- BS, West China Univ. Med. Sci. , Pharmacy (1987)

## Research & Scholarship

### CURRENT RESEARCH AND SCHOLARLY INTERESTS

My lab mainly studies the protective effect of postconditioning against stroke. Reperfusion (the restoration of blood flow) is one of the first choices for ischemic stroke treatment. However, reperfusion can also cause overproduction of reactive oxygen species (ROS) or free radicals that lead to reperfusion injury. Limiting the damage caused by reperfusion is a key issue for stroke treatment. We were the first to demonstrate that interrupting the early hyperemic response after reperfusion reduces infarction after stroke, a novel phenomenon called postconditioning. Since postconditioning is performed after reperfusion, it has great potential for clinical application. In addition, we also study protective effect of preconditioning and mild hypothermia. The rationale for studying three means of neuroprotection is that we may discover mechanisms that these treatments have in common. Conversely, if they have differing mechanisms, we will be able to offer more than one treatment for stroke and increase a patient’s chance for recovery. Our researches include studying roles of caspase-dependent and independent apoptotic pathway, PKC pathways and Akt pathway, among others, in the ischemic damage development after stroke.

## Teaching

### COURSES

**2019-20**

- Experimental Stroke: NSUR 70Q (Win)

**2018-19**

- Experimental Stroke: NSUR 70Q (Win)

**2017-18**

- Experimental Stroke: NSUR 70Q (Win)

### STANFORD ADVISEES

**Postdoctoral Faculty Sponsor**

Hansen Chen

### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Neurosciences (Phd Program)

## Publications

### PUBLICATIONS

- **Distinctive Effects of T Cell Subsets in Neuronal Injury Induced by Cocultured Splenocytes In Vitro and by In Vivo Stroke in Mice** *STROKE*
  Gu, L., Xiong, X., Zhang, H., Xu, B., Steinberg, G. K., Zhao, H.
  2012; 43 (7): 1941-1946

- **The Akt signaling pathway contributes to postconditioning's protection against stroke; the protection is associated with the MAPK and PKC pathways** *JOURNAL OF NEUROCHEMISTRY*
  Gao, X., Zhang, H., Takahashi, T., Hsieh, J., Liao, J., Steinberg, G. K., Zhao, H.
  2008; 105 (3): 943-955

- **Limb remote-preconditioning protects against focal ischemia in rats and contradicts the dogma of therapeutic time windows for preconditioning** *NEUROSCIENCE*
  Ren, C., Gao, X., Steinberg, G. K., Zhao, H.
  2008; 151 (4): 1099-1103

- **Delayed postconditioning protects against focal ischemic brain injury in rats** *PLoS ONE*
  Ren, C., Gao, X, Niu, G, Yan, Z, Chen, X, Zhao, H
  2008

- **Interrupting reperfusion as a stroke therapy: ischemic postconditioning reduces infarct size after focal ischemia in rats** *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*
  Zhao, H., Sapolsky, R. M., Steinberg, G. K.
  2006; 26 (9): 1114-1121

- **Akt contributes to neuroprotection by hypothermia against cerebral ischemia in rats** *JOURNAL OF NEUROSCIENCE*
  Zhao, H., Shimohata, T., Wang, J. Q., Sun, G. H., Schaal, D. W., Sapolsky, R. M., Steinberg, G. K.
  2005; 25 (42): 9794-9806

- **Ischemic post-conditioning facilitates brain recovery after stroke by promoting Akt/mTOR activity in nude rats** *JOURNAL OF NEUROCHEMISTRY*
  Xie, R., Wang, P., Ji, X., Zhao, H.
  2013; 127 (5): 723-732

- **T Cells Contribute to Stroke-Induced Lymphopenia in Rats** *PLOS ONE*
  Gu, L., Xiong, X., Wei, D., Gao, X., Krams, S., Zhao, H.
  2013; 8 (3)

- **Hurdles to Clear Before Clinical Translation of Ischemic Postconditioning Against Stroke** *TRANSLATIONAL STROKE RESEARCH*
  Zhao, H.
  2013; 4 (1): 63-70

- **The protective effects of T cell deficiency against brain injury are ischemic model-dependent in rats** *NEUROCHEMISTRY INTERNATIONAL*
  Xiong, X., Gu, L., Zhang, H., Xu, B., Zhu, S., Zhao, H.
  2013; 62 (3): 265-270

