

## BIOGRAPHICAL SKETCH

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NAME David A. Prince	POSITION TITLE Professor of Neurology and Neurological Sciences
eRA COMMONS USER NAME (credential, e.g., agency login) PRINCE.DAVID	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
University of Vermont, Burlington VT	BS	1952	
Univ. of Vermont, College of Medicine		1952-54	Medicine
Univ. of Pennsylvania, School of Medicine	M.D.	1956	Medicine
Neurology residency, Mt. Sinai Hosp., NYC		1957-58; 1960-62	
Chief, neurology service, Tripler US Army Hosp.		1958-60	
NIH postdoctoral fellowship, Stanford Sch. Of Medicine		1962-63	

Statement: I have been involved in research and training programs in Neuroscience and epilepsy since I arrived at Stanford in 1962. I have had a large number of per- and postdoctoral trainees, many of whom have had successful careers in clinical and basic neuroscience. My lab has generated >200 peer-reviewed publications in which electrophysiological and anatomical approaches were used to study the intact and epileptogenic brain.

### A. Positions and Honors

- 1956-1957 Rotating Internship, Mt. Sinai Hospital, New York, NY
- 1957-1958 Assistant Resident in Neurology, Mt. Sinai Hospital, NY
- 1960-1962 Assistant Resident and Chief Resident in Neurology, Mt. Sinai Hospital, NY
- 10/62-6/63 NIH Special Fellowship in Neurophysiology, Stanford Univ. Sch. of Med.
- 10/63-8/68 Assistant Professor of Medicine (Neurology) Stanford Univ. Sch. of Med.
- 9/68-8/70 Associate Professor of Medicine (Neurology), Stanford Univ. Sch. of Med.
- 9/70-6/71 Associate Professor and Acting Chairman, Dept. of Neurology, Sch. of Med.
- 6/71-12/89 Professor and Chairman, Dept. of Neurology, Stanford Univ. Sch. of Med.
- 4/89-12/89 Professor and Chairman, Dept. of Neurology & Neurological Sci., Stanford Univ. School of Medicine
- 6/1/83-pres. Edward F. and Irene T. Pimley Professor of Neurology and Neurological Sciences, Stanford University School of Medicine

### Other Experience and Professional Memberships:

- 1964 Diplomate in Neurology, American Board of Psychiatry, American EEG Society
- 1976-78 Council Member, American EEG Society
- 1970-72 Secretary, American Epilepsy Society
- 1973 President, American Epilepsy Society
- 1974-76 Council Member, American Neurological Association
- 1971-1989 Association of University Professors of Neurology

1968-69 President, Bay Area Neurophysiological Group  
1990-94 Member, Advisory Board, Max Plank-Institute for Psychiatry  
Consulting Editor: Epilepsy Research  
Editorial Board: Advances in Neuroscience, Epilepsy Research  
Member, Society for Neuroscience  
2008 Elected Honorary Member, American Neurological Association

### Honors

Phi Beta Kappa, Alpha Omega Alpha, Sigma Xi, Guggenheim Foundation Fellowship, Lennox Award, and Research Recognition Award in Basic Neuroscience from American Epilepsy Society, Sachs Lecturer, Javits Neuroscience Investigator Award, 1987, 1994, George Bishop Lecturer, Bronte Lecturer, Servier Lecturer, Special Lecturer, Society for Neuroscience, 2009

### C. Selected Peer-Reviewed Publications (from a total of 237)

#### Most relevant to the current application

Sun, Q-Q., Huguenard, J.R., and Prince, D.A. Neuropeptide Y receptors differentially modulate GIRK channels and HVA  $Ca^{2+}$  channels in rat thalamic neurons. *J. Physiol.*, 531(1):67-79, 2001.

Sun, Q-Q., Akk, G., Huguenard, J.R., and Prince, D.A. Differential regulation of GABA release and neuronal excitability mediated by neuropeptide  $Y_1$  and  $Y_2$  receptors in rat thalamic neurons are correlated by GABA<sub>A</sub> subunit expression. *J. Physiol.* 531(1):81-94, 2001.

