

## **Dr. ANDREA MARIO POMPEO ROMANI**

Office Address: Dept. Physiology & Biophysics - E528  
Case Western Reserve University  
Cleveland, OH, 44106-4970  
phone: (216)-368.1625 (off.); (216)-368.5518 (lab.)  
fax: (216)-368.5586  
e-mail: [amr5@po.cwru.edu](mailto:amr5@po.cwru.edu)

### **Education**

**October 1973-July 1977:** Humanities with honors, Trapani, Italy.

**October 1977-July 1984:** M.D. cum Laude, University of Siena, Italy.

**October 1986-September 1990:** Ph.D. in Experimental and Molecular Pathology, Universities of Turin and Siena, Italy.

### **Appointments in Case Western Reserve University**

**September 1989-June 1991:** Post-Doctoral Fellow, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University, Cleveland, OH, USA

**July 1991-December 1991:** Research Associate, Department of Physiology and Biophysics, Case Western Reserve University, School of Medicine, Cleveland, OH, USA.

**January 1992-December 1992:** Research Associate, Istituto di Patologia Generale (Institute of General Pathology), School of Medicine, University of Siena, Siena, Italy

**December 15 1992-July 2006:** Assistant Professor, Department of Physiology and Biophysics, Case Western Reserve University, School of Medicine, Cleveland, OH, USA.

**July 2006-present:** Associate Professor, Department of Physiology and Biophysics, Case Western Reserve University, School of Medicine, Cleveland, OH, USA.

### **Appointments at other Institutions**

**December 2012-present:** Adjunct Associate Professor, Department of Chemistry Cleveland State University, Cleveland, OH, USA.

### **Fellowships and Awards**

**July 1990-June 1991:** "Hormonal Regulation of Mg<sup>2+</sup> in cardiac cells", American Heart Association, Ohio Section.

### **Active Memberships in Professional and Scientific Societies**

1990-present: Biophysical Society

1991-present: American Physiology Society

1996-present: American Society Cell Biology

The Oxygen Society

Research Society on Alcoholism

Endocrinology Society

### **Past Memberships in Professional and Scientific Societies**

1986-1991: Italian Society of General Pathology

1986-1991: Italian Society of Biochemistry

1993-2005: American Association for the Advance of Science

1998-2005: American Diabetes Association

### Current Collaborations

- Dr. Nagy, Dept. Pathobiology, and Director P20 Alcohol Center, Cleveland Clinic Foundation (*Alcohol Liver Disease: Kupffer cells and EtOH*)
- Dr. Szweda, Oklahoma Medical Research Foundation, Oklahoma City (*Protein modification by 4HNE*)
- Drs. Jin, Wayne University, Detroit (*Cytoskeleton and adhesion modifications by ethanol*)
- Dr. Colleen Croniger, Dept. Nutrition, Case Western Reserve University (*Liver Metabolism*)
- Dr. George Dubyak, Dept. Physiology & Biophysics, Case Western Reserve University (*Pyrophosphate*)
- Dr. Charles O'Neill, Emory University, Atlanta, Georgia (*Pyrophosphate and vascular calcification*)
- Dr. Marco Brotto, University of Kansas City-Missouri (*Alcoholic muscle toxicity*)

### Teaching and Related Activities

#### **1. Courses taught at Institute of General Pathology, School of Medicine, University of Siena, Siena, Italy**

- 1984-1989, and 1991-1992: *General Pathology*, School of Medicine, Univ. Siena, Italy, 25 hours
- 1984-1989, and 1991-1992: *Immunology*, School of Medicine, Univ. Siena, Italy, 25 hours
- 1986-1989, and 1991-1992: *Immunology*, School of Dentistry, Univ. Siena, Italy, 25 hours
- 1984-1989, and 1991-1992: *Pathological Bases of Endocrine Diseases*, School of Medicine, Univ. Siena, Italy, 25 hours

#### **2. Ph. D. Courses taught at Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University, Cleveland, OH. All the courses were organized for small groups (8 to 12 students)**

