

MSTP STUDENT DESCRIPTION

NAME: Christopher V. DeSimone

e-Mail address: cvd@buffalo.edu

Undergraduate College/University attended: Niagara University

Major: Dual B.S. Biochemistry and B.S. Biology

Years in MSTP (1-8): 6th year

DEPARTMENT: Physiology and Biophysics

THESIS ADVISOR: Dr. Michael J. Morales (<http://www.acsu.buffalo.edu/~moralesm/>)

RESEARCH DESCRIPTION:

PhD Thesis title: **Molecular basis of HpTx2 gating modifier toxin interaction with Kv4.3; the channel responsible for the cardiac transient outward current**

Date of Completion of PhD: May 2008

Research Description:

Pro-arrhythmic effects have been of great concern in drug treatment of cardiac arrhythmias. These side effects of treatment stem from the lack of specificity of the drug for its target. Gating modifier toxins inhibit potassium channels at sites away from the pore, and thus bind at regions that are less conserved than the pore. A gating modifier toxin that is selective for inhibition of a single type of potassium channel that plays a role in the cardiac action potential repolarization, would spare the pro-arrhythmic side effects of treatment. The length of the cardiac action potential duration would be prolonged and arrhythmogenesis and its propagation may be suppressed. Therefore, my research is geared toward studying a gating modifier (HpTx2) type of inhibitor of Kv4.3, which is a potassium channel that plays a role in the early phase of the cardiac action potential. Understanding the basis of the interaction between the toxin and the channel will provide the selected target in developing a drug that mimics the effects of the toxin. Thus, having the potential to be an anti-arrhythmic drug without the pro-arrhythmic side effects. In order to study this channel we have made a recombinant toxin (rHpTx2gs) of HpTx2 from the Heteropoda venatoria spider. The benefit to using the recombinant toxin for probing the channel structure and function, is that it is specific for Kv4.3 and therefore provides a means to selectively target it. This recombinant toxin inhibits the Kv4.3 channel selectively, through gating modification of the channel. My research is aimed at understanding this interaction between this gating modifier toxin and the Kv4.3 channel.

PUBLICATIONS / ABSTRACTS PRESENTED:

Publications, Presentations, and Abstracts

Publications

DeSimone, CV, YC Lu, VE Bondarenko, & MJ Morales (2009). S3b amino acid substitutions and ancillary subunits alter the affinity of *Heteropoda* toxin 2 for Kv4.3. *Mol. Pharm.* in press.

Christopher V. DeSimone, Vladimir E. Bondarenko and Michael J. Morales. HpTx2 Interaction With Kv4.3 and Kv4.1 Reveals Differences in Gating Modification. 2009. In preparation for submission to Biophysical Journal.

The State University at Buffalo School of Medicine and Biomedical Sciences. Doctoral dissertation May 2008:
Binding Studies of the Gating Modifier toxin rHpTx2 with Kv4.3

The 2003 Miami Nature Biotechnology Winter Symposium: 50 Years on: From the double helix to molecular medicine. Volume 14, Proceedings of the Miami Nature Biotechnology Winter Symposium Short Reports. Porphyrim localization and apoptosis induction in RIF cells in culture. Christopher V. DeSimone and Robert S. Greene. Department of Biology, Niagara University, PO Box 2032 Niagara University NY 14109, USA. <http://www.med.miami.edu/mnbws/Greene107.html>.

Poster presentations

Biophysical Society meeting 2009

Christopher V. DeSimone, YiChun Lu, Vladimir E. Bondarenko and Michael J. Morales. S3b amino acid substitutions and ancillary subunits alter the affinity of *Heteropoda* toxin 2 for Kv4.3. University at Buffalo-SUNY, Buffalo, NY, USA

Biophysical Society meeting 2009

Christopher V. DeSimone, Vladimir E. Bondarenko and Michael J. Morales. HpTx2 Interaction With Kv4.3 and Kv4.1 Reveals Differences in Gating Modification. University at Buffalo-SUNY, Buffalo, NY, USA

Biophysical Society meeting 2008

HpTx2 binding and gating modification of Kv4 channels are dependent on distinct amino acids in S3b. Christopher V. DeSimone, YiChun Lu, Vladimir E. Bondarenko, Michael J. Morales. University at Buffalo-SUNY, Buffalo, NY, USA

Sigma XI research conference 2008. HpTx2 binding and gating modification of Kv4 channels are dependent on distinct amino acids in S3b. Christopher V. DeSimone, YiChun Lu, Vladimir E. Bondarenko, Michael J. Morales. University at Buffalo-SUNY, Buffalo, NY, USA

17th Upstate New York Cardiac Electrophysiology Society 2007
Binding studies of the gating modifier rHpTx2 on Kv4.3. Christopher V.

