

## CURRICULUM VITAE OF MICHAEL GRIFFIN, Ph.D.

### Work Address

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## EDUCATION

1977 - 1983

University of California at San Francisco  
Department of Pharmacology and Toxicology  
Ph.D. degree awarded Dec. 1983 GPA 3.95

Thesis: Chronic opiate regulation of adenylate cyclase activity in neuroblastoma x glioma NG108-15 hybrid cells

1972 - 1976

University of California at San Diego  
Bachelor of Arts degree awarded Dec. 1976 GPA 3.54  
Major in Chemistry Minor in Psychology  
Specialization in Biochemistry GPA 4.00  
Honors: Magna Cum Laude, Deans List, Provosts Honor List (6)

## PROFESSIONAL EXPERIENCE

1990 - present

Current Title: Researcher Step V, Dept of Pharmacology UCI School of Medicine

Research: Comparison of Native and Cloned Muscarinic Receptors in Smooth Muscle and Genetically Altered Tissue Culture Cells. Signal transduction modeling

1999 – present: Professor

1993 – 1999 Associate Professor

1987 – 1993 Assistant Professor

Schmid School of Science and Technology, Chapman University  
One University Way Orange CA 92866 (714) 977-6864

Teaching: Courses taught: Biochemistry, Metabolic Pathways, Micronutrient Metabolism, General Chemistry I and II, Organic Chemistry, Drugs Rx Us, Toxicology, Medicinal Chemistry, Introduction to Environmental Science, Freshman Seminar, Foundations of Science and Honors Program.

1984 - 1987

Title: Postdoctoral Associate in Pharmacology

Yale University, 333 Cedar St. New Haven, CT. 06510 (203) 785-4372  
Supervisor: Dr. John Perkins, Prof./Chairman

Research: Elucidation of the molecular mechanisms responsible for the desensitization and down-regulation of  $\beta$ -adrenergic receptors in human astrocytoma 1321N1 cells.

1977 - 1983

Title: Graduate Student in the Department of Pharmacology

University of California, San Francisco San Francisco, CA. 94143 (415) 476-1951

Supervisor; Dr. Horace Loh, Prof.

Research: Elucidation of the molecular mechanisms involved in long term opiate induced increases of adenylate cyclase activity.

## **PUBLICATIONS**

27. Ehlert FJ, Suga H, Griffin MT. (2011); Quantifying agonist activity at G protein-coupled receptors. *J Vis Exp.* Dec 26;(58):e3179. doi: 10.3791/3179.

26. Ehlert FJ, Griffin MT, and Suga H (2011) Analysis of Functional Responses at G Protein Coupled Receptors: Estimation of Relative Affinity Constants for the Inactive Receptor State *J Pharmacol Exp Ther* Aug;338(2):658-70.

25. Ehlert FJ, Suga H, and Griffin MT (2011) Analysis of Agonism and Inverse Agonism in Functional Assays with Constitutive Activity: Estimation of Orthosteric Ligand Affinity Constants for Active and Inactive Receptor States. *J Pharmacol Exp Ther* Aug;338(2):671-86.

24. Griffin, M.T., Matsui, M., Ostrom, R., and Ehlert, F.J. (2009) The guinea pig ileum lacks the direct, high-potency,  $M_2$ -muscarinic, contractile mechanism characteristic of the mouse ileum. *Naunyn-Schmied Arch Pharmacol* Oct: 380(4):327-335

23. Figueroa K.W., Griffin M.T., and Ehlert F.J. (2009) Selectivity of Agonists for the Active State of  $M_1$  to  $M_4$  Muscarinic Receptor Subtypes. *J Pharmacol Exp Ther.* Jan;328(1):331-42.

22. Ehlert, F.J., and Griffin, M.T., (2008) Two-State Models and the Analysis of the Allosteric Effect of Gallamine at the  $M_2$  Muscarinic Receptor. *J Pharmacol Exp Ther.* 325(3):1039-60.

21. Griffin, M.T., Figueroa, K.W., Liller, S., and Ehlert, F.J. (2007) Estimation of Agonist Activity at G Protein Coupled Receptors: Analysis of  $M_2$  Muscarinic Receptor Signaling Through  $G_{i/o}$ ,  $G_s$  and  $G_{15}$ . *J. Pharmacol. Exp. Ther.* 321:1193-1207

20. Ehlert, F.J., Griffin, M.T., Abe, D.M., Vo, T.H., Taketo, M.M., Manabe, T., and Matsui, M. (2005)  $M_2$  Muscarinic Receptors Mediate Contraction through Indirect Mechanisms in Mouse Urinary Bladder. *J. Pharmacol. Exp. Ther.* 313: 368-378

