

Biosketch
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Roy Ervin Twyman, M.D.

Present Position:

**Vice President, CNS Franchise Development, Clinical R&D
Johnson and Johnson Pharmaceutical Research and Development, LLC (J&JPRD)
1125 Trenton-Harbourton Rd, Titusville, NJ, USA 08560**

Education:

1978 B.S. Electrical Engineering, Purdue University, W. Lafayette, Indiana, USA
Honors Engineering and Electrical Engineering programs
1982 M.D., University of Kentucky, Lexington, Kentucky, USA
1983 Medicine Internship, University of Kentucky, Lexington, Kentucky, USA
1986 Neurology Residency, University of Michigan, Ann Arbor, Michigan, USA
Chief Resident, Neurology
1988 Neuroelectrophysiology and Epilepsy Fellowship, University of Michigan,
Ann Arbor, Michigan, USA

Academic Positions:

1977-8 Electrical Engineering Assistant
Union Carbide Corporation, Oak Ridge, Tennessee, USA
1988 Instructor, Dept. of Neurology
University of Michigan, Ann Arbor, Michigan, USA
1989 Assistant Professor, Dept. of Neurology
University of Michigan, Ann Arbor, Michigan, USA
1992 Assistant Professor, Depts. of Neurology, Pharmacology and Toxicology
Investigator, Program in Human Molecular Biology and Genetics
Investigator, Neuroscience Program
University of Utah, Salt lake City, Utah, USA
1995 Associate Professor with tenure, Depts. of Neurology, Pharmacology and Toxicology
Investigator, Huntsman Cancer Institute
Investigator, Program in Human Molecular Biology and Genetics
Investigator, Neuroscience Program
University of Utah, Salt Lake City, Utah, USA

Pharmaceutical Industry Experience:

1998-2002 Increasing responsibilities from Project Physician, Medical Leader, Clinical Leader, Neurology Franchise
Medical Leader, CNS/Pain Therapeutic Area, Clinical R&D, J&JPRD
2004 Franchise Development, CNS/Pain Therapeutic Area, Clinical R&D, J&JPRD

Other Current/Recent National and Industry-related Experience:

2005-2007 National Academy of Sciences Institute of Medicine, Drug Forum Committee – J&J representative
2006-2009 National Academy of Sciences Institute of Medicine, Neuroscience Forum Core member
2007-2008 Foundation for the National Institutes of Health, Biomarkers Consortium, Neuroscience subcommittee
2007-2011 FDA Peripheral and Central Nervous System Drugs Advisory Committee Member, Industry representative
2008 National Academy of Sciences, National Research Council, The Third Frontier Project, Committee Member

Licensures, Certifications and Patents:

1983 National Board of Medical Examiners
1988 American Board of Psychiatry and Neurology

Various Several patents on GABA receptors, autoantibodies to glutamate receptors, and those related to Johnson & Johnson compounds

Scholastic Awards and Honors:

1974 Purdue University Engineering Scholarship
1976 Eta Kappa Nu (National Electrical Engineering Honorary)
1976 Tau Beta Pi (National Engineering Honorary)
1981 Alpha Omega Alpha (National Medical Honorary)
1986-1998 American Academy of Neurology Pharmacology Award
1997&1998 University of Utah Neurology Department Teacher of the Year
1997 Elected to American Neurological Association
1998 American Epilepsy Society Merritt Putnam Symposium invited speaker

Current Professional Affiliations:

- American Neurological Association (elected 1997)
- American Academy of Neurology

Select Academic Bibliography:

