

Current projects and Publications

Parminder J.S. Vig, PhD

Professor of Neurology and Biochemistry

Associate Professor of Neurobiology and Anatomical Sciences

Funded Projects:

National Institutes of Health (NINDS): RO3

Targeted Delivery of S100B inhibitory peptides to SCA1 Mouse Cerebellum. **(MPI)**

Principal Investigator, March 2010-April 2013

Currier Spinocerebellar Research Fund Do glial proteins modulate ataxin-1 phosphorylation. **Principal Investigator, Jan 2010-open**

Cure Ataxia.org: Ataxia: Ataxia Research at UMMC. **Principal Investigator, Dec. 2010 –open**

Balance Disorders Inc: Dopamine D2 Receptor Agonist Bromocriptine as a Potential Therapeutic for SCA1. **Principal Investigator, 07/01/2011 – 06/30/2012**

Pending/under preparation:

Intramural Research Support Program, UMMC. Targeting therapeutics to cerebellum using heat sensitive polypeptide carriers. **Principal Investigator**

The Micheal J. Fox Foundation Title: Validation of ASIC1a as a Therapeutic Target for Parkinson's Disease **Principal Investigators: Bidwell and Vig**

National Institutes of Health (NINDS): R21, Targeting cerebellum with thermally sensitive therapeutic peptides. **(MPI) Principal Investigator: Vig and Raucher**

National Institutes of Health (NINDS): R01, Dopamine against as therapeutics for SCA1. **Principal Investigator: Vig**

Previous:

National Ataxia Foundation: Cytokines in Human Neurodegenerative Disorders. **Principal Investigator 1993-1994 (\$2,045)**

National Ataxia Foundation: In vivo effects of insulin-like growth factor-I on cerebellar degeneration in lurcher mouse. **Principal Investigator 1994-1995 (\$5,000).**

Pediatrics Research Support Grant: Glial cell responses in the spinal cord during motor neuron degeneration produced by B-iminodipropionitrile in rats. **Co-Investigator 1994-1995 (\$ 10,000).**

UMC Seed Money: Role of Calcium Binding proteins in hippocampal degeneration in developing mice following intrauterine exposure to domoic acid. Principal Investigator 1994-1997 (\$5,000)

National Ataxia Foundation: Calcium binding proteins in patients with spinocerebellar ataxias. Principal Investigator 1995-1996 (\$5,000)

National Institute of Health Training Grant to Jackson State University. Research Mentor for MS degree: 1992 (Supplies \$4,000)

National Institute of Health Training Grant to Jackson State University. Research Mentor for MS degree 1994 (Supplies \$4,000)

National Institute of Health Training Grant to Jackson State University. Research Mentor for MS degree 1996 (Supplies \$4,000).

National Ataxia Foundation : Role of polyglutamine peptides in cerebellar degeneration. Principal Investigator 1996-1997 (\$10,500).

National Ataxia Foundation: Expression of calcium-binding proteins in Purkinje cells of SCA-1 transgenic mice. Principal Investigator 1997-1998 (\$8,000)

Biomedical Research Support Grant, Univ. Miss Med. Center: Do Purkinje cells need calcium binding proteins to survive? Principal Investigator 1997-1998 (\$12,000)

National Ataxia Foundation: Do Purkinje cells from spinocerebellar ataxia-1 transgenic mice survive in culture? Principal Investigator 1998-1999 (\$9,000)

National Ataxia Foundation: Effects of insulin-like growth factor-1 (IGF-1) on Purkinje cell survival in SCA-1 transgenic mice Principal Investigator, Jan 2000- July 2001 (\$20,000)

National Ataxia Foundation: SCA-1 Calbindin D28k null double mutant mice. Role of calbindin in ataxin-1 mediated Purkinje cell degeneration Principal Investigator, Jan 2001-June 2003 (18,424)

National Institute of Health (NINDS) Supplement Grant: Testing of candidate drug treatments for neurodegeneration in rodent models. Principal Investigator, Oct 2003-Dec 2004 (\$74,000)