Browne, S., Kang, J., Akk, G., Chiang, L., Schulman, H., Huguenard, J.R., and Prince, D.A. Kinetic and pharmacological properties of GABA<sub>A</sub> receptors in single thalamic neurons are correlated with GABA<sub>A</sub> subunit expression. *J. Neurophysiol.* 86:2312-2321, 2001

Xiang, Z., Huguenard, J.R., and Prince, D.A. Synaptic inhibition of pyramidal cells evoked by different interneuronal subtypes in layer V of rat visual cortex. *J. Neurophysiol.* 88:740-750, 2002.

Li, H., and Prince, D.A. Synaptic activity in chronically injured, epileptogenic sensory-motor neocortex, *J. Neurophysiol.*, 88:2-12, 2002.

Sun, Q-Q., Huguenard, J.R., and Prince, D.A. Somatostatin inhibits thalamic network oscillations in vitro: action on the GABAergic neurons of the reticular nucleus. *J. Neurosci.* 22:5374-5386, 2002.

Bacci, A., Huguenard, J.R., and Prince, D.A. Functional autaptic neurotransmission in fast-spiking interneurons: a novel form of feedback inhibition in the neocortex, *J. Neurosci.*, 23:859-866, 2003.

Bacci, A., Huguenard, J.R., and Prince, D.A. Differential modulation of synaptic transmission by neuropeptide Y in rat neocortical neurons, *PNAS*, 99:17125-17130, 2003.

Bandrowski, A.E., Huguenard, J.R. and Prince, D.A. Baseline glutamate levels affect group I and II mGluRs in layer V pyramidal neurons of rat sensorimotor cortex, *J. Neurophysiol.* 89:1308-1316, 2003.

Xiang, Z. and Prince, D.A. Heterogeneous actions of serotonin on interneurons in rat visual cortex, *J. Neurophysiol.* , 89:1278-1287, 2003.

Sun, Q-Q., Huguenard, J.R. and Prince, D.A. Vasoactive polypeptide (VIP) and pituitary adenylate cyclase-activating polypeptide (PACAP) activate  $I_h$  currents and depolarize thalamocortical neurons in vitro, *J. Neurosci.*, 23(7):2751-8. 2003.

Kharazia, V.N., Jacobs, K.M. and Prince, D.A. GluR1 and calbindin expression are altered in interneurons of neocortical microgyral malformations, *Neurosci.*, 120:207-218, 2003.

Graber, K.D., and Prince, D.A. A critical period for prevention of neocortical post-traumatic epileptogenesis in rats, *Annals of Neurology*, 55:860-870, 2004.

Bacci, A., Rudolph, W., Huguenard, J.R., and Prince, D.A. Major differences in inhibitory synaptic transmission onto two neocortical interneuron subclasses. *J. Neurosci.*, 23(29):9664-9674. 2003.

Sun QQ, Baraban S, Prince DA and Huguenard JR (2003) Target-specific NPYergic synaptic inhibition and its network consequences within the mammalian thalamus, *J. Neurosci.*, 23(29):9639-9649, 2003.

Sun, Q-Q, Huguenard, J.R. and Prince, D.A. Barrell Cortex Microcircuits: Thalamocortical feedforward inhibition in spiny stellate cells is mediated by a small number of fast-spiking interneurons, *J. Neurosci.*, 26(4):1219-1230, 2006.

Bacci, A., Huguenard, J.R., and Prince, D.A. Long-lasting self-inhibition of neocortical interneurons mediated by endocannabinoids, *Nature*, 431:312-316, 2004.

Jacobs, KM and Prince, D.A. Excitatory and inhibitory postsynaptic currents in a rat model of epileptogenic microgyria, *J. Neurophysiol.* 93:687-696, 2005.218.

Li, H., Bandrowski A.,E., and Prince, D.A. Cortical injury affects short-term plasticity of evoked excitatory synaptic currents, *J. Neurophysiol.*, 93:146-156, 2005.