19. Ehlert, F.J., Ching-Hsuan, J., Leung, K., Lee, A.G., Shehnaz, D., and Griffin, M.T. (2005) Comparison of the Antimuscarinic Action of *p*-Fluorohexahydrosiladifenidol in Ileal and Tracheal Smooth Muscle *J. Pharmacol. Exp. Ther.* 312: 592-600

18. Griffin, M.T., Matsui, M., Shehnaz, D., Ansari, K.Z., Taketo, M.M., Manabe, T., and Ehlert, F.J. (2004) Muscarinic Agonist-Mediated Heterologous Desensitization in Isolated Ileum Requires Activation of Both Muscarinic M<sub>2</sub> and M<sub>3</sub> Receptors. *J. Pharmacol. Exp. Ther.* 308: 339-349
17. Matsui, M., Griffin, M.T., Shehnaz, D., Taketo, M.M., and Ehlert, F.J. (2003) Increased Relaxant Action of Forskolin and Isoproterenol Against Muscarinic Agonist-Induced Contractions in Smooth Muscle from M<sub>2</sub> Receptor Knockout Mice. *J. Pharmacol. Exp. Ther.* 305:1: 106-113
16. Griffin, M.T., Hsu, J.C., Shehnaz, D., and Ehlert, F.J.: (2003) Comparison of Pharmacological Antagonism of M<sub>2</sub> and M<sub>3</sub> Muscarinic Receptors Expressed in Isolation and in Combination. *Biochem. Pharmacol* 65: 1227-1241
15. Ehlert, F.J., Ansari, K.Z., Shehnaz, D., Sawyer, G.W., and Griffin, M.T. (2001) Acetylcholine-Induced Desensitization of the Muscarinic Contractile Response in Guinea-Pig Ileum is Inhibited by Pertussis Toxin Treatment. *J. Pharmacol. Exp. Ther.* 299:3: 1126-1132
14. Ehlert, F.J. and Griffin, M.T. (2001) Estimation of Agonist Activity and Relative Efficacy at G Protein-coupled Receptors: Mutational Analysis and Characterization of Receptor Subtypes. *Analytical Pharmacology* 2; 1: 34-47
13. Ehlert, F.J., Griffin, M.T., Sawyer, G.W., and Bailon, R. (1999): A Simple Method for Estimation of Agonist Activity at Receptor Subtypes: Comparison of Native and Cloned M<sub>3</sub> Muscarinic Receptors in Guinea Pig Ileum and Transfected Cells. *J. Pharmacol. Exp. Ther.* 289; 981-992
12. Ehlert, F.J. and Griffin, M.T. (1998): The Use of Irreversible Ligands to Inactivate Receptor Subtypes: 4-DAMP Mustard and Muscarinic Receptors in Smooth Muscle. *Life Sciences* 62; 1659-1664
11. Ehlert, F.J., Griffin, M.T., and Glidden, P. (1996): The Interaction of the Enantiomers of Aceclidine with Subtypes of the Muscarinic Receptor. *J. Pharmacol. Exp. Ther.* 279; 1335-1344
10. Esqueda, E.E., Gerstin, E.H., Griffin, M.T., Ehlert, F.J. (1996): Stimulation of cAMP Accumulation and Phosphoinositide Hydrolysis by M<sub>3</sub> Muscarinic Receptors in the Rat Peripheral Lung. *Biochem Pharmacol.* 52; 643-658
9. Ehlert, F.J., Oliff, H.S., and Griffin, M.T. (1996): The Quaternary Transformation Products of N-(3-Chloropropyl)-4-Piperidinyl Diphenylacetate and 4-DAMP Mustard Have Differential Affinity for Subtypes of the Muscarinic Receptor. *J. Pharmacol. Exp. Ther.* 276; 405-410
8. Griffin, M.T., Thomas, E.A., and Ehlert, F.J. (1993): Kinetics of Activation and *In Vivo* Muscarinic Receptor Binding of N-(2-Bromoethyl)-4-Piperidinyl Diphenylacetate; an Analogue of 4-DAMP Mustard. *J. Pharmacol. Exp. Ther.* 266; 301-305
7. Griffin, M.T. and Ehlert, F.J. (1992) ; Specific Inhibition of Isoproterenol-Stimulated Cyclic AMP Accumulation by M<sub>2</sub> Muscarinic Receptors in Rat Intestinal Smooth Muscle. *J. Pharmacol. Exp. Ther.* 263: 221-225