Mississippi Functional Genomics Network: The role of nitric oxide in domoic acid induced epilepsy. Co-Investigator, Oct. 2003-Sept. 2004 (\$30,000)

National Institutes of Health (NINDS): Mechanism Ataxin-1 Mediated Purkinje Cell Death. Principal Investigator, Feb 2003-Jan 2008 (\$713,000)

National Ataxia Foundation: Role of Bergmann Glia in Purkinje Cell Development and Pathology in SCA1 Principal Investigator, Jan 2008-June 2009 (\$35,000)

Intramural Grant Support Program, UMC: Is ASIC1a involved in altered Purkinje cell spine density in SCA1? Principal Investigator, Oct 2008- Nov 2009 (\$29,500)

Pending Patents

Therapeutic use of dopamine D2 receptor agonists for treating SCA1.

Provisional Patent Applications (Potential for getting a patent)

Thermally targeted delivery of therapeutic peptides to the cerebellum for treating spinocerebellar ataxias and other neurodegenerative diseases.

Drs. Vig and Raucher and Hearst filed a non-provisional patent application to THE UNITED STATES PATENT AND TRADEMARK OFFICE entitled "COMPOSITION AND METHODS FOR TARGETED DELIVERY OF A THERAPEUTIC COMPOUND TO THE BRAIN OR SPINAL CORD OF A SUBJECT FOR TREATMENT OF NEURODEGENERATIVE DISEASES"

Record of Invention (Potential for getting a patent)

Angiotensin II and related peptides as therapeutics for treating cerebellar ataxias.

Publications (Journal Articles):

1. Kanwar KC and **Vig PJS**: Intestinal absorption of zinc in the fluoridated environment IRCS Med. Sci. 1983; 11:762.
2. Kanwar KC, **Vig PJS** and Kalla NR: In vitro inhibition of testosterone synthesis in the presence of fluoride ions. IRCS Med. Sci. 1983; 11:813-814.
3. Nath R, **Vig PJS**, Gulati S, Sharma M, Ravi K, and Paliwal VK: Biological and environmental monitoring of heavy metals with special reference to cadmium. In: Agarwal VP, Rana SVS, eds Sci Dev Environ. India; 1987: 113-116
4. **Vig PJS**, Singh S, Prashar S, Gulati S, Paliwal VK and Nath R: Environmental impact of heavy metals on health (An analysis of food, water, air and blood samples). In: Environmental Pollution and Health Hazards in India, New Delhi: Ashish Publishing House, Kumar R, ed, 1987: 138-146.
5. Ravi K, Paliwal VK, **Vig PJS**, Sharma M and Nath R: Do isometallothioneins regulate enzyme metabolism? Speculations Sci. Technol 1988; 11:59-61.