Non-Industry Related, Peer Reviewed Academic Publications

- McClellan AM., Twyman R.E. Receptor system response kinetics reveal functional subtypes of native murine and recombinant human GABAA receptors. *Journal of Physiology*. 515 (Pt 3):711-27, 1999.
- Bamber B.A., Beg A.A., Twyman R.E. Jorgensen EM. The *Caenorhabditis elegans* unc-49 locus encodes multiple subunits of a heteromultimeric GABA receptor. *Journal of Neuroscience*. 19(13):5348-59, 1999.
- Donevan, S.D., Beg, A., Gunther, J.M., Twyman, R.E. The methylglutamate, SYM 2081, is a potent and highly selective agonist at kainate receptors. *J. of Pharmaceutical and Experimental Therapeutics*, 285(2):539-45, 1998.
- Lavoie, A.M., Tingey, J.J. Harrison, N.L, Pritchett, D.B., Twyman, R.E. Opening and deactivation rates of recombinant GABA-A receptor channels are dependent on alpha subunit composition. *Biophysical Journal* 73:2518-2526, 1997.
- Carlson, N.G., Gahring, L.C., Twyman, R.E. Rogers, S.W. Identification of amino acids in the glutamate receptor, GluR3, important for antibody binding and receptor activation. *Journal of Biological Chemistry*, 272: 11295-11301, 1997.
- Gahring, L.C., Rogers, S.W., and Twyman, R.E. Autoantibodies to glutamate receptor subunit GluR2 in non-familial olivopontocerebellar degeneration. *Neurology*, 48:494-500, 1997.
- Lavoie, A.M. and Twyman, R.E. Direct evidence for diazepam modulation of GABA-A receptor microscopic affinity. *Neuropharmacology* 35:1383-1392, 1996.
- Rogers, SW, Twyman, RE, Gahring, LC. (1996). The role of autoimmunity to glutamate receptors in neurological disease. *Molecular Medicine Today* 2:76-81. (Journal Cover Article)
- Gahring L.C., Twyman, R.E., Greenlee, J. and Rogers, S.W. Autoantibodies to neuronal glutamate receptors in patients with paraneoplastic neurodegenerative syndrome enhance receptor activation. *Molecular Medicine* 1:245-253, 1995. (Journal Cover Article)
- Twyman, R.E., Gahring, L.C., Spiess, J., and Rogers, S.W. Glutamate receptor antibodies activate a subset of receptors and reveal an agonist binding site. *Neuron* 14:755-762, 1995. (Journal Cover Article)
- Rogers, C.J., Twyman, R.E., Macdonald, R.L. Benzodiazepine and beta-carboline regulation of kinetic properties of the GABAA receptor channel of mouse spinal neurones in culture. *Journal of Physiology*, 475:69-82, 1994.
- Skeen, G.A., White, H.S. and Twyman, R.E. The dihydropyridine Nitrendipine reduces N-methyl - D-aspartate (NMDA)-evoked currents of rodent cortical neurons through a direct interaction with the NMDA receptor associated ion channel. *Journal of Pharmaceutical and Experimental Therapeutics*, 1994.
- Twyman, R.E. GABA-A receptor opening rates in excised patches of mouse cortical neurons. *Japanese Journal of Physiology*, 44:87-90, 1994.
- Skeen, G.A., Twyman, R.E., and White, H.S. The dihydropyridine nitrendipine modulates NMDA-mediated calcium flux into mammalian neurons. *Molecular Pharmacology* 44:443-450, 1993.
- Twyman, R.E., Green, R.M., and Macdonald, R.L. Kinetics of open channel block of GABAA receptor channels by penicillin. *Journal of Physiology* 445:97-128, 1992.