- **Using hormetic strategies to improve ischemic preconditioning and postconditioning against stroke.** *International journal of physiology, pathophysiology and pharmacology*
  Zhao, H., Joo, S., Xie, W., Ji, X.
  2013; 5 (2): 61-72

- **Lithium Treatment Reduces Brain Injury Induced by Focal Ischemia with Partial Reperfusion and the Protective Mechanisms Dispute the Importance of Akt Activity** *AGING AND DISEASE*
  Takahashi, T., Steinberg, G. K., Zhao, H.
  2012; 3 (3): 226-233

- **PHOSPHORYLATED MITOGEN-ACTIVATED PROTEIN KINASE/EXTRACELLULAR SIGNAL-REGULATED KINASE 1/2 MAY NOT ALWAYS REPRESENT ITS KINASE ACTIVITY IN A RAT MODEL OF FOCAL CEREBRAL ISCHEMIA WITH OR WITHOUT ISCHEMIC PRECONDITIONING** *NEUROSCIENCE*
  Takahashi, T., Steinberg, G. K., Zhao, H.
  2012; 209: 155-160

- **Prokineticin 2 is an endangering mediator of cerebral ischemic injury** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Cheng, M. Y., Lee, A. G., Culbertson, C., Sun, G., Talati, R. K., Manley, N. C., Li, X., Zhao, H., Lyons, D. M., Zhou, Q., Steinberg, G. K., Sapolsky, R. M.
  2012; 109 (14): 5475-5480

- **The Chronic Protective Effects of Limb Remote Preconditioning and the Underlying Mechanisms Involved in Inflammatory Factors in Rat Stroke** *PLOS ONE*
  Wei, D., Ren, C., Chen, X., Zhao, H.
  2012; 7 (2)

- **From rapid to delayed and remote postconditioning: the evolving concept of ischemic postconditioning in brain ischemia.** *Current drug targets*
  Zhao, H., Ren, C., Chen, X., Shen, J.
  2012; 13 (2): 173-187

- **An Insult-Inducible Vector System Activated by Hypoxia and Oxidative Stress for Neuronal Gene Therapy** *TRANSLATIONAL STROKE RESEARCH*
  Cheng, M. Y., Lee, I., Jin, M., Sun, G., Zhao, H., Steinberg, G. K., Sapolsky, R. M.
  2011; 2 (1): 92-100

- **The Protective Effects of Ischemic Postconditioning against Stroke: From Rapid to Delayed and Remote Postconditioning.** *The open drug discovery journal*
  Zhao, H. n.
  2011; 5: 138–47

- **Limited Therapeutic Time Windows of Mild-to-Moderate Hypothermia in a Focal Ischemia Model in Rat.** *Stroke research and treatment*
  Zhao, H., Steinberg, G.
  2011; 2011: 131834-?

- **The Akt Pathway Is Involved in Rapid Ischemic Tolerance in Focal Ischemia in Rats** *TRANSLATIONAL STROKE RESEARCH*
  Gao, X., Zhang, H., Steinberg, G., Zhao, H.
  2010; 1 (3): 202-209

- **Limb remote ischemic postconditioning protects against focal ischemia in rats** *BRAIN RESEARCH*
  Ren, C., Yan, Z., Wei, D., Gao, X., Chen, X., Zhao, H.
  2009; 1288: 88-94

- **The protective effect of early hypothermia on PTEN phosphorylation correlates with free radical inhibition in rat stroke** *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*
  Lee, S. M., Zhao, H., Maier, C. M., Steinberg, G. K.
  2009; 29 (9): 1589-1600

- **Ischemic postconditioning as a novel avenue to protect against brain injury after stroke** *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*
  Zhao, H.
  2009; 29 (5): 873-885

- **Activating delta PKC antagonizes the protective effect of ERK1/2 inhibition against stroke in rats** *BRAIN RESEARCH*
  Castaneda, D., Zhao, H., Mochly-Rosen, D., Steinberg, G. K.
  2009; 1251: 256-261

- **Improving Tumor-Targeting Capability and Pharmacokinetics of Tc-99m-Labeled Cyclic RGD Dimers with PEG(4) Linkers** *MOLECULAR PHARMACEUTICS*
  Wang, L., Shi, J., Kim, Y., Zhai, S., Jia, B., Zhao, H., Liu, Z., Wang, F., Chen, X., Liu, S.