6. **Vig PJS**, Bhatia M, Gill KD and Nath R: Cadmium inhibits brain calmodulin: In vitro and in vivo studies. *Bull Environ Contam Toxicol*. 1989; 43: 541-547.
7. **Vig PJS**, Bhatia M, Gill KD and Nath R: Cadmium inhibits brain calmodulin activity in monkey brain. *J Appl Toxicol* 1989; 9:313-316.
8. **Vig PJS**, Mehrotra BD and Desai D: Chlordecone interaction of calmodulin binding with phosphodiesterase. *J Appl Toxicol* 1990; 10:55-57.
9. Yallapragada PR, **Vig PJS** and Desai D: Differential effects of triorganotins on calmodulin activity. *Toxicol Environ Health* 1990; 29:317-327.
10. **Vig PJS**, Mehrotra BD and Desai D: Holothurin: An activator of bovine brain phosphodiesterase. *Res Comm Chem Pathol Pharmacol* 1990; 67:419-422.
11. **Vig PJS**, Paliwal VK and Nath R: A comparative study of direct current plasma atomic emission spectrometry and atomic absorption spectrophotometry for biological monitoring of trace metals. In: Dillon HK, Ho MH, eds, *Biological Monitoring of Exposure to Chemicals: Metals*. New York: John Wiley, 1991: 163-171.
12. **Vig PJS** and Nath R: In Vivo effects of cadmium on calmodulin and calmodulin regulated enzymes in rat brain. *Biochemistry International* 1991; 23:927-934.
13. **Vig PJS**, Yallapragada PR, Kodavanti PRS and Desai D: Modulation of calmodulin properties by amiodarone and its major metabolite desethylamiodarone. *Pharmacol Toxicol* 1991; 68:26-33.
14. **Vig PJS**, Yallapragada PR, Trotman CH, Mehrotra BD and Desai D: Effect of organochlorine and organotin compounds on active conformation of calmodulin. *J Environ Sci Health A* 1991; 26:521-534.
15. Kodavanti PRS, Cameron JA, Yallapragada PR, **Vig PJS** and Desai D: Inhibition of Ca^{2+} transport associated with cAMP-dependent protein phosphorylation in rat cardiac sarcoplasmic reticulum by triorganotins. *Arch Toxicol* 1991; 65:311-317).
16. **Vig PJS**, Ravi K and Nath R: Interaction of metals with brain calmodulin purified from normal and cadmium exposed rats. *Drug Chem Toxicol* 1991; 14:207-218.
17. Desai D, **Vig PJS**, Subramony SH and Currier RD: Inositol 1,4,5-trisphosphate receptors and protein kinase C in olivopontocerebellar atrophy. *Brain Res* 1991; 552:36-40.
18. Yallapragada PR, **Vig PJS**, Kodavanti PRS and Desai D: In vivo effect of triorganotins on calmodulin activity in rat brain. *J Toxicol Environ Health* 1991;

34:229-237.

19. **Vig PJS** and Desai D: Modulation of protein kinase C activity by amiodarone and desethylamiodarone. *NeuroToxicology* 1991; 12:595-602.
20. Pala I, Srinivasan A, **Vig PJS** and Desai D: In vitro effects of organophosphorus compounds on calmodulin activity. *J Appl Toxicol* 1991; 11:391-395.
21. Desai D, Pentylala SN, Trotman CH, **Vig PJS**, and Sekhon BS: Combined effects of carbon tetrachloride and chlordecone on calmodulin activity in gerbil brain. *J Toxicol Environ Hlth* 1991; 34:219-228.
22. **Vig PJS**, Subramony SH, Currier RD and Desai D: Inositol 1,4,5-trisphosphate metabolism in the cerebella of Lurcher mutant mice and patients with olivopontocerebellar atrophy. *J Neurological Sci* 1992; 110:139-143.
23. Desai D, Subramony SH, **Vig PJS** and Currier RD: Phosphoinositide second messenger system in human OPCA and the mouse model. In: Eds. Harding A, Deufel T, *Advances in Neurology*, vol. 61, New York: Raven Press 1993: 167-173.
24. Pentylala SN, **Vig PJS**, Sekhon BS and Desai D: Effect of carbon tetrachloride on inositol 1,4,5-trisphosphate dependent and independent regulation of rat brain microsomal Ca^{2+} -fluxes. *Cellular Signalling* 1994; 6: 561-567.
25. **Vig PJS**, Pentylala SN, Chetty CS, Rajanna B and Desai D: Lead alters inositol polyphosphate receptor activities: Protection by ATP. *Pharmacology and Toxicology* 1994; 75:17-22.
26. **Vig PJS**, Desai D, Joshi P, Subramony SH and Fratkin JD: Decreased insulin-like growth factor-I-mediated protein tyrosine phosphorylation in human olivopontocerebellar atrophy and lurcher mutant mouse. *J Neurological Sci*.1994; 124 38-44.
27. **Vig PJS**, Desai D, Joshi P, Subramony SH and Fratkin JD: Increased cerebellar endothelin-1 receptor binding in neurologic mutant mouse lurcher. *Res. Comm. Mol. Pathol. & Pharmacol.*1995; 89:307-316.
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29. Desai D and **Vig PJS**. Phosphoinositide derived second messengers and calcium homeostasis in neurodegeneration. In *ATrace and Toxic Elements in Nutrition and Health*. Eds. M Abdulla, SB Vohra and M Athar. Wiley Eastern Ltd.