- Twyman, R.E., and Macdonald, R.L. Neurosteroid modulation of GABAA receptor single channel kinetics. *Journal of Physiology* 456:215-245, 1992.
- Porter, N.M., Angelotti, T.P., Twyman, R.E. and Macdonald, R.L. Kinetic properties of $\alpha 1\beta 1$ γ -aminobutyric acidA receptor channels stably expressed in Chinese hamster ovary cells: regulation by pentobarbital and picrotoxin. *Molecular Pharmacology* 42:872-881, 1992.
- Twyman, R.E., and Macdonald, R.L. Kinetic properties of the glycine receptor main- and sub-conductance states of mouse spinal cord neurones in culture. *Journal of Physiology* 435:303-331, 1991.
- Twyman, R.E., Rogers, C.J., and Macdonald, R.L. Intraburst kinetic properties of the GABAA receptor main conductance state of mouse spinal cord neurones in culture. *Journal of Physiology* 423:193-220, 1990.
- Porter, N.M., Twyman, R.E., Uhler, M.D., and Macdonald, R.L. Cyclic AMP-dependent protein kinase decreases GABAA receptor current in mouse spinal cord cells. *Neuron* 5:789-796, 1990.
- Twyman, R.E., Rogers, C.J., and Macdonald, R.L. Differential mechanisms for enhancement of GABA by diazepam and phenobarbital: a single channel study. *Annals of Neurology* 25:213-220, 1989.
- Twyman, R.E., Rogers, C.J., and Macdonald, R.L. Pentobarbital and picrotoxin have reciprocal actions on single GABA-Cl⁻ channels. *Neuroscience Letters* 96:89-95, 1989.
- Macdonald, R.L., Rogers, C.J., and Twyman, R.E. Kinetic properties of chloride channels gated by gamma-aminobutyric acid in mouse spinal cord neurons in cell culture. *Journal of Physiology* 410:479-499, 1989.
- Macdonald, R.L., Rogers, C.J., and Twyman, R.E. Barbiturate modulation of kinetic properties of GABAA receptor channels in mouse spinal neurons in culture. *Journal of Physiology* 417:483-500, 1989.
- Levine, S.R., Twyman, R.E., and Gilman, S. The role of anticoagulation in cavernous sinus thrombosis. *Neurology* 38:517-22, 1988.
- Richfield, E.K., Twyman, R.E., and Berent, S. Neurologic syndrome following bilateral damage to the head of the caudate nuclei. *Annals of Neurology* 22:768-71, 1987.
- Johnson, G.L., Twyman, R.E., Todd, E.P., Cottrill, C.M., and Noonan, J.A. Echocardiographic classification of complete atrioventricular canal defect. *American Heart Journal*, 101-5:612-18, 1981.

Book Chapters

- Donevan, S.D. and Twyman, R.E. "Glutamate receptors in Epileptogenesis." In *Contemporary Neuropharmacology: Pathogenesis, Neurotransmitters and Drug Action*, Gross, R.A. and Greenamyre, J.T., Eds., Humana Press, 1998.
- Macdonald R.L., Twyman RE: "Kinetic properties and regulation of GABAA receptor channels." In *Ion Channels Volume IV*, T. Narahashi (ed.), Chapt. 10, pp. 315-344, Plenum Press, New York, 1992.
- Macdonald R.L., Twyman RE, Ryan-Jastrow T, Angelotti TP: "Regulation of GABAA receptor channels by anticonvulsant and convulsant drugs and by phosphorylation." In *Workshop on the Neurobiology of Epilepsy*, P. Engle (ed.), *Epilepsy Research, Supp.* 9:265-277, 1992.
- Macdonald, R.L., Ryan-Jastrow, T., Porter, N.M., Rock, D.M. and Twyman, R.E. "Kinetic properties of NMDA receptor channels: mechanisms of CPP and MK-801 antagonism." In *Excitatory Amino Acids 1990 Symposium*, B.S. Meldrum, F. Moroni, R.P. Simon and J.H. Woods, (eds.) FIDIA Research Foundation Symposium Series, 6:329-340, Raven Press, 1991.
- Twyman, R.E. and Macdonald, R.L. "Antiepileptic drug regulation of GABAA receptor channels." In *GABA Mechanisms in Epilepsy*, G Tunnicliff, B.U. Raess, (eds.), Chapt 4, pp 89-104, Wiley Liss, New York, 1991.
- Macdonald, R.L. and Twyman, R.E. "Biophysical properties and regulation of GABAA receptor channels." In *"GABA and Inhibitory Synaptic Transmission in the Brain"*, R.W. Olsen (ed.), *Seminars in the Neurosciences*, 3:219-230, 1991.
- Macdonald, R.L. and Twyman, R.E. "GABAA/benzodiazepine and glycine receptors." In *Current Opinion in Neurology and Neurosurgery*, D.B. Calne (ed.), 4:538-543, Current Science Ltd, London, England, 1990.
- Macdonald, R.L., Twyman, R.E., Rogers, C.J., and Weddle, M.G. "Pentobarbital regulation of the kinetic properties of GABA receptor chloride channels." In *Chloride Channels and their Modulation by Neurotransmitters and Drugs*, *Biochemical Advances in Pharmacology*, Raven Press, 1988.