Jin, Xiaoming, Huguenard, J.R., and Prince, D.A. Impaired CL- extrusion in layer V pyramidal neurons of chronically injured epileptogenic cortex, *J. Neurophysiol.*, 93:2117-2126, 2005.

Halabisky, B., Shen, F., Huguenard, J.R., and Prince, D.A. Electrophysiological classification of somatostatin-positive interneurons in mouse sensorimotor cortex, *J. Neurophysiol.* 96: 834-845, 2006.

Jin, X., Prince, D.A. and Huguenard. J.R. Enhanced excitatory synaptic connectivity in layer V pyramidal neurons of chronically injured epileptogenic neocortex in rats. *J. Neurosci.*, 26:4891-4900, 2006.

Tani, H., Bandrowski, A.E., Parada, I., Wynn, M., Huguenard, J.R., Prince, D.A. and Reimer, R.J. Modulation of epileptiform activity by glutamine and system A transport in a model of post-traumatic epilepsy. *Neurobiol. Disease*, 25 (2):230-238, 2007.

Sun, Q-Q, Huguenard, J.R., and Prince, D.A. Reorganization of barrel circuits leads to thalamically-evoked cortical epileptiform activity. *Thalamus and Related Systems*, 3:261-273, 2008. PMC2184932

Prince, D.A., Parada, I., Scalise, K., Graber, K., Jin, X. and Shen, F. Epilepsy following cortical injury: Cellular and molecular mechanisms as targets for potential prophylaxis. *Epilepsia*, 50(2):30-40, 2009. PMC2710960

Marinelli, S., Pacioni, S., Bisogno, T., DiMarzo,V., Prince, D.A. Huguenard, J.R. and Bacci, A.I. The endocannabinoid-2-arachidonoylglycerol is responsible for the slow self-inhibition in neocortical neurons, *J. Neurosci.*, 28(50):13352-13541, 2008. PMC2615383

Chu, Y, Parada, I and Prince, DA. Temporal and topographic alterations in expression of the  $\alpha 3$  isoform of  $\text{Na}^+/\text{K}^+$ -ATPase in the rat freeze lesion model of microgyria and epileptogenesis. *Neuroscience*, 162(2):339-48, 2009. PMCID-PMC In Process.

Paz, J.T., Christian, C.A., Parada, I., Prince, D.A., Huguenard, J.R. Focal cortical infarcts alter intrinsic excitability and synaptic excitation in the reticular thalamic nucleus, *Journal of Neuroscienc,e* 39(15) 5465-5479, 2009. PMC2861582

Zhang W., Yamawaki R., Wen X., Uhl J., Diaz J., Prince D.A., Buckmaster P.S.. Surviving hilar somatostatin interneurons enlarge, sprout axons, and form new synapses with granule cells in a mouse model of temporal lobe epilepsy. *J Neurosci.*, 11;29(45):14247-56, 2009. PMC 2802278

Chu, Y., Jin, X., Parada, I., Pesic, A., Stevens B., Barres, B.A, and Prince, D.A. Enhanced synaptic connectivity and epilepsy in C1q knockout mice, *PNAS*, 107(17):7975-80, 2010. PMC 2867906

Halabisky, B., Parada, I., Buckmaster, P.S., Prince, D.A. Excitatory input onto hilar somatostatin interneurons is increased in a chronic model of epilepsy., *J. Neurophysiol.*, 4(4):2214-2223, 2010. PMCID-PMC In Process.

Faria, L.C. and Prince, D.A. Presynaptic inhibitory terminals are functionally abnormal in a rat model of posttraumatic epilepsy. *J. Neurophysiology*, ;104(1):280-290, 2010. PMC 2904216

Jin, X., Huguenard, J.R., and Prince, D.A. Reorganization of inhibitory synaptic circuits in rodent chronically injured epileptogenic neocortex, *Cereb Cortex*, Sep 20. 21(5):1094-1104, 2011. PMC 3077430

