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## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

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NAME Davis, Thomas P.	POSITION TITLE Professor of Pharmacology, BIO-5 Institute and Program in Neurosciences and Physiological Sciences.		
eRA COMMONS USER NAME davistp			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Loyola University of Los Angeles	BS	1973	Biology
University of Nevada	MS	1975	Physiology/Biochemistry
University of Missouri, Columbia	PhD	1978	Physiol./Anal. Biochem
Abbott Laboratories, N. Chicago, IL	Postdoc	1978-80	Analytical Biochemistry

### **A. PERSONAL STATEMENT:**

The Davis Laboratory has spent the past 30 years, continuously funded by N.I.H. RO1 basic science research grants. Our scientific and research focus is in developing "state of the art" methods/procedures/tools for quantifying/studying the *in vivo* integrity of the blood brain barrier/neurovascular unit (and associated drug transporters) as altered by pathological disease states associated with brain injury (stroke/hypoxia) and peripheral pain. We remain dedicated to our mission of maintaining the strongest basic science program in drug delivery research while educating undergraduate, graduate and post-doctoral fellows to advance our field. In the course of our research into the molecular, biochemical and pathophysiological mechanisms associated with maintenance and disruption of the blood-brain barrier/neurovascular unit and endothelial cell tight junction proteins and transporters, we have been cited by our peers for "paradigm shifting" discoveries and meritorious mentoring of the "next generation" of biomedical researchers

### **B. PROFESSIONAL EXPERIENCE:**

1978-80 Analytical Biochemist, Therapy Monitoring Venture Group, Abbott Laboratories, North Chicago, Illinois.

1981-86 Assistant Professor, Pharmacology and Director, Laboratory of Analytical and Peptide Chemistry, University of Arizona Health Sciences Center, Tucson, Arizona. Member, Arizona Cancer Center and Neuroscience Graduate Interdisciplinary Program.

1986-91 Associate Professor, Pharmacology and Director, Laboratory of Analytical and Peptide Chemistry, University of Arizona Health Sciences Center, Tucson, Arizona. Member, Arizona Cancer Center and Neuroscience Program.

1991-present Professor, Medical Pharmacology and Director, Laboratory of Blood Brain Barrier Research, University of Arizona Health Sciences Center, Tucson, Arizona. Member, Arizona Cancer Center, Neurosciences and Physiological Sciences Training Program.

1991-present Professor, Medical Pharmacology, Program in Neurosciences and Program in Physiological Sciences, University of Arizona College of Medicine, Tucson.

2007-present Professor, BIO 5 Research Institute, University of Arizona, Tucson.

### **HONORS:**

1969-73, Loyola University Academic Scholarship; 1975, David Bruce Dill Award and Scholarship; Phi Beta Kappa, Gamma Sigma Delta and Sigma XI Honor Societies; Associate Editor, *Current Pharmaceutical Design*, 2008 to present. Editor, 2014. Editorial Advisory Board, *Fluids and Barriers of the CNS*. 2010 to present; *Peptides*, 1984 to present. Editor, *Life Sciences*, 1988 to 2006. Fellow, American Institute of Chemists, 1987. Fellow, International Neuropeptide Society, 1997. Certified Professional Chemist, 1990. Member, Neurological Sciences III study section, N.I.H. 1994-1998. Member, Brain Disorders Clinical Neurosciences II Study Section, N.I.H., 1998-2003. Co-organizer with the Office of Research Integrity, "Management of Biomedical Research Laboratories"- A National Conference, October 1-3, 1998. Member and Awardee, Loyola Marymount University College of

Science and Engineering Wall of Fame. October, 2003. Distinguished Alumnus of the Year, 2012, St. Francis High School.

Elected Chair, Gordon Research Conference, "Barriers of the CNS", Tilton, NH.

Member, Acute Neural Injury and Epilepsy Study Section, N.I.H., 2010-2016.

Founders Day Lecture and Awardee, University of Arizona College of Medicine, 2011.