2009; 6 (1): 231-245

- **Blocking glucocorticoid and enhancing estrogenic genomic signaling protects against cerebral ischemia** *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*
  Cheng, M. Y., Sun, G., Jin, M., Zhao, H., Steinberg, G. K., Sapolsky, R. M.
  2009; 29 (1): 130-136
- **Positron Emission Tomography Imaging of Poststroke Angiogenesis** *STROKE*
  Cai, W., Guzman, R., Hsu, A. R., Wang, H., Chen, K., Sun, G., Gera, A., Choi, R., Bliss, T., He, L., Li, Z., Maag, A. D., Hori, et al
  2009; 40 (1): 270-277
- **Delayed Postconditioning Protects against Focal Ischemic Brain Injury in Rats** *PLOS ONE*
  Ren, C., Gao, X., Niu, G., Yan, Z., Chen, X., Zhao, H.
  2008; 3 (12)
- **Protective effects of ischemic postconditioning compared with gradual reperfusion or preconditioning** *JOURNAL OF NEUROSCIENCE RESEARCH*
  Gao, X., Ren, C., Zhao, H.
  2008; 86 (11): 2505-2511
- **Dual roles of the MAPK/ERK1/2 cell signaling pathway after stroke** *JOURNAL OF NEUROSCIENCE RESEARCH*
  Sawe, N., Steinberg, G., Zhao, H.
  2008; 86 (8): 1659-1669
- **Inhibiting caspase-3 activity blocks beta-catenin degradation after focal ischemia in rat** *NEUROREPORT*
  Zhang, H., Gao, X., Yan, Z., Ren, C., Shimohata, T., Steinberg, G. K., Zhao, H.
  2008; 19 (8): 821-824
- **Synthesis of a potent and selective F-18-Labeled delta-opioid receptor antagonist derived from the Dmt-Tic pharmacophore for positron emission tomography imaging** *JOURNAL OF MEDICINAL CHEMISTRY*
  Ryu, E. K., Wu, Z., Chen, K., Lazarus, L. H., Marczak, E. D., Sasaki, Y., Ambo, A., Salvadori, S., Ren, C., Zhao, H., Balboni, G., Chen, X.
  2008; 51 (6): 1817-1823
- **Molecular imaging as the main part of our decision-making and treatment strategies in stroke** *FRONTIERS IN BIOSCIENCE-LANDMARK*
  Kashefi, A., Zhao, H., Chen, X.
  2008; 13: 1535-1556
- **Hypothermia blocks β-catenin degradation after focal Ischemia in rat, Brian Research** *Brain Research*
  Zhang, H., Ren, C, Gao, X, Takahashi, T, Sapolsky, RM, Steinberg, GK , Zhao, H
  2008: 182-7
- **The protective effect of ischemic postconditioning against ischemic injury: From the heart to the brain** *JOURNAL OF NEUROIMMUNE PHARMACOLOGY*
  Zhao, H.
  2007; 2 (4): 313-318
- **General versus specific actions of mild-moderate hypothermia in attenuating cerebral ischemic damage** *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*
  Zhao, H., Steinberg, G. K., Sapolsky, R. M.
  2007; 27 (12): 1879-1894
- **Viral caspase inhibitor p35, but not crmA, is neuroprotective in the ischemic penumbra following experimental stroke** *NEUROSCIENCE*
  Sung, J. H., Zhao, H., Roy, M., Sapolsky, R. M., Steinberg, G. K.
  2007; 149 (4): 804-812
- **Suppression of delta PKC activation after focal cerebral ischemia contributes to the protective effect of hypothermia** *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*
  Shimohata, T., Zhao, H., Sung, J. H., Sun, G., Mochly-Rosen, D., Steinberg, G. K.
  2007; 27 (8): 1463-1475
- **epsilon PKC may contribute to the protective effect of hypothermia in a rat focal cerebral ischemia model** *STROKE*
  Shimohata, T., Zhao, H., Steinberg, G. K.
  2007; 38 (2): 375-380

