COLLEEN E. CLANCY, Ph.D.
Department of Physiology and Biophysics
Institute for Computational Biomedicine
Weill Medical College of Cornell University
1305 York Avenue BOX 140
New York, NY 10021
646-962-6374
clc7003@med.cornell.edu

POSITIONS HELD

Weill Medical College of Cornell University, New York, NY
Assistant Professor of Medicine. 2005 –
Assistant Professor of Physiology and Biophysics, and the Institute for Computational Biomedicine. 2004 –
Theoretical approaches to structure-function relationships in cardiac and neuronal ion channels.
Systems integration: from gene to disease.

Columbia University, New York, NY
Associate Research Scientist. Department of Pharmacology. 2003-2004
Structure-function relationships in neuronal and cardiac ion channels using computational and experimental approaches.

EDUCATION

Columbia University, New York, NY
Postdoctoral training. Department of Pharmacology. August 2001-2003
Laboratory of Dr. Robert Kass.
Structure-function relationships in cardiac ion channels using computational and experimental approaches.

Case Western Reserve University, Cleveland, OH
Ph.D. Department of Physiology and Biophysics. 2001
Laboratory of Dr. Yoram Rudy.
Dissertation: Computational models of congenital abnormalities in ion channels: Linking defects to abnormal cellular function.

Union College, Schenectady, NY
B.S. Mathematics and Biology 1994
Honors research in Biology
Laboratory of Dr. Joseph Salvo.
Thesis: Bioremediation of polychlorinated biphenyls (PCBs) by indigenous microorganisms.

PUBLICATIONS:

• Xu, J. and **Clancy, C.E**. "Ionic Mechanisms of Bursting in CA3 Hippocampal Pyramidal Neurons: A Model Study". *In revision.*

• **Clancy, C.E.,** Zhu, Z. I., and Rudy, Y. "Pharmacogenetics and anti-arrhythmic drug therapy: A theoretical investigation"**. American Journal of Physiology.** 2007. Jan;292(1):H66-75.

• Choe, C.U., Schulze-Bahr, E., Neu, A., Xu, J., Zhu, Z.I., Sauter, K., Bahring, R., Priori, S., Guicheney, P., Monnig, G., Neapolitano, C., Heidemann, J., **Clancy, C.E**., Pongs, O., Isbrandt, D. C-terminal HERG (LQT2) mutations disrupt IKr channel regulation through 14-3-3. ***Human Molelcular Genetics****.* 2006. 15(19):2888-902.

• Zhu, Z. I., and **Clancy, C.E.** Invited editorial. "From mutation to clinical presentation: Mechanisms in the black box". ***Journal of Molecular and Cellular Cardiology.*** 2005. 38(6):965-8.

• Terrenoire*, C., **Clancy*, C.E.,** Cormier*, J.W., Sampson, K. and R.S. Kass. "Autonomic control of cardiac action potentials; Role of potassium channel kinetics in response to sympathetic stimulation". ***Circulation Research (ultrarapid communication).*** *2005*. 96(5):e25-3. **equal contribution*

• Royer A., Demolombe, S., El Harchi, A., Le Quang, K., Piron, J., Toumaniantz, G., Mazurais, Bellocq, C., Lande, G., Terrenoire, C., Motoike, H.K., Chevallier, J., Loussouarn, G., **Clancy, C.E.,** Escande, D., Charpentier, F. "Expression of human ERG K+ channels in the mouse heart exerts anti-arrhythmic activity. ***Cardiovascular Research****. 2005*. 65(1):128-37.

• **Clancy,C.E.** and R.S. Kass. Invited review. "K^+ and Na^+ cardiac ion channel mutations: from DNA to ECG." ***Physiological Reviews****. 2005*. 85: 33-47.