6. Thomas, E.A., Hsu, H.H., Griffin, M.T., Hunter, A.L., and Ehlert, F.J. (1992): Conversion of N-(2-Chloroethyl)-4-piperidinyl Diphenylacetate (4-DAMP Mustard) to an Aziridinium Ion and Its Interaction with Muscarinic Receptors in Various Tissues. *Mol Pharmacol.* 41: 718-726
5. Griffin, M.T., Law, P.Y. and Loh, H.H. (1986): Effect of Phospholipases on Chronic Opiate Action in Neuroblastoma x Glioma NG108-15 Hybrid Cells. *J. Neurochem.* 47: 1098-1105
4. Griffin, M.T., Law, P.Y. and Loh, H.H. (1985): Involvement of Both Inhibitory and Stimulatory Guanine Nucleotide Binding Proteins in the Expression of Chronic Opiate Regulation of Adenylate Cyclase Activity in NG108-15 Cells. *J. Neurochem.* 45: 1585-1589
3. Griffin, M.T., Law, P.Y. and Loh, H.H. (1985): Neuroblastoma x Glioma NG108-15 Hybrid Cells Cultured in Serum-Free Chemically Defined Medium: Effects on Acute and Chronic Opiate Regulation of Adenylate Cyclase Activity. *Brain Res.* 360: 370-373
2. Griffin, M.T., Law, P.Y. and Loh, H.H. (1983): Modulation of Adenylate Cyclase Activity by an Endogenous Cytosolic Factor Following Chronic Opiate Exposure in Neuroblastoma x Glioma NG108-15 Hybrid Cells. *Life Sci.* 33: 365-368
1. Law, P.Y., Griffin, M.T., Koehler J.E. and Loh, H.H. (1983): Attenuation of Enkephalin Activity in Neuroblastoma x Glioma NG108-15 Hybrid Cells by Phospholipases. *J. Neurochem.* 40: 267-275

## **BOOK CHAPTERS**

- Ehlert FJ, Pak KJ, Griffin MT. (2012); Muscarinic agonists and antagonists: effects on gastrointestinal function. *Handb Exp Pharmacol.* (208):343-74.
- Ehlert, F.J., Thomas, E.A., Gerstin, E.H., Griffin, M.T. (1997): Muscarinic Receptor Subtypes in Smooth Muscle pp 87-147 ed. Eglen, R.M., CRC Press, Boca Raton, LA 87-147
- Law, P.Y., Griffin, M.T. and Loh, H.H. (1984): Mechanisms of Multiple Cellular Adaptation Processes in Clonal Cell Lines During Chronic Opiate Treatment. In: NIDA Research Monograph 54 (Mech. Tolerance Depend): 119-135

## **PAPERS/POSTERS/ABSTRACTS PRESENTED**

18. Effect of McN-A-343 on adenylate cyclase activity in CHO cells transfected with the M<sub>2</sub> and M<sub>3</sub> muscarinic receptors. Southern California American Chemical Society Undergraduate Research Conference. Chapman University April 24, 2010. Beatty, J. Taylor, K. and Griffin, M.T.
17. Selectivity of Agonists For The Active State of M<sub>1</sub>-M<sub>4</sub> Receptor Subtypes.

52<sup>nd</sup> Annual Western Pharmacology Society Meeting Acapulco, Mexico February 8 – 12<sup>th</sup> 2009  
Figueroa, K.W., Griffin, M. and Ehlert, F.J.

16. The Tandem Two-Site Model Explains Affinity-Only Modulation of Agonist Activity by Gallamine at the M<sub>2</sub> Muscarinic Receptor. Neuroscience Meetings San Diego, CA Nov 4-7, 2007  
Ehlert F.J., Griffin M. T.

15. McN-A-343 Directs Signaling Through the M<sub>2</sub> Muscarinic Receptor-G(α15) Complex Relative to that of G(i) FASEB Meetings, Washington DC. May 1-4, 2007 The FASEB Journal 21; 570.5  
Ehlert, F.J., Griffin, M.T., and Figueroa, K.W.

14. Coupling of Muscarinic Receptor Subtypes to Phosphoinositide Hydrolysis in Mouse Ileum and Urinary Bladder. Neurosciences Meeting Nov 8-12, 2005 Washington D.C.  
Tran, J.A., Matsui, M., Griffin, M.T., and Ehlert, F.J.