DeSimone, YiChun Lu, Vladimir E. Bondarenko, Michael J. Morales.
University at Buffalo-SUNY, Buffalo, NY, USA

Biophysical Society meeting 2007

Molecular determinants of rHpTx2gs interaction with Kv4.3. Author
Block: Christopher V. DeSimone, YiChun Lu, Vladimir E. Bondarenko,
Michael J. Morales. University at Buffalo-SUNY, Buffalo, NY, USA

American Physican Scientist Association/American Society for Clinical
Investigation Joint meeting 2007. Molecular determinants of rHpTx2gs
interaction with Kv4.3. Christopher V. DeSimone, YiChun Lu, Vladimir
E. Bondarenko, Michael J. Morales. University at Buffalo-SUNY,
Buffalo, NY, USA

Biophysical Society meeting 2006. Differences in Voltage-Dependent
Interaction of HpTx2 with Kv4 Channels. Vladimir E. Bondarenko, PhD,
Vladislav V. Zarayskiy, PhD, Michael J. Morales, PhD. University at
Buffalo-SUNY, Buffalo, NY, USA, ²Boston University School of
Medicine, Boston, MA, USA. (*name was on poster; abstract submitted
to meeting before I contributed to study)

Eastern College Science Conference 2003. In vitro characterization of the
apoptotic process using photoactive porphyrins in a cell-free nuclear
extract. Christopher V. DeSimone and Robert S. Greene Department of
Biology, Niagara University PO Box 2032 Niagara University NY
14109, USA.

Niagara University Arts and Sciences conference 2003. In vitro
characterization of the apoptotic process using photoactive porphyrins in
a cell-free nuclear extract. Christopher V. DeSimone and Robert S.
Greene Department of Biology, Niagara University PO Box 2032
Niagara University NY 14109, USA.

Eastern College Science Conference 2001

Apototoic localization of porphyrin photodynamic therapy on radiation-
induced fibrosarcoma cells. Michelle Good, Raymond W. Delluci,
Christopher V. DeSimone, and Dr. Robert S. Greene Department of
Biology, Niagara University, PO Box 2032 Niagara University, NY

Platform Presentations

Presented research at the Eastern College Science Conference (2003)
In vitro characterization of the apoptotic process using photoactive
porphyrins in a cell-free nuclear extract. Christopher V. DeSimone and
Robert S. Greene Department of Biology, Niagara University PO Box
2032 Niagara University NY 14109, USA.

Presented research at the TriBeta regional conference (2003)
In vitro characterization of the apoptotic process using photoactive
porphyrins in a cell-free nuclear extract.. Christopher V. DeSimone and
Robert S. Greene Department of Biology, Niagara University PO Box

2032 Niagara University NY 14109, USA.

PROFESSIONAL/EDUCATIONAL MEETINGS ATTENDED (name of meeting, dates of attendance, location):

Biophysical Society Meeting, Long Beach, California, March 2007
Sigma XI research conference, Buffalo, May 2008
American Physician Scientist Association Annual Meeting, Chicago, April 2007
Biophysical Society Meeting, Baltimore, March 2007
MD/PhD WNY conference Rochester (2005)
MD/PhD WNY conference Buffalo (2006)
MD/PhD WNY conference Syracuse (2007)
NYS Center of Excellence's Academic Industry and Life Sciences Symposium (2006)
Leon Farhi memorial symposia (2005)
Hermann Rahn memorial lectures (2005, 2006)
Suk-Hi Hong memorial lectures (2006, 2007)
MD/PhD WNY conference Rochester (2008)

AWARDS / HONORS:

American Heart Association Pre-Doctoral fellowship;
Northeastern Affiliate-2 year fellowship (2006-2008)
Mark Diamond Research Fund Grant (2006-2007)
GSEU Professional Development Award (2006)
Gilbert D. Moore Fellowship Award (2005)
Rochester Academy of Sciences Grant (2003)
AMA foundation grant for APSA finance committee (2006-2007)
Pre-Doctoral Fellowship grant from the American Heart Association Northeast Affiliate
Tascione Travel Grant
Medical School Dean's letter years 1 and 2
Finalist in Student Research Achievement Award poster competition at 2008 Biophysical society meeting

MEDICAL SCHOOL ACTIVITIES:

American College of Physicians (2009)
American Association of Family Physicians (2008-2009)
American Medical Association student member (2006-2009)
American Physiological Society (2006-2008)
American Heart Association Basic Sciences Council (2006-2007)
American Heart Association Clinical Cardiology Council (2007-2008)
American Physician Scientists Association UB Institutional Representative (2006-2007)
American Physician Scientists Association finance committee member (2006-2007)
Biophysical Society member (2006-2007)
Center for Research in Cardiovascular Medicine; working in both the Cell and Molecular Physiology lab and Cardiac Electrophysiology lab (2005-2007)
Center for Cellular and Systems Electrophysiology at UB SMBS (2005-2007)
Mentored undergraduate in cardiac electrophysiology research (2008)
President of the Physiology and Biophysics Graduate Student Association (2006-2007)

MD/PhD interview assistant (for prospective MD/PhD. students of UB) (2005-2008)
GI physiology teacher for 451/551 at UB SMBS Graduate School (2006)
University at Buffalo School of Medicine and Biomedical Sciences Second Look Day assistant (2008)
Heart Smart (2004)
Big Sib/Little Sib- Medical students (2005-2007)
Lighthouse Clinic (2004, 2008)
Member of Dr. Suk-Hi Hong Physiology and Biophysics Memorial lecture Committee (2005-2007)
Module student representative for improvement in Neuroscience module (2005)
Flag Football (2003-2004)
Intramural basketball (2004)
Bowling league- 200+ average (2006-2007)
Niagara Reservoir Flag football champions (2008)
University at Buffalo Intramural softball league champions (2007)
Niagara Frontier Softball Tournament champions (2007)
Bowling league- 200+ average (2006-2007)
Lord's Day dinner/soup kitchen (2004, 2008)

EXTRACURRICULAR INTERESTS:

Playing competitive sports, fishing, collecting sports cards, visiting sports stadiums, movies, playing drums, music, karaoke, watching Niagara University and University at Buffalo basketball teams.