`• **Clancy,C.E.** and R.S. Kass. "Theoretical investigation of the neuronal Na^+ channel SCN1A: Abnormal gating and epilepsy." ***Biophysical Journal****. 2004. 86(4): 2606-14.*

• Tateyama, M., Rivolta, I., **Clancy, C.E.** and Kass, R.S. Modulation of cardiac Na^+ channel gating by protein kinase A in disease-linked mutations. ***Journal of Biological Chemistry****. 2003. 278(47): 46718-46726.*

• **Clancy,C.E.** and R.S. Kass. Invited review. "Pharmacogenomics and Epilepsy." ***Pharmacogenomics.*** *2003 Nov;4(6): 747-51*.

• Glaaser, I.W., Kass, R.S. and **Clancy, C.E.** Invited review. Mechanisms of Genetic Arrhythmias: from DNA to ECG. ***Progress in Cardiovascular Diseases****. 2003. 46(3): 259-70.*

• **Clancy, C.E.**, Tateyama, M., Liu, H., Wehrens, X.H.T. and Kass, R.S. Non-equilibrium gating in cardiac Na^+ channels: an original mechanism of arrhythmia. ***Circulation****. 2003, Vol. 107:2233-2237.*

• Liu, H., **Clancy,C.E.**, Cormier, J.W. and Kass, R.S. Invited review. Mutations in Cardiac Sodium Channels: Clinical Implications. ***American Journal of Pharmacogenomics***. *2003;3(3):173-9.*

• **Clancy,C.E.**, Kurokawa, J., Tateyama, M., Wehrens, X.H.T. and Kass, R.S. Invited review. K^+ channel structure-activity relationships and mechanisms of drug-induced QT prolongation. ***Annual Review of Pharmacology and Toxicology***. *2003, Vol. 43:441-461.*

• **Clancy,C.E.** and R.S. Kass. Invited commentary, "Defective cardiac ion channels: from mutations to clinical syndromes." ***Journal of Clinical Investigation****. 2002:110 (1075-77).*

• Splawski, I., Timothy, K., Tateyama, M. **Clancy, C.E.,** Malhotra, A., Beggs, A., Cappuccio, F., Sagnella, G.A. Kass, R.S., and Keating, M.T. African sodium channel polymorphism implicated in sudden death from cardiac arrhythmias. ***Science****. 2002:297:1333-1336.*

•**Clancy, C.E**., Tataeyama, M. and Kass, R.S. Novel insights into the molecular mechanisms of bradycardia-triggered arrhythmias in the Long QT-3 syndrome. ***Journal of Clinical Investigation.*** *2002:110:1251-1262.*

• Rivolta, I., **Clancy, C.E**., Tateyama, M., Liu, H., Priori, S.G., and Kass, R.S. A novel LQT-3 mutation (I1768V): evidence for LQT-3 phenotypic heterogeneity. ***Physiological Genomics*** *2002:10: 191-197.*

• Liu, H., Tateyama, M., **Clancy, C.E.**, Abriel, H. and Kass, R.S. Channel openings are necessary but not sufficient for use-dependent block of cardiac Na^+ channels by flecainide: evidence from the analysis of disease-linked mutations. ***Journal of General Physiology***. *2002 Jul;120(1):39-51.*

• **Clancy, C.E.** and Rudy, Y. A Na^+ channel mutation that causes both Brugada and Long-QT syndrome phenotypes: A simulation study of mechanism. ***Circulation****: 2002:105:1208-1213.*

• Nuyens, D., Stengl, M., Dugarmaa, S., Rossenbacker, T. Compernolle, V., Rudy , Y., Smits J.F., Flameng, W., **Clancy , C.E**. , Moons, L., Vos, M.A., Dewerchin, M., Benndorf, K., Collen, D., Carmeliet, E. and Carmeliet, P. Sudden heart rate accelerations or premature beats cause life threatening arrhythmias in mice with Long-QT3 syndrome. ***Nature Medicine****. 2001: 7:9. 1021-1027.*

• **Clancy, C.E.** and Rudy, Y. Cellular consequences of HERG mutations in the Long QT Syndrome: Precursors to sudden cardiac death*.* ***Cardiovascular Research***. *2001:50:2. 301-313.*