13. Contractile Role of M<sub>2</sub> Muscarinic Receptors in Urinary Bladder Smooth Muscle. Annual Meeting for the International Incontinence Society. Paris, France Aug 23-26, 2004  
Ehlert F, Griffin M, Manabe T, Taketo M, Matsui M

12. Can M<sub>2</sub> Receptors Stimulate Phospholipase C Activity? Southern California American Chemical Society Undergraduate Research Conference Loyola Marymount University April 24, 2004. Student presenter: Amy Gustafson

11. Role of M<sub>2</sub> and M<sub>3</sub> Muscarinic Receptors in Short-Term Desensitization of the Contractile Response in Isolated Ileum Neurosciences Meeting Nov 8-12, 2003 New Orleans, LA  
Griffin, M.T., Matsui, M, Shehnaz, D., Ansari, K.Z., Taketo, M.M., Manabe, T., Ehlert, F.

10. Pharmacological characterization of a Cell Line Expressing both M<sub>2</sub> and M<sub>3</sub> Muscarinic Receptors. 2001 Neurosciences Meeting Nov 11-14, 2001 San Diego, CA

9. Acetylcholine-Mediated Desensitization of Muscarinic Agonist-Induced Contraction in the Guinea Pig Ileum is Prevented by Pertussis Toxin. The Ninth International Symposium Subtypes of Muscarinic Receptors Nov 12-15, 2000 Houston, Texas Abstract published in Life Sciences

8. Characterization of Muscarinic Agonists with Equiactive Molar Ratios: Comparison of Native and Cloned M<sub>3</sub> Receptors in Guinea Pig Ileum and CHO Cells. Abstract presented at Western Pharmacology Meetings Jan 21-27, 1998 Mazatlan Mexico.

7. The Interaction of the Enantiomers of Aceclidine with Subtypes of the Muscarinic Receptor. The Seventh International Symposium Subtypes of Muscarinic Receptors Nov 12-15, 1996 Vienna, Virginia Abstract published in Life Sciences

6. Kinetics of solvolysis and *in vivo* muscarinic receptor binding of N-(2-bromoethyl)-4-piperidinyl diphenylacetate; an analogue of 4-DAMP mustard. The Fifth International Symposium Subtypes of Muscarinic Receptors Oct 22-24, 1992 Newport Beach, CA Abstract published in Life Sciences Vol 52: 587

5. Inhibition of cyclic AMP accumulation in rat intestinal smooth muscle slices by oxotremorine-M. The American Society for Pharmacology and Experimental Therapeutics Meetings Aug 20-24, 1991 San Diego, CA
4. Specific Inhibition of Isoproterenol-Stimulated Cyclic AMP Accumulation by M<sub>2</sub> Muscarinic Receptors in Rat Intestinal Smooth Muscle. UCI Pharmacology Symposium April 1991 Newport Beach CA
3. Acute and chronic opiate regulation of adenylate cyclase in NG108-15 cells. Western Pharmacology Society Feb. 4-8, 1984 Reno, NV.
2. Regulation of adenylate cyclase by a cytosolic factor following chronic opiate treatment in NG108-15 hybrid cells. International Narcotic Research Conference June 26-30, 1983 Garmisch, Germany
1. Membrane lipid modification of chronic opiate effects in NG108-15 cells. Federation of American Societies for Experimental Biologists April 4-8, 1982 New Orleans, LA.

## **PROFESSIONAL ASSOCIATIONS**

Society for Neuroscience  
 American Association of University Professors

## **AWARDS and FELLOWSHIPS**

Chapman Faculty Research Award 2012, 2011, 2010, 2009, 2008, 2006, 2004, 2001, 1999, 1998, 1997, 1994, 1989, 1988  
 Co-investigator NIH/National Institute of General Medical Sciences (NIGMS) R01 GM69829  
 Title: Agonist activity at G-protein coupled receptors \$640,000 2005-2009  
 Co-investigator National Institutes of Health Grant PHS-NIH Neurological Disorder and Stroke NS-30882 Title: Autonomic Muscarinic Receptor Signaling Mechanisms \$644,725 1997-2001  
 Co-investigator National Institutes of Health Grant R01 NS-30882-01 \$538,456 1992-96  
 Faculty Sponsored Student Research Award 2003-2004  
 Grant in Aid Award 2003-2004  
 Hua-Cheng Wang Fellowship 1991-1993  
 Chapman University Scudder Award, 2001  
 Chapman University Excellence Award 1994  
 Residence Life Faculty Appreciation Award 2006  
 National Research Service Award T32 NS07166-05 1984-1985  
 National Research Service Award T32 GM07175-03-07 1979-1983  
 Earl C. Anthony Patent Fund Award 1982-1983  
 Pharmaceutical Manufacturers Association Foundation Award (PMAF) 1982

## **REFERENCES**

Dr. John Perkins, Prof., Dean

Dr. Fred Ehlert, Professor

Southwestern Graduate School  
U of Texas Southwestern Medical Center  
5323 Harry Hines Blvd  
Dallas, TX 75235 - 9041  
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