- 1998-1999: *Molecular Organization of the cell (Phol532 - Director: Dr. Gualberto)*, 6 hours
- 1998-2000: *Membrane Physiology (Phol472 - Director)*, 8 hours
- 1998-2000: *Molecular Organization of the cell (Phol532 - Director)*, 8 hours
- 1999-2002: *Physiology of Organ Systems (Phol480 - Director)*, 12 hours
- 2005-2008: *Cardiovascular Physiology (Phol514 - Director: Dr. Harvey)*, 8 hours
- 2006-2007: *Translational Physiology (Phol500 - Director: Dr. Cefaratti)*, 3 hours
- 2007- present: *Physiology of Organ Systems (Phol480 - Director)*, 22 hours
- 2010- present: *Cardiovascular Physiology (Phol514 - Director: Dr. Chandler)*, 10 hours
- 2011 - present: *Masters in Medical Physiology – Coordinator of the Endocrinology Block*, 24 hours
- 2011 - present: *Master in Medical Physiology – Coordinator of the Reproductive Physiology Block*, 16 hours

#### **3. Courses taught at the School of Medicine, Case Western Reserve University, Cleveland, OH.**

- 1995-2007: **Endocrinology**, 2<sup>nd</sup> year small study groups (Director: Dr. Murphy), 8 hours
- 1996-2007: **Endocrinology**, 1<sup>st</sup> year small study groups (Director: Dr. Murphy/Dubyak), 4 hours
- 1996-2007: **Homeostasis I**, small study groups (Director: Dr. Dubyak), 4 hours
- 2000-2007: **Cardiovascular Physiology**, small study groups (Director: Dr. Harvey), 4 hours
- 2005-present: **Block 2- Endocrinology** (new medical school curriculum, small IQ groups), 6 hours
- 2005-present: **Block 4- Cardiovascular** (new medical school curriculum, small IQ groups), 6 hours

### Professional Service

#### **1. Departmental Service**

##### **1.1 Undergraduate Activities**

- 1996 - present: **Director** of Summer Undergraduate Research Program (SURP), Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University
- 1996 - present: **Coordinator** between SURP program, Department of Physiology and Biophysics, and Summer Program for Undergraduate Research (SPUR) - Howard Hughes, Case Western Reserve University.
- 2010 - present: **Director** of NSF-REU (Research Experience for Undergraduates) in Biology: Training Grant in Protein Dynamics, Department of Physiology and Biophysics, Case Western Reserve University

### 1.2 Graduate Activities

- 1996 - present: **Thesis Committee Member** for Master and PhD students (see detailed list below), and **Academic Advisor** for three PhD students in the Department of Physiology and Biophysics, Case Western Reserve University
- 2008 - present: **Director** Graduate Students Admission Committee, Department of Physiology and Biophysics, Case Western Reserve University.
- 2011 - present: **Assistant Director** of the program Masters in Medical Physiology, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.
- 2011 - present: **Member** of the Masters in Medical Physiology Admission Committee, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.
- 2011 - present: **Academic Advisor** for 25 students enrolled in the program *Masters in Medical Physiology*, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.

### 1.3 Administrative Activities

- 1995 - 2004: **Director** of Facility and Equipment Committee, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.
- 2001 - present; **Director** System Physiology Journal Club, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.
- 2002 - 2005: **Coordinator** Seminar Series for the Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.
- 2006 - Present: **Member** of the Education Committee, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.
- 2006 - present: **Member** of the Committee on Appointments, Promotions and Tenure (*CAPT*), Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.
- 2008 - 2009: **Member** of Space and Facility Committee during the renovation of the Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.
- 2008 - present: **Director** Graduate Students Admission Committee, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.
- 2009 - present: **Member** of the Committee for the departmental WEB site renovation, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University
- 2011 - present: **Member** of the Masters in Medical Physiology Admission Committee, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.

### 1.4 Facility Director Activities

- 2011 - present: **Director** of the Atomic Absorbance Facility, Department of Physiology and Biophysics, School of Medicine, Case Western Reserve University.

## 2. Institutional Service (Case Western Reserve University)

- 2005 - present: **Member** DOES Committee.
- 2008 - present: **Member and Interviewer** BSTP (Biomedical Science Training Program) Graduate Students Admission Committee (PhD Program).
- 2008 - present: **Interviewer** for School of Medicine candidates.
- 2009 - present: **Interviewer** for MSTP (Medical Scientist Training Program) candidates for the MD/PhD program.
- 2011 - present: **Interviewer** for OMFS (Oral-Maxillo Facial Surgery School) candidates for the OMFS/School of Dentistry program.