New Delhi. London, 1995: pp. 194-200.

30. Joshi P, **Vig PJS**, Veerisetty V, Cameron JA, Sekhon BS, Desai D. Increased nitric oxide synthase activity in daunorubicin treated rat brain *Pharmacol Toxicol* 1996; 78:99-103.
31. **Vig PJS**, Fratkin JD, Desai D, Currier RD, Subramony SH. Decreased parvalbumin immunoreactivity in surviving Purkinje cells of patients with spinocerebellar ataxia - 1. *Neurology* 1996; 47: 249-253.
32. Paulson HL, Perez MK, Trotter Y, Trojanowski JQ, Subramony SH, Das SS, **Vig P**, Mandel J-L, Fischbeck KH, Pittman RN. Intranuclear inclusions of expanded polyglutamine protein in spinocerebellar ataxia type 3. *Neuron* 1997;19: 333-344.
33. **Vig PJS**, Subramony SH, Burright EN, Fratkin JD, McDaniel DO, Desai D, Qin Z. Reduced immunoreactivity to calcium-binding proteins in Purkinje cells precedes onset of ataxia in spinocerebellar ataxia-1 (SCA-1) transgenic mice. *Neurology* 1998; 50: 106-113.
34. Subramony SH, **Vig PJS**. Clinical aspects of SCA-1. In: Wells RD, Warren ST, eds, *Genetic instabilities and hereditary neurological diseases*. San Diego: Academic Press, pp. 231-239 (1998).
35. Rao JV, Desai D, **Vig PJS**, Venkateswarlu Y, Marine biomolecules inhibit rat brain nitric oxide synthase. *Toxicol.* 129: 103-112 (1998)
36. M Pande, J A Cameron, **P J S Vig** and D Desai. Phencyclidine block of Ca²⁺ ATPase in rat heart sarcoplasmic reticula. *Toxicology* 129: 95-102 (1998).
37. **Vig, PJS**, Subramony SH, Burright EN, Fratkin JD, McDaniel DO, Desai D, Qin Z: Reduced immunoreactivity to calcium-binding proteins in Purkinje cells precedes onset of ataxia in spinocerebellar ataxia-1. *Neurology* 50(1): 106-113 (1998)
38. Subramony SH, **Vig PJS**. Clinical aspects of SCA-1. In: Wells RD, Warren ST, eds, *Genetic instabilities and hereditary neurological diseases*. San Diego: Academic Press, pp. 231-239 (1998).
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40. Pala I, Srinivasan A, **Vig P J S** and Desai D. Modulation of calmodulin and protein kinase C activities by penicillium mycotoxins. *Intl. J. Toxicology* 18 :91-

96 (1999).