• **Clancy, C.E.** and Rudy, Y. Linking a genetic defect to its cellular phenotype in a cardiac arrhythmia. ***Nature****. 1999: 400. 566-569.*

• **Clancy, C.E.,** Mendoza, M.G., Naismith, T.V., Kolman, M., and Egelhoff, T.E. Identification of an MHCK A-related myosin kinase in *Dictyostelium*. ***Journal of Biological Chemistry***. *1997:272: (18) 11812-11815.*

• **Clancy, C.E.,** and M.Frame. Fractal geometry of restricted sets of circle inversions. ***Fractals***. *1996:3:689-99.*

BOOKS and BOOK CHAPTERS:

Clancy C.E. and Kass R.S**. Editors.** Handbook of Experimental Pharmacology: "Basis and Treatment of Cardiac Arrhythmias." Springer-Verlag GmbH & Co. KG. Berlin Heidelberg. 2006.

Glaaser, I.W. and **Clancy, C.E.** Chapter, "Cardiac Na+ channels as therapeutic targets for antiarrhythmic agents" in: Handbook of Experimental Pharmacology: "Basis and Treatment of Cardiac Arrhythmias." Springer-Verlag GmbH & Co. KG. Berlin Heidelberg. 2006.

INVITED PRESENTATIONS:

Thomas Jefferson University - Computational Biology Afternoon Tea (CBAT) Seminar Series. "Mutations and electrical disease: Insights from model studies" Philadelphia, PA. May 2007**.**

International Society of Electrocardiology (ISCE). Session: "Genetic Mutations and Arrhythmia: Simulation from DNA to ECG". Cancun, Mexico. April, 2007.

Mount Sinai School of Medicine, Department of Pharmacology and Systems Therapeutics. "Theoretical approaches to pharmacogenetics and antiarrhythmic therapy". New York, NY. April, 2007.

Universitaet Hamburg - Universitaetsklinikum Eppendorf. "Genetic defects and electrically based diseases: Insights from theoretical models". Hamburg, Germany. March 2007.

Weill Cornell Medical College in Qatar. "Phamarcogenomics and antiarrhythmia therapy: Insights from theory". Doha, Qatar. November 2006.

Mathematical Biosciences Institute: Cardiac Electrophysiology and Arrhythmia Program. Subtleties of Na^+ channel gating revealed by theoretical modeling: Understanding genetic perturbations and disease". Columbus, OH. September 2006.

National Institutes of Health NHLBI/ORD Workshop on Rare Inherited Arrhythmias. "Mechanisms of Arrhythmia Caused by Na+ Channel Mutations: Insights From Theoretical Models". Bethesda, MD. September 2006.

Kavli Institute for Theoretical Physics: Cardiac Dynamics Program. "Ion channelopathies: from mutation to ECG". Santa Barbara, CA. July 2006.

Gordon Research Conference: Cardiac Regulatory Mechanisms. " Genetics and arrhythmia mechanisms: Insights from theoretical models". Colby Sawyer College. New London, NH. July 2006.

Weill Cornell Medical College in Qatar. "Math instead of Mice: Computational Biology, Genetics and Disease". Doha, Qatar. October 2005.