## 3. Inter-Institutional Service

- 2008-present: **Member** of the Steering Committee for the P20 on Ethanol Liver Pathology (Laura Nagy, Director), Cleveland Clinic Foundation and Case Western Reserve University.

#### **4. National Service**

2005 – ISEF Judge, Cleveland  
2009 - present: Member of the Strategic Alliances and Outreach Committee, Oxygen Society (SFRBM)  
2010 - present: Member of Junior Awards Committee (SFRBM)  
2010 - present: NSF-REU panel Reviewer  
2011 – Present: NSF-Graduate Fellowships Reviewer  
2012 - ISEF judge, Pittsburgh

#### **5. Editorial Board**

2005 - present: Archives of Biochemistry and Biophysics  
2008 - present: Magnesium Research  
2010 – present: World Journal of Gastro-Intestinal Physio-Pathology  
2010 – Present: Journal of Membrane Science & Technology  
2011 – Present: TheScientificWorldJOURNAL – Hepatology Section

#### **6. Regular Peer Reviewer for**

Archives of Biochemistry and Biophysics  
Biochemical Pharmacology  
Cardiovascular Research  
Free Radicals in Biology and Medicine  
Journal of Cellular Biochemistry  
Magnesium Research  
TheScientificWorldJOURNAL – Hepatology Section

#### **7. Ad-Hoc Peer Reviewer for**

American Journal Physiology – Cardiovascular Section  
Biochemical Biophysical Acta,  
Circulation Research  
Endocrinology  
Journal of Clinical Endocrinology and Metabolism  
Journal Pharmacology & Experimental Therapeutics  
Life Science  
Metabolism

#### **8. National Grant Reviewer for**

2004: NIH – ICI: Special Emphasis panel  
2004 - 2007: American Heart Association - Ohio Valley section 4B:  
2004 - present: American Institute of Biological Science (DoD) - Alcohol panel  
2005: NIH – ICI: Special Emphasis panel  
2006: NIH - ZRG1-CB-D(40) - Special Emphasis Panel  
2007 - present: Oak Ridge Associated Universities (ORAU)  
2008 - present: American Institute of Biological Science (DoD) - Clinical trial panel

#### **9. International Grant Reviewer for**

1998 - present: Medical Research Council (U.K.)  
Swiss Research Council (Switzerland)  
TOP grant Proposal (Netherlands)  
National Research Council (South Africa)  
OKTA (Hungary)

## **10. Meeting Reviewer**

- 2002 - present: Free Radicals in Biology and Medicine (SFRBM): Reviewer of Oral Communications to Annual Meeting  
2013 – present: Endocrine Society: Reviewer of Oral Communications to Annual Meeting

## **11. Meeting and Special Journal Organizer**

- 2005: Session on ‘Regulation of Cellular Functions by Magnesium’ Gordon Conference on Biological Effects of Magnesium  
2007: Editor Guest for Special Issue on “Magnesium Regulation and Function”, *Archives of Biochemistry and Biophysics*

## **Post Doctoral Advisor**

- Dr. Christie Cefaratti, May 2002-May 2005, currently Scientific Consultant for Takeda Pharmaceuticals  
Dr. Amy Nulton-Persson, June 2006 – May 2007  
Dr. Ana T. Tomaszewska, Oct 2006 – May 2007, currently at ETH Zentrum, Zurich, Switzerland  
Dr. Bozena A Konopnicka, Oct 2006 – May 2007, currently at Hospital Laboratory, Warsaw, Poland

## **Thesis Advisor**

- Carmela Marfella, Master in Physiology (1993-1996)  
Dr. Donald Keenan, MD/Ph.D (1995-1998), Assistant Professor, Department of General Surgery, Univ. of Pittsburgh, Pittsburgh, Pennsylvania  
Dr. Christie Luca - PhD (1995-2000), Scientific Advisor for Takeda Pharmaceuticals  
Dr. Ossama Lashin – PhD (2001-2004), Internal Medicine, University Hospital of Cleveland, Cleveland, OH  
Nicole Baitz – Master in Cell Physiology (2003-2005)  
Amy Shafqat – Master in Physiology (John Carroll University, April 2010 -March 2011)  
Zienab Etwebi – Master in Physiology (May 2010 – May 2011)  
Chesinta Voma – PhD in Physiology (Cleveland State University, September 2011 – present)