### **C. SELECTED PEER-REVIEWED PUBLICATIONS (FROM 212):**

- Witt, K.A., R.D. Egleton, J.D. Huber and **T.P. Davis**. Insulin enhancement of opioid peptide transport across the blood-brain barrier and assessment of analgesic effect. *J. Pharmacology. Exp. Therap.* 295(3):972-978, 2000. [\[PubMed\]](#)
- Huber, J.D., K.A. Witt, S. Hom, R.D. Egleton, K.S. Mark, and **T.P. Davis**. Inflammatory pain alters blood-brain barrier permeability and tight junctional protein expression. *American J. Physiology-Heart and Circulatory Physiology.* 280:H1241-H1248, 2001. [\[PubMed\]](#)
- Egleton, R.D., S.A. Mitchell, J. Huber, M.M. Palian, R. Polt, and **T.P. Davis**. Improved Blood-Brain Barrier Penetration and Enhanced Analgesia of an Opioid Peptide by Glycosylation. *J. Pharmacol. Exp. Therap.* 299(3):967-972, 2001. [\[PubMed\]](#)
- Hom, S, R.D. Egleton, T.J. Abbruscato and **T.P. Davis**. Effect of reduced flow on blood-brain barrier transport systems. *Brain Research* 890(1):38-48, 2001. [\[PubMed\]](#)
- Witt, K.A., J.D. Huber, R.D. Egleton, M.J. Roberts, M.D. Bentley, L. Guo, H. Wei, H.I. Yamamura and **T.P. Davis**. Pharmacodynamic and pharmacokinetic characterization of poly(ethylene glycol) conjugation to Met-enkephalin analogue DPDPE. *J. Pharmacol. Exp. Therap.* 298(2):848-856, 2001. [\[PubMed\]](#)
- Huber, J.D., R.D. Egleton and **T.P. Davis**. Molecular physiology and pathophysiology of blood-brain barrier tight junction. *Trends in the Neurosciences* 24(12):719-725, 2001. [\[PubMed\]](#)
- Mark, K.S. and **T.P. Davis**. Cerebral microvascular changes in permeability and tight junctions induced by hypoxia- reoxygenation. *American J. Physiology-Heart and Circulatory Physiology* 282(4):H1485-H1494, 2002. [\[PubMed\]](#)
- Brown, R.C. and **T.P. Davis**. Calcium modulation of adherens and tight junction function: a potential mechanism for blood-brain barrier disruption after stroke. *Stroke* 33(6):1706-1711, 2002. [\[PubMed\]](#)
- Hau, V., J. Huber, R. Egleton and **T.P. Davis**. The effect of guanidino modification and proline substitution on the *in vitro* stability and BBB permeability of endomorphin II. *J. Pharm. Sci.* 91(10):2140-2149. 2002. [\[PubMed\]](#)
- Huber, J.D., V.S. Hau, C.R. Campos, R.D. Egleton and **T.P. Davis**. Blood-brain barrier tight junctions are altered during a 72-h exposure to lambda-carrageenan-induced inflammatory pain. *American J. Physiology-Heart and Circulatory Physiology* 283(4):H1531-H1537, 2002. [\[PubMed\]](#)
- Hawkins, B.T., R.C. Brown and **T.P. Davis**. Smoking and ischemic stroke: A role for nicotine? *Trends in Pharmacological Sciences* 23(2):78-82, 2002. [\[PubMed\]](#)
- Huber, J., V.S. Hau, K.S. Mark, R.C. Brown, C.R. Campos and **T.P. Davis**. Viability of microvascular endothelial cells to direct exposure of formalin, lambda-carrageenan and complete Freund's adjuvant. *European J. Pharmacology* 450(3):297-304, 2002. [\[PubMed\]](#)
- Huber, J.D., R.D. Egleton and **T.P. Davis**. Conjugation of low molecular weight polyethylene glycol to biphalin enhances antinociceptive profile. *J. Pharm. Sci.* 92:1377-1385, 2003. [\[PubMed\]](#)
- Egleton, R.D., C.R. Campos, J.D. Huber, R.C. Brown and **T.P. Davis**. Differential effects of diabetes on rat choroid plexus ion transporter expression. *Diabetes* 52:1496-1501, 2003. [\[PubMed\]](#)
- Brown, R.C., K.S. Mark, R.D. Egleton, J.D. Huber, A.R. Burroughs and **T.P. Davis**. Protection against hypoxia-induced increase in blood-brain barrier permeability: Role of Tight Junction Proteins and NF kappa B. *Journal of Cell Science* 116(4):693-700, 2003. [\[PubMed\]](#)
- Wolka, A., J.D. Huber and **T.P. Davis**. Pain and the Blood Brain Barrier: obstacles to drug delivery. *Advanced Drug Delivery Reviews* 55(8):987-1006, 2003. [\[PubMed\]](#)
- Brown, R.C., K.S. Mark and **T.P. Davis**. Protection against hypoxia-induced blood brain barrier disruption: Changes in intracellular calcium. *American Journal of Physiology- Cell Physiology* 286(5):C1045-1052, 2004. [\[PubMed\]](#)
- Hawkins, B.T., T.J. Abbruscato, R.D. Egleton, R.C. Brown, J.D. Huber, C.R. Campos, and **T.P. Davis**. Nicotine increases *in vivo* blood-brain barrier permeability and alters cerebral microvascular tight junction protein distribution. *Brain Research* 1027:48-58, 2004. [\[PubMed\]](#)