Cornell University, Department of Biological Sciences. Departmental Seminar. " Genetics and sudden cardiac death: Insights from computational biology". Ithaca, NY. October 2005.
Yale University, Department of Mathematics. Math Career Forum Inaugural Lecture. "Math instead of Mice: Computational Biology, Genetics and Disease". New Haven, CT. April 2005.
State University of New York Downstate Medical Center. Special Seminar in Computational Biomedicine. "From genetic mutations to clinical syndromes: Insights from theoretical models". Brooklyn, New York. January 2005.
Cardiostim 2004 "14th World Congress on Cardiac Electrophysiology and Cardiac Techniques". Arrhythmogenic consequences of potassium channel mutations. Nice, France. June 2004.
Cardiostim 2004 "14th World Congress on Cardiac Electrophysiology and Cardiac Techniques". Models of genetic sudden death. Nice, France. June 2004.
INSERM U533 Faculté de Médecine. "Ion channels and Disease: Insights from theoretical models". Nantes, France. December 2003.
Kavli Institute for Theoretical Physics Program on "Pattern Formation in Physics and Biology". Modeling ventricular arrhythmias. Santa Barbara, CA. October 2003.
Kavli Institute for Theoretical Physics Program on "Pattern Formation in Physics and Biology". Sodium channel kinetics. Santa Barbara, CA. October 2003.
American Heart Association 75th Scientific Sessions. Understanding consequences of sodium-channelopathies with the use of mathematical models. Chicago, IL. November 2002.
Biomedical Engineering Society Meeting. "Long-QT Syndromes: Theoretical exploration of kinetics". Durham, NC. October 2001.
Medical Biotechnology Center. University of Maryland. "Computational models of molecular defects in ion channels". Baltimore, MD. December 2000.
Physiome Sciences. "Linking congenital defects to abnormal cellular function". Princeton, NJ. November 2000.

ABSTRACTS:

• Zhu, Z. and **Clancy, C.E**. 2006. L-type Ca2+ channels and T-wave alternans: Insights from disease-linked mutations and theoretical modeling. Oral Presentation at Heart Rhythm Society Meeting. Boston, MA.

• Xu, J. and **Clancy, C.E**. 2006. A role for complex hippocampal dendritic branching in epilepsy triggers. Biophysical Society Meeting. Salt Lake City, UT.

• Xu, J. and **Clancy, C.E**. 2005, A Theoretical Investigation of bursting in CA3 hippocampal neurons. Society for Neuroscience Annual Meeting. Baltimore, MD.

• Cormier, J.W., Sampson, K.J., **Clancy, C. E**., et al. 2005. Targeted regulation of IKs during adrenergic control of cardiac electrical activity: a computational study. Biophysical Society Meeting. 88 (1): 10A-10A Part 2 Suppl.

•**Clancy, C.E**., Terrenoire, C. and Kass, R.S. 2004. A Long-QT mutation alters the response of I_{Ks} to β-adrenergic stimulation and disrupts action potential adaptation: A simulation study. Molecular Biology of Cardiac Disease. Keystone Symposia, Keystone, CO.

•**Clancy, C.E**., and Kass, R.S. 2003. Theoretical investigation of a mutation underlying epilepsy in the brain Na+ channel SCN1A. Biophysical Society Meeting. San Antonio, TX.

•**Clancy, C.E**. 2002. Cardiac sodium channel mutations: Insights from theoretical models. American Heart Association 75th Scientific Sessions. Chicago, IL.

•**Clancy, C.E**., Wehrens, X.H.T, Rivolta, I., Tataeyama, M. and Kass, R.S. 2002. Investigation of cardiac SCN5A inactivation gating: Insights from mutations implicated in the Long-QT Syndrome. Biophysical Society Meeting. San Francisco, CA.

•**Clancy, C.E**., Tataeyama, M. Rivolta, I., and Kass, R.S. 2002. The mechanism of rate dependence the non-inactivating component of the cardiac I_{Na}. Biophysical Society Meeting. San Francisco, CA.

• Wehrens, X.H.T., Rossenbacker, T., **Clancy, C.E**., Jongbloed, R.J.E., Vos, M.A., Doevendans, P.A., Kass, R.S. 2002. A novel mutation L619F in the cardiac Na+ channel SCN5A underlies Long-QT Syndrome (LQT3): A role for the II-III linker in inactivation gating. Biophysical Society Meeting. San Francisco, CA.

• **Clancy, C.E.** and Rudy, Y. 2000. A single mutation in the cardiac sodium channel is sufficient to cause both the Brugada and Long-QT syndrome phenotypes. Platform presentation. American Heart Association 73rd Scientific Session. New Orleans, LA.