41. Pande M, Cameron JA, **Vig PJS**, Ali SF, D Desai. Inhibition of calcium ATPase by phencyclidine in rat brain. *Mol Cell Biochem* 194:(1-2) 173-177 (1999).
42. Desai D, Pande M, **Vig PJS**, Cameron JA, Ali SF. In vitro and in vivo inhibition of rat brain nitric oxide synthase activity by phencyclidine. *Int. J. Toxicol.* 18, 245-250 (1999)
43. **Vig PJS**, McDaniel DO, Subramony S H, Qin Z. The effects of calbindin D-28K and parvalbumin antisense oligonucleotides on the survival of cultured Purkinje cells. *Res Commun Mol Pathol Pharmacol.* 103: (3) 249-259 (1999)
44. Subramony SH, **Vig PJS**, McDaniel DO. Dominantly inherited ataxias. *Semin Neurol* 19: (4) 419-425 (1999)
45. **Vig P J S**, Subramony SH, Qin Z, McDaniel DO, Fratkin J. Relationship between ataxin-1 nuclear inclusions and Purkinje cell specific proteins in SCA-1 transgenic mice. *J Neurol Sci.* 15; 174: (2) 100-110 (2000)
46. Feng Y, LeBlanc MH, LeBlanc EB, Parker CC, Fratkin JD, Qian XB, Patel DM, Huang M, Smith EE, **Vig PJS**. Desmethyl tirilazad improves neurologic function after hypoxic ischemic brain injury in piglets. *Crit Care Med.*, 28. 1431- 1438 (2000)
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48. Subramony SH, **Vig PJS**. Spinocerebellar ataxia 3 In: *The Cerebellum and its Disorders*. Eds: Manto M-U, Pandolfo M, Cambridge Univ. Press, pp. 428-439 (2002)
49. Logan S, Cameron JA, **Vig PJS**. Calmodulin activity in aging rat heart. *Biomed. Sci. Instrum*, 39: 561-566 (2003)
50. McDaniel DO, Barber WH, Nguyen C, Rhodes SW, May WL, McDaniel LS, **Vig PJS**, Jemeson LL Butkus DE. Combined analysis of cytokine genotype polymorphism and the level of expression with allograft function in African-American Renal Transplant Patients. *Transp Immuno* 11: 107-119 (2003)
51. Akifumi Mizutani, Lei Wang, Harini Rajan, **PJS Vig**, William A Alaynick, Joshua P Thaler and Chih-Cheng Tsai. BOAT, an AXH domain protein, suppresses the cytotoxicity of mutant ataxin-1. *EMBO J.* 24: 3339-3351 (2005).
52. **P J S Vig**, S.H. Subramony, D R D'Souza, J. Wei, M E Lopez. Intranasal

- administration of IGF-I improves behavior and Purkinje cell pathology in SCA1 mice. *Brain Res. Bull.* 69:574-579, (2006).
53. D.R. D'Souza, J. Wei, M. E. Lopez, J.D. Hebert, S.H. Subramony, **P.J.S.Vig** Tissue transglutaminase crosslinks ataxin-I: Possible role in SCA1 pathogenesis. *Neuroscience Letters* 409: 4-9 (2006)
 54. **PJS Vig**, M E Lopez, J Wei, D R D'Souza, S H. Subramony, J Henegar and J D Fratkin. Glial S-100B Vacuoles in Purkinje Cells: Earliest Morphological Abnormality in SCA1 Transgenic Mice. *J. Neurological Sci.* (Online: Free Access) 23: 166-174 (2006).
 55. Pande M, Harps A, Sundaram M, **Vig PJS**. Role of nitric oxide in domoic acid induced hippocampal degeneration. *J. Neurological Sci.* (Online: Free Access) 24: 16-24 (2007).
 56. Salameh JR, Talbott LM, May W, Gosheh B, **Vig PJS**, McDaniel DO. Role of biomarkers in incisional hernias. *Am. Surg.* 73: 561-567 (2007).
 57. Vig, PJS, Shao, Q, Lopez, ME, (2009). Glial response to polyglutamine-mediated stress. *Biosci. Hypotheses* 2, 148-150.
 58. **Vig PJS** (2009) S100B - A common connection between depression and cerebellar disorders. . *Biosci. Hypotheses* 2, 343 -344.
 59. **PJS Vig**, Q Shao, SH Subramony, M E Lopez and E Safaya, (2009) Bergmann Glial S100B activates myo-inositol monophosphatase 1 and co-localizes to Purkinje Cell Vacuoles in SCA1 Transgenic Mice. *Cerebellum* 8, 231- 244.
 60. Pentyala S, Ruggeri J, Veerajju A, Yu Z, Bhatia A, Desai D, **Vig P**, Microsomal CA^{2+} flux modulation as an indicator of heavy metal toxicity. *Indian J. of Exper. Biology* 48:737-743 (2010)
 61. Hearst S, Lopez M, Shao Q, Liu Y, **Vig PJ** (2010). Dopamine D2 receptor signaling modulates mutant ataxin-1 S776 phosphorylation and aggregation . *J. Neurochem* 1143 Aug (3):706-716
 62. Fratkin JD, **Vig PJS** (2012). Neuropathology of degenerative ataxias. *Handb Clin Neurol*, 103:111-125.
 63. **Vig PJS**, Hearst S, Shao Q, Lopez ME, Murphy II HA and Safaya S (2011). Glial S100B protein modulates mutant ataxin-1 aggregation and toxicity: TRTK12 peptide, a potential candidate for SCA1 therapy *Cerebellum* 10(2):254-266
 64. Hearst SM, Walker LR, Shao Q, Lopez M, Raucher D, **Vig PJS** (2011). The Design and Delivery of a Thermally Responsive Peptide to Inhibit S100B Mediated Neurodegeneration. *Neuroscience* 2011 Dec 1;197:369-80