- Hau, V.S., J.D. Huber, C.R. Campos, R.T. Davis and **T.P. Davis**. Effect of lambda carrageenan induced inflammatory pain on brain uptake of codeine and antinociception. *Brain Research* 1018:257-264, 2004. [\[PubMed\]](#)
- Brown, R.C. and **T.P. Davis**. Hypoxia/Aglycemia alters expression of occludin and actin in brain endothelial cells. *Biochemical and Biophysical Research Communications* 327:1114-1123, 2005. [\[PubMed\]](#)
- Egleton, R.D. and **T.P. Davis**. Development of Neuropeptide Drugs that Cross the Blood- Brain Barrier. *NeuroRx* 2(1); 44-53, 2005. [\[PubMed\]](#)
- Brooks, T.A., B.T. Hawkins, J.D. Huber, R.D. Egleton and **T.P. Davis**. Chronic inflammatory pain leads to increased blood-brain barrier permeability and tight junction protein alterations. *American J. Physiology (Heart and Circulatory)* 289(2): H738-H743, 2005. [\[PubMed\]](#)
- Hawkins, B.T., R.D. Egleton and **T.P. Davis**. Modulation of cerebral microvascular permeability by endothelial nicotinic acetylcholine receptors. *American J. Physiology (Heart and Circulatory)* 289(1): H212-H219, 2005. [\[PubMed\]](#)
- Hawkins, B. T. and **T.P. Davis**. The blood-brain barrier/neurovascular unit in health and disease. *Pharmacological Reviews* 57:173-185, 2005. [\[PubMed\]](#)
- Huber, J.D., C.R. Campos, K.S. Mark and **T.P. Davis**. Alterations in blood-brain barrier ICAM-1 expression and microglial activation following lambda carrageenan induced inflammatory pain. *American Journal of Physiology (Heart and Circulatory)* 290(2):H732-40, 2006. [\[PubMed\]](#)
- Witt, K.A. and **T. P. Davis**. CNS drug delivery: opioid peptides and the blood-brain barrier. *Aaps J* 8(1): E76-88, 2006. [\[PubMed\]](#)
- Hom, S., Fleegal, M.A., Egleton, R.D., Campos, C.R., Hawkins, B.T. and **T. P. Davis**. Comparative changes in the blood-brain barrier and cerebral infarction of SHR and WKY rats. *Am J Physiol Regul Integr Comp Physiol* 292(5): R1881-92, 2007. [\[PubMed\]](#)
- McCaffrey, G., Staatz, W.D., Quigley, C.A., Nametz, N., Seelbach, M.J., Campos, C.R., Brooks, T.A., Egleton, R.D. and **T.P. Davis**. Tight junctions contain oligomeric protein assembly critical for maintaining blood-brain barrier integrity in vivo. *J Neurochem* 103(6): 2540-2555, 2007. [\[PubMed\]](#)
- Seelbach, M.J., Brooks, T.A., Egleton, R.D. and **T. P. Davis**. Peripheral inflammatory hyperalgesia modulated morphine delivery to the brain: a role for P-glycoprotein. *J. Neurochem* 102(5): 1677-90, 2007. [\[PubMed\]](#)