• **Clancy, C.E.** and Rudy, Y. 2000. A single channel based model of cardiac I_{Kr} and its role in action potential repolarization. Poster presentation. World Congress on Medical Physics and Bioengineering. Chicago, IL.
• **Clancy, C.E.** and Rudy, Y. 2000. Theoretical investigation of the effects of LQT2 mutations on the cardiac ventricular action potential. Poster presentation. Biophysical Society Meeting. New Orleans, LA.
• **Clancy, C.E.** and Rudy, Y. 1999. The cellular electrophysiological consequences of the DKPQ sodium channel mutation in the long-QT syndrome. Platform presentation. Biophysical Society Meeting. Baltimore, MD.
• Naismith, T.N., Kolman, M.K., **Clancy, C.E.,** and Egelhoff, T.E. 1997. Family of novel protein kinases participates in control of myosin localization in *Dictyostelium*. American society of cell biology. Bethesda, MD.
• **Clancy, C.E.,** and Frame, M. 1995. Symbolic dynamics and grammatical complexity of circle inversion groups. Northeast Dynamics Meeting. University of Hartford, West Hartford, CT.
• Frame, M. and **Clancy, C.E.** 1995. Fractal geometry of restricted sets of circle inversions. The Mandelbrot Symposium. Curacao, Dutch Antilles.
• Frame, M. and **Clancy, C.E.** 1995. Fractal footprints of chaos. AMS/MAA National meeting: Special session on fractal geometry and chaotic dynamics. San Francisco, CA.
• **Clancy, C.E.,** and M. Frame. 1994. Fractal characteristics of the limit sets of families of circle inversions. Steinmetz Symposium on Undergraduate Research. Schenectady, NY.
• **Clancy, C.E.,** and K. Fish. 1994. Bioremediation of polychlorinated biphenyls (PCBs) by Woods Pond microorganisms. Steinmetz Symposium on Undergraduate Research. Schenectady, NY.
• **Clancy, C.E.,** and M. Frame. 1994. Fractal characteristics of the limit sets of inversion groups. Hudson River Undergraduate Mathematics Conference. Loudonville, NY.

RESEARCH PROJECTS ONGOING OR COMPLETED DURING THE LAST 3 YEARS:

"Ionic Mechanisms of Epilepsy" (07/01/04 - 06/31/05)
Principal Investigator: Colleen E. Clancy
Institution: Weill Medical College of Cornell University
Agency and Type: National Epilepsy Foundation. Junior Investigator Research Grant.
Summary: This proposal aims to define a role for neuronal Na+ channels in hippocampal CA3 excitability and epilepsy

"Mechanisms of sinoatrial node excitability: A role for Na+ channels" (7/05/05- 06/31/08)
Principal Investigator: Colleen E. Clancy
Institution: Weill Medical College of Cornell University
Agency and Type: American Heart Association. Heritage Affiliate. Scientist Development `Grant.
Summary: This proposal aims to define a role for neuronal Na+ channels central and peripheral sinoatrial nodal pacemaking.

"Computational approaches to genetic disease" (10/01/05 - 09/31/07)
Principal Investigator: Colleen E. Clancy
Institution: Weill Medical College of Cornell University
Agency and Type: Alfred P. Sloan Foundation. Research Fellow in Computational Molecular Biology
Summary: This proposal aims develop anatomically complex hippocampal CA3 model neurons.

"Theoretical Investigation of T-wave Alternans: Connecting the L-type Calcium Channel to Arrhythmia" (07/01/06 - 06/31/08)
Principal Investigator: Zheng I. Zhu
Mentor: Colleen E. Clancy
Institution: Weill Medical College of Cornell University
Agency and Type: American Heart Association. Heritage Affiliate. Post-doctoral Fellowship.
Summary: The project aims to understand Ca2+ channel mutations and T-wave alternans.

"Pharamacogenomics and antiarrhythmic therapy" (04/01/07 - 03/31/12)
Principal Investigator: Colleen E. Clancy
Institution: Weill Medical College of Cornell University
Agency and Type: National Institutes of Health, NHLBI R01 HL085592.
Summary: The project aims to develop computational models of antiarrhythmic therapy.