- **Gene therapy using SOD1 protects striatal neurons from experimental stroke** *NEUROSCIENCE LETTERS*
  Davis, A. S., Zhao, H., Sun, G. H., Sapolsky, R. M., Steinberg, G. K.
  2007; 411 (1): 32-36

- **Conditions of protection by hypothermia and effects on apoptotic pathways in a model of permanent middle cerebral artery occlusion** *Journal of Neurosurgery*
  Zhao, H., Wang, J, Shimohata, T, Sun, G, Yenari, MA, Sapolsky R.M, Steinberg, G.K
  2007; 107 (3): 636-41

- **Phosphoinositide-3-kinase/Akt survival signal pathways are implicated in neuronal survival after stroke** *MOLECULAR NEUROBIOLOGY*
  Zhao, H., Sapolsky, R. M., Steinberg, G. K.
  2006; 34 (3): 249-269

- **Hypothermia blocks ischemic changes in ubiquitin distribution and levels following stroke** *NEUROREPORT*
  Liu, J., Zhao, H., Sung, J., Sun, G., Steinberg, G. K.
  2006; 17 (16): 1691-1695

- **Biphasic cytochrome c release after transient global ischemia and its inhibition by hypothermia** *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*
  Zhao, H., Yenari, M. A., Cheng, D., Sapolsky, R. M., Steinberg, G. K.
  2005; 25 (9): 1119-1129

- **Chaperones, protein aggregation, and brain protection from hypoxic/ischemic injury** *JOURNAL OF EXPERIMENTAL BIOLOGY*
  Giffard, R. G., Xu, L. J., Heng, Z., Carrico, W., Ouyang, Y. B., Qiao, Y. L., Sapolsky, R., Steinberg, G., Hu, B. R., Yenari, M. A.
  2004; 207 (18): 3213-3220

- **Glycogen synthase kinase 3 beta inhibitor Chir025 reduces neuronal death resulting from oxygen-glucose deprivation, glutamate excitotoxicity, and cerebral ischemia** *EXPERIMENTAL NEUROLOGY*
  Kelly, S., Zhao, H., Sun, G. H., Cheng, D. Y., Qiao, Y. L., Luo, J., Martin, K., Steinberg, G. K., Harrison, S. D., Yenari, M. A.
  2004; 188 (2): 378-386

- **Bcl-2 transfection via herpes simplex virus blocks apoptosis-inducing factor translocation after focal ischemia in the rat** *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*
  Zhao, H., Yenari, M. A., Cheng, D., Barreto-Chang, O. L., Sapolsky, R. M., Steinberg, G. K.
  2004; 24 (6): 681-692

- **Catalase over-expression protects striatal neurons from transient focal cerebral ischemia** *NEUROREPORT*
  Gu, W. P., Zhao, H., Yenari, M. A., Sapolsky, R. M., Steinberg, G. K.
  2004; 15 (3): 413-416

- **Mild postischemic hypothermia prolongs the time window for gene therapy by inhibiting cytochrome C release** *STROKE*
  Zhao, H., Yenari, M. A., Sapolsky, R. M., Steinberg, G. K.
  2004; 35 (2): 572-577

- **Cellular and molecular events underlying ischemia-induced neuronal apoptosis** *DRUG NEWS & PERSPECTIVES*
  Zheng, Z., Zhao, H., Steinberg, G. K., Yenari, A. A.
  2003; 16 (8): 497-503

- **Bcl-2 overexpression protects against neuron loss within the ischemic margin following experimental stroke and inhibits cytochrome c translocation and caspase-3 activity** *JOURNAL OF NEUROCHEMISTRY*
  Zhao, H., Yenari, M. A., Cheng, D. Y., Sapolsky, R. M., Steinberg, G. K.
  2003; 85 (4): 1026-1036

- **Prospects for the treatment of stroke using gene therapy.** *Expert review of neurotherapeutics*
  Zhao, H., Yenari, M. A., Sapolsky, R. M., Steinberg, G. K.
  2003; 3 (3): 357-372

- **Prospects for the treatment of stroke using gene therapy** *Expert Rev. Neurotherapeutics*
  Zhao, H., Yenari, M. A., Sapolsky, R. M., Steinberg, G.K
  2003; 3 (3): 357-372