- Brooks, T.A., Nametz, N., Charles, R. and **T.P. Davis**. Diclofenac attenuates the regional effect of lambda-carrageenan on blood-brain barrier function and cytoarchitecture. *J Pharmacol Exp Ther* 325(2): 665-73, 2008. [\[PubMed\]](#)
- Campos, C.R., Ocheltree, S.M., Hom, S., Egleton, T.D. and **T.P. Davis**. Nociceptive inhibition prevents inflammatory pain induced changes in the blood-brain barrier. *Brain Res* 1221: 6-13, 2008. [\[PubMed\]](#)
- McCaffrey, G., Seelbach, M.J., Staatz, W.D., Nametz, N., Quigley, C., Campos, C.R., Brooks, T.A. and **T.P. Davis**. Occludin oligomeric assembly at tight junctions of the blood-brain barrier is disrupted by peripheral inflammatory hyperalgesia. *J Neurochem* 106(6): 2395-409, 2008. [\[PubMed\]](#)
- Willis, C.L. and **T.P. Davis**. Chronic inflammatory pain and the neurovascular unit: a central role for glia in maintaining BBB integrity? *Curr Pharm Des* 14(16): 1625-43, 2008. [\[PubMed\]](#)
- Ronaldson P.T., DeMarco K.M., Sanchez-Covarrubias L., Solinsky C.M. and **T. P. Davis**. Transforming growth factor (TGF)- $\beta$  signaling alters substrate permeability and tight junction protein expression at the blood-brain barrier during inflammatory pain. *J Cereb Blood Flow Metab* .29, 1084-1098. 2009.
- Ronaldson, P.T., K.M. DeMarco, L. Sanchez-Covarubias, C.M. Solinsky and T.P. Davis. Transforming growth factor Beta signaling alters permeability and tight junction protein expression at the blood brain barrier during inflammatory pain. *J. Cerebral Blood Flow and Metabolism* 29,6. 1084-1098.2009.
- Ronaldson, P.T., J. D. Finch, K.M. DeMarco, C.M. Solinsky, C. E. Quigley and T.P. Davis. Inflammatory Pain signals an increase in functional expression of organic anion transporting polypeptide 1a4 at the blood brain barrier. *J. Pharmacology Experimental Therapeutics*. 336,3. 827-839.2011.
- Lochhead, J.J., G. McCaffrey, C. Quigley, J. Finch, K. DeMarco, T.P. Davis and P. T. Ronaldson. Tempol modulates changes in xenobiotic permeability and occludin oligomeric assemblies at the blood brain barrier during inflammatory pain. *Amer. J. of Physiology: Heart and Circ Physiology*. 302:H582-H593. 2011.
- Ronaldson, P.T. and T.P. Davis. Targeting Blood Brain Barrier Changes during Inflammatory Pain: An Opportunity for Optimizing CNS Drug Delivery. *Therapeutic Delivery*. 2:1015-1041. 2011.