HONORS AND PROFESSIONAL ACTIVITIES

1999. Best in Cardiovascular Research. Research Day, Case Western Reserve University.
1999. Service to the community. Given by Superior Elementary School. East Cleveland, Ohio.
1999. Outstanding Service Award. Association of Cleveland Physiologists and the Department of Physiology and Biophysics.
1999-2001 NIH trainee. T32 HL07887-03. Heart-Lung Physiology.
2001. "Rising Stars: Ph.D.'s to watch": "Physiologist Models the Human Heart and Reaches Out as a Mentor," by Ana Marie Cox. The Chronicle of Higher Education, 7 September 2001.
2002. Feature profile, "Math of the heart" in Union College Alumni Magazine.
2005–06. Alfred P. Sloan Foundation. Research Fellow in Computational Molecular Biology. "Computational approaches to genetic disease".
2006. Invited Chair. Heart Rhythm Society Meeting. Session: "Simulating Physiologic Processes: What Do We Learn". Boston, MA
2006. Invited Participant NHLBI / NIH Office of Rare Diseases (ORD) Workshop on Recognition and Treatment of Rare Inherited Arrhythmias. Bethesda, MD
2006-7. Session organizer and Invited Chair. International Society of Electrocardiology (ISCE). Session: "Computer Simulations: From Ion-Channels to the Electrocardiogram". Cancun, Mexico.
2007. Session organizer and Participant in NIH NHLBI Workshop on "Systems Approach to Understanding Electromechanical Activity in the Human Heart". Bethesda, MD

TEACHING EXPERIENCE

• Molecules, Genes and Cells. Post lecture conferences and small group conferences for medical students. Weill Cornell Medical College in Qatar. Doha, Qatar. 2005, 2006.
• Physiological genomics of the cardiovascular system. Lecture on gene regulation of ion channels and arrhythmia. Weill Medical College of Cornell University. Spring 2005.
• Molecules, Genes and Cells. Small group conferences for medical students. Weill Medical College of Cornell University. 2004, 2005, 2006
• Congenital Long-QT Syndrome. Small group lecture for medical students. Columbia University. Nov. 2003.
• Part-time faculty at Cleveland State University. Department of Collegiate Studies. MTH087 and MTH088. Jan. 1999- Dec. 2000.
• Cardiac Electrophysiology and LQTs. Small group lecture for 1st year medical students. CWRU. Dec. 2000.
• Founder and Director. Tutoring program for science and math education enrichment in elementary students at Superior Elementary, East Cleveland. Recruitment and organization of 40+ tutors for individual mentoring in order to improve performance on the Ohio State Proficiency Exam. Fall 1998-2001.
• "Cardiac Electrophysiology". HCEM pre-medical education program for minority undergraduates. Summer 1996.

PROFESSIONAL SERVICE

2006- Chair of the Physiology, Biophysics and Systems Biology (PBSB) curriculum committee. This committee aims to develop standards, schedules and courses for PBSB graduate students.
2006- Course developer and organizer for "Cell Physiology" offered as part of the PBSB program curriculum.

2006-7. Grant review at the National Institutes of Health. In the National Heart, Lung and Blood Institute.

EDITORIAL SERVICE

- Reviewer for *Journal of Clinical Investigation*
- Reviewer for *Circulation*
- Reviewer for *Circulation Research*
- Reviewer for *Medical and Biological Engineering and Computing*
- Reviewer for *American Journal of Physiology*
- Reviewer for *Journal of General Physiology*
- Reviewer for *British Journal of Pharmacology*
- Reviewer for *Journal of Biological Chemistry*
- Reviewer for *Trends in Cardiovascular Medicine*
- Reviewer for *Journal of Neurophysiology*
- Reviewer for *Current Pharmaceutical Design*
- Reviewer for *Journal of Molecular and Cellular Cardiology*
- Reviewer for *Biophysical Journal*
- Reviewer for *Annals of Biomedical Engineering*
- Reviewer for *Cardiovascular Research*
- Reviewer for *The Lancet Neurology*
- Reviewer for *The Journal of Physiology*