- **Gene therapy and hypothermia for stroke treatment** *6th International Conference on Neuroprotective Agents*
  Yenari, M. A., Zhao, H., Giffard, R. G., Sobel, R. A., Sapolsky, R. M., Steinberg, G. K.
  NEW YORK ACAD SCIENCES.2003: 54–68

- **Gene transfer of HSP72 protects cornu ammonis 1 region of the hippocampus neurons from global ischemia: Influence of Bcl-2** *ANNALS OF NEUROLOGY*
  Kelly, S., Zhang, Z. J., Zhao, H., Xu, L. J., Giffard, R. G., Sapolsky, R. M., Yenari, M. A., Steinberg, G. K.
  2002; 52 (2): 160-167

- **Mild post-ischemic hypothermia prolongs the time window for gene therapy**
  Zhao, H., Yenari, M. A., Sapolsky, R. M., Steinberg, G. K.
  LIPPINCOTT WILLIAMS & WILKINS.2002: 347–47

- **Extracellular glutamate changes in rat striatum during ischemia determined by a novel dialysis electrode and conventional microdialysis** *NEUROCHEMISTRY INTERNATIONAL*
  Sugahara, M., Asai, S., Zhao, H., Nagata, T., Kunimatsu, T., Ishii, Y., Kohno, T., Ishikawa, K.
  2001; 39 (1): 65-73

- **Two distinct components of initial glutamate release synchronized with anoxic depolarization in rat global brain ischemia** *NEUROREPORT*
  Asai, S., Kunimatsu, T., Zhao, H., Nagata, T., Takahashi, Y., Ishii, Y., Kohno, T., Ishikawa, K.
  2000; 11 (13): 2947-2952

- **Quantitative evaluation of extracellular glutamate concentration in postischemic glutamate re-uptake, dependent on brain temperature, in the rat following severe global brain ischemia** *BRAIN RESEARCH*
  Asai, S., Zhao, H., Kohno, T., Takahashi, Y., Nagata, T., Ishikawa, K.
  2000; 864 (1): 60-68

- **Nicergoline enhances glutamate re-uptake and protects against brain damage in rat global brain ischemia** *EUROPEAN JOURNAL OF PHARMACOLOGY*
  Asai, S., Zhao, H., Yamashita, A., Jike, T., Kunimatsu, T., Nagata, T., Kohno, T., Ishikawa, K.
  1999; 383 (3): 267-274

- **Phosphorylation of c-Jun and its localization with heme oxygenase-1 and cyclooxygenase-2 in CA1 pyramidal neurons after transient forebrain ischemia** *JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM*
  Matsuoka, Y., Okazaki, M., Zhao, H., Asai, S., Ishikawa, K., Kitamura, Y.
  1999; 19 (11): 1247-1255

- **Transient in vivo membrane depolarization and glutamate release before anoxic depolarization in rat striatum** *BRAIN RESEARCH*
  Kunimatsu, T., Asai, S., Kanematsu, K., Zhao, H., Kohno, T., Misaki, T., Ishikawa, K.
  1999; 831 (1-2): 273-282

- **Neither L-NAME nor L-arginine changes extracellular glutamate elevation and anoxic depolarization during global ischemia and reperfusion in rat** *NEUROREPORT*
  Zhao, H., Asai, S., Ishikawa, K.
  1999; 10 (2): 313-318

- **Minimal effect of brain temperature changes on glutamate release in rat following severe global brain ischemia: a dialysis electrode study** *NEUROREPORT*
  Asai, S., Zhao, H., Takahashi, Y., Nagata, T., Kohno, T., Ishikawa, K.
  1998; 9 (17): 3863-3868

- **Effects of brain temperature on CBF thresholds for extracellular glutamate release and reuptake in the striatum in a rat model of graded global ischemia** *NEUROREPORT*
  Zhao, H., Asai, S., Kohno, T., Ishikawa, K.
  1998; 9 (14): 3183-3188

- **Real-time monitoring of the effects of normothermia and hypothermia on extracellular glutamate re-uptake in the rat following global brain ischemia** *NEUROREPORT*
  Zhao, H., Asai, S., Kanematsu, K., Kunimatsu, T., Kohno, T., Ishikawa, K.
  1997; 8 (9-10): 2389-2393