- Mc Caffrey, G., Staatz, W., Ronaldson, P.T., Finch, J.D., DeMarco, K.M., Laracuenta, M., and T.P. Davis. P-glycoprotein trafficking at the blood brain barrier altered by peripheral inflammatory hyperalgesia. *J. Neurochemistry*. 1471-1495. 2012.
- Mc Caffrey, G., and T.P. Davis. Physiology and pathophysiology of the blood brain barrier : P-glycoprotein and occludin trafficking as therapeutic targets to optimize CNS drug delivery. *Journal of Investigative Medicine*. 60,8. 1131-1140. 2012.
- Williams, P.D., Zlokovic, B.V., Griffin, J.H., Pryor, K.E., and T. P. Davis. Preclinical safety and pharmacokinetic profile of 3K3A-APC, a novel, modified Activated Protein C for Ischemic Stroke. *Current Pharmaceutical Design*. 18, 27. 4215-4222. 2012.
- Wang, Y., Z. Zhang, N. Chow, T.P. Davis, J.H. Griffin, M. Chopp, and B.V. Zlokovic. An activated protein C analog with reduced anticoagulant activity enhances tPA treatment for ischemic stroke in rodents. *Stroke*. 43: 2444-2449. 2012.
- Ronaldson, P.T., and T.P. Davis. Gabapentin and diclofenac reduce opioid consumption in patients undergoing tonsillectomy : A result of altered CNS delivery ? *Archives of Trauma Research*. 2(2), 97-98. 2013.
- Ronaldson, P.T. and T.P. Davis. Targeted drug delivery to treat pain and cerebral hypoxia. *Pharmacological Reviews*. 65,1. 291-314. 2013.
- Slosky, L.M., B.J. Thompson, L. Sanchez-Covarubias, Y. Zheng, M. Laracuenta, T. W. Vanderah, P.T. Ronaldson and T. P. Davis. Acetaminophen modulates P- glycoprotein functional expression at the blood-brain barrier by a constitutive androstane receptor–dependent mechanism. *Molecular Pharmacology*. 84,5. 774-786. 2013.
- Sanchez-Covarubias, L., T.P. Davis and P.T. Ronaldson. Drug transporters at CNS Barrier Sites: Obstacle or Opportunity for drug delivery? *Current Pharmaceutical Design*. 2013, June 19. epub.
- Guo, H., R.D. Bell, S. Wang, A. Sagare, N. Chow, T.P. Davis, J.H. Griffin, S.A. Goldman and B.V. Zlokovic. An activated protein C analog stimulates neuronal production by human neuronal progenitor cells via PAR1-PAR3-S1P-Akt pathway. *J. Neuroscience*. 33,14. 6181-6190. 2013.
- Mosnier, L.O., J.A. Fernandez, T.P. Davis, B.V. Zlokovic and J.H. Griffin. Influence of the 3K3A-activated protein C variant on the plasma clot lysis activity of tPA and of tPA on the variant's anticoagulant activity. *J Thrombosis Haemostasis*. 11,11.2059-2062.2013.
- Sanchez-Covarrubias, L., L.M. Slosky, P.T. Ronaldson, T. W. Vanderah, and T.P. Davis. P-glycoprotein modulates morphine uptake into the CNS: a role for the non-steroidal anti-inflammatory drug diclofenac. *PLOS One*. In Press. 2013.
- Ronaldson, P.T., and T.P. Davis. Gabapentin and diclofenac reduce opioid consumption in patients undergoing tonsillectomy: A result of altered CNS delivery? *Arch Trauma Res*. 2, 2. 97-98. 2013.
- Lyden, P., H. Levy, S. Weymer, K. Pryor, W. G. Kramer, J. H. Griffin, T. P. Davis and B.V. Zlokovic. Phase 1 Safety, Tolerability and Pharmacokinetics of 3K3A-APC in Healthy Adult volunteers. *Current Pharmaceutical Design*. 19. 2013.

#### **D. RESEARCH SUPPORT ONGOING TODAY (NIH) :**

- **N.I.H. R01-NS42652- Years 12-17.** 7/1/2002-6/30/2018. Thomas P. Davis, P.I. **“Blood-Brain Barrier Changes Induced by Pain.”** P.I. In this grant we study the saturable versus non-saturable drug transporter mechanisms associated with opioid and non opioid drug delivery at the BBB. We also characterize the signaling mechanisms for endothelial cell based BBB transporters and tight junction proteins during peripheral pain states. Finally, we study the effect of “over the counter ” pain therapeutics, such as acetaminophen, on opioid drug delivery/drug drug interaction, at the BBB, in pain states.
- **N.I.D.A. R01-DA11271- Years 12-18.** 8/1/1997-7/31/2015. Thomas P. Davis, P.I. **“Blood to CNS Drug Uptake in Pain.”** This grant is designed to study tight junction and transporter protein trafficking changes that affect endothelial cell permeability, leak and drug delivery to the CNS as a result of peripheral inflammatory pain and reaction oxygen species. This grant also studies the molecular signaling mechanisms associated with the key transporter, P-glycoprotein, and occludin/claudin tight junction protein trafficking at the BBB , in pain states.