65. **Vig PJS**, Wei J, Shao Q, Lopez ME, Halperin R, Gerber J. Suppression of Calbindin-D28k Expression Exacerbates SCA1 Phenotype in a Disease Mouse Model. *Cerebellum*. 2011 Nov 11. PMID: 22076800.
66. **PJS.Vig**, J Wei, Q Shao, ME Lopez, SH Subramony and R Halperin, Overexpression of IGF-I suppresses SCA1 phenotype in the transgenic mouse model. *J. Neurosci.* (Under preparation)
67. **PJS.Vig**, S. Hearst, Q Shao, ME Lopez. Effects of Angiotensin II Treatment and Acid-Sensing Ion Channel 1a Knockdown on SCA1 Purkinje Cells. (Under preparation).

Abstracts and presentations

1. **Vig PJS**, Paliwal V, Nath R. A comparative study of direct current plasma atomic emission spectrometry and atomic absorption spectrophotometry for biological monitoring of trace metals. American Chemical Society 1985, Miami, FL.
2. Nath R, Gulati S, **Vig PJS**, Gill KD. Indian Academy of Neurosciences 1986, Aligarh, India.
3. Nath R, **Vig PJS**, Gulati S, Ravi, D, Paliwal VK. Seminar on Science, Development and Environment. 1986, Muzaffarnagar, India.
4. **Vig PJS**, Ravi K, Gulati S, Sharma M, Nath R. Inhibition of calmodulin activity in brain of cadmium exposed monkeys under different nutritional stress conditions. *Toxicol Lett* 1986;31:187A.
5. **Vig PJS**, Ravi K, Gill KD, Nath R. Indian Academy of Neuroscince 1897, Tirupathi, India.
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10. Chetty CS, Rajanna B, **Vig PJS**, Desaiah D. Metal cations stimulate inositol trisphosphate receptor binding in rat cerebellum. FASEB Journal 1990;4:A1014.
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- inositol 1,4,5-trisphosphate receptors and protein kinase C activity. *The Toxicologist* 1991; 11: 331.
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 35. Joshi P, **Vig PJS**, Veerisetty V, Cameron JA, Desaiah D. Increased nitric oxide

- synthases activity in rat brain treated with daunorubicin. *FASEB Journal* 1993;7:243.
36. Uzodinma JE, Barnes P, Sekhon BS, Cameron JA, **Vig PJS**, Desai D. Increased endothelin receptor binding in spontaneously hypertensive rats. *FASEB Journal* 1993;7:550.
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 41. Vig PJS, Desai D, Sekhon BS, Houze LP, Cameron JA. Daunomycin inhibits insulin-like growth factor-I-dependent protein tyrosine phosphorylation. *FASEB Journal* 1994;8:A97.
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 45. Desai D, Joshi P, **Vig PJS**, Subramony SH, Currier RD. Cerebellar nitric oxide synthase activity in patients with spinocerebellar ataxia-1. *Neurology* 1994;44:A369.
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