Frédéric Manseau, Marinelli, S, Schwaller, B, Prince, D.A., Huguenard, J.R. and Bacci, A. Desynchronization of neocortical networks by asynchronous release of GABA at autaptic and

synaptic contacts from fast-spiking interneurons, PLoS Biology, 28;8(9). pii: e1000492, 2010. PMC2946936

Anderson, T., Huguenard, J.R., and Prince, D.A. Differential effects of Na<sup>+</sup>/K<sup>+</sup> ATPase blockade on cortical layer V neurons, J. Physiol., 588(22):4401-4414, 2010. PMC3008847

Faria, L.C., Parada, I. and Prince D.A. Interneuronal calcium channel abnormalities in posttraumatic epileptogenic neocortex. Neurobiol Dis. 2012 Feb;45(2):821-8. Epub 2011 Dec 7. PMID-PMC In Process.

Ma, Y. And Prince, D.A. Functional alterations in GABAergic fast-spiking interneurons in chronically injured epileptogenic neocortex, Neurobiol. Dis. (2012), doi:10.1016/j.nbd.2012.03.027.

Li H, Graber KD, Jin S, McDonald W, Barres BA, Prince DA, Gabapentin decreases epileptiform discharges in a chronic model of neocortical trauma. Neurobiol Dis. 2012 Jul 2;48(3):429-438. [Epub ahead of print]

## **D. Research Support**

### **Ongoing Research Support:**

#### **1 R01 NS39579-12**

NIH/NINDS

Modulation of Neocortical Interneuronal Function

04/01/2010 - 03/31/2014

The major goals of this project are to assess mechanisms of modulation of function in neocortical interneurons, e.g., via autapses and neurotransmitters.

Role: PI

#### **2 R01 NS06477: 46**

NIH/NINDS

08/01/2010-07/31/2014

Cellular Mechanisms in Epileptogenesis

The major goals of this grant are to identify mechanisms underlying the prolonged gating of GABA<sub>A</sub> receptor mediated responses in the thalamic reticular nucleus and test whether the reticular nucleus survives thalamic injury subsequent to cortical lesions and participates in the reorganization of thalamic circuits following injury.

Role: Co-PI

#### **CURE: Citizens United for Research Epilepsy**

Prevention of Neocortical Posttraumatic Epileptogenesis

11/01/09-10/31/2012

The major aim is to develop strategies to prevent posttraumatic epilepsy with gabapentin, BDNF activation or other molecules.

Role: PI

### **Completed Research Support:**

#### **2 P50 NS12151-36**

NIH/NINDS

Epilepsy Research Program: Project I

07/15/2007 - 06/30/2012

Abnormalities in Fast Spiking Interneurons of Chronically Epileptogenic Cortex

The major goal of these experiments is to define alterations in pre- and postsynaptic inhibitory mechanisms that occur at autaptic and synaptic sites in chronically epileptogenic

neocortex due to decreases in Na<sup>+</sup>-K<sup>+</sup> ATPase and abnormalities in synaptic boutons within the axons of fast-spiking interneurons.

Role: PI

1 R01 NS39579-09

NIH/NINDS

Modulation of Neocortical Interneuronal Function

04/01/2005 - 03/31/2010

The major goals of this project are to assess mechanisms of modulation of function in neocortical interneurons, e.g., via autapses and neurotransmitters.

Role: PI

CURE: Citizens United for Research in Epilepsy

10/01/2007-03/30/2010

Prevention of Neocortical Posttraumatic Epileptogenesis

The major goals of these experiments are to identify strategies for prevention of posttraumatic epilepsy in a rat model. We will assess effects of blocking NMDA receptors and enhancing metallothionein I either by direct application or the use of genetically modified animals.

Role: PI

2 R01 NS06477-44

NIH/NINDS

Cellular Mechanisms in Epileptogenesis

08/01/2006 - 07/31/2010

The major goals of this grant are to identify mechanisms underlying the prolonged gating of GABA<sub>A</sub> receptor mediated responses in the thalamic reticular nucleus and test whether the reticular nucleus survives thalamic injury subsequent to cortical lesions and participates in the reorganization of thalamic circuits following injury.

Role: Co-PI