## **Thesis Committee Member**

- Carmela Marfella (Master in Physiology, 1997)  
Krista Kivilo  
Anastasios Konstatakos  
David Lucas (Ph.D., 1999)  
Kenneth Humphries (Ph.D., 1999), Assistant Professor, Oklahoma Medical Center  
Pranav Dhalal (Ph.D., 2000)  
Hesham Sadek (Ph.D., 2004), Assistant Prof., Dept. Cardiology, Austin Medical School, Austin, TX  
Linda Kunster (Ph.D., 2004)  
Marie Zafirooulos (Master in Physiology, 2006)  
Julie Rennison (Ph.D., 2008), Research Associate, Cleveland Clinic Foundation, Cleveland, OH  
Barbara Kuri (Ph.D., 2009), Assistant Professor, TriC Community College, Cleveland  
Benjamin Sommerlot (Ph.D. Biology, 2008 - 2010)<sup>#</sup>  
Chepchumba Yego (Ph.D., 2010), Post Doctoral Fellow at NIH  
Domenic Tony Prosdocimo (Ph.D., 2010), Research Associate, Cardiovascular Institute, Case Western Reserve University  
Nick Cianciola (Ph.D., 2010), Research Associate in Microbiology, Case Western Reserve University  
Milana Leygerman (Master in Physiology, 2011)  
Jacqueline Hill (PhD in Physiology, 2012)  
Michael Simmonson (PhD in Physiology, 2012)  
Julie Chang (MS in Biology, CWRU, March 2013)  
Kate Fu (2013 – present)

**Ad-Hoc International Thesis Committee Member**

Rebecca van Wjik (Master, 2008) - Cape Town University, South Africa  
Melvin M. Govender (Ph.D.,2011) - University of Kwazulu-Natal, South Africa  
Shamal Vinesh Ramesar (PhD. 2011) University of Kwazulu-Natal, South Africa

**Lab Rotations Advisor - Graduate Students**

John Hwa (1992), Assistant Professor, Dept. Pharmacology, Dartmouth, NH  
Bradley McConnell (1993), Assistant Professor, Dept. Pharmacology, Univ. of Texas, Houston, TX  
Carmela Marfella (1993)<sup>#</sup>  
Christie Luca (1994), Scientific Advisor for Takeda Pharmaceuticals  
Krista Kivilo (1996)  
Anastasios Konstantakos (1996-1997)  
Hesham Shadek (1997-1998), Assistant Professor, Dept. Cardiology, Austin Medical School, Austin, TX  
Theresa E. Fagan (1998-1999), Scientific Advisor for GenTech  
Ossam Lashin (2000), Assistant Prof., Internal Medicine, University Hospital, Cleveland  
Amr El Touky (2002), Resident in Internal Medicine, Mayo Clinic, Rochester, MN.  
Nichole Baitz (2003), Researcher in Biotech Co..  
Wichit Suthammarak (Oct. - Nov. 2005), BSTP student  
Lisa M. Torres (summer 2006), recipient Cryle fellowship for medical student, Case Western Reserve Univ.  
Jeffrey Look (Oct. 2006 - April 2007), Ph.D. Student  
Lisa M Torres (summer 2007), Research training for Medical Student, MD, Case Western Reserve Univ.  
Zienab Etwebi (Jan - April 2010), Master Student  
Ken Gresham (May - June 2010), Ph.D. Student  
Carl B. Gillombardo (Nov. 2011 - June 2012), Ph.D. Student – withdrawn as July 2012

**Lab Rotations Advisor – Masters in Medical Physiology Students**

Gabriela Cox (Law), March 2013 - present  
Samantha Long, May 2013 - present

**Undergraduate and Summer Student Advisor**

Elisabeth A. Dowell (summer student 1990 and 1991), MD, Case Western Reserve University, Family Practice, Tucson, AZ  
Francesca Fragomeni (summer student 1993), MD  
Veronica Matthews (undergraduate 1994)  
Brian Grinberg (summer student 1994)  
Veronica Matthews (undergraduate 1995)  
Sangeeta Karle (summer student 1995), Master Immunology, John Hopkins Univ.  
Patrick Tessman (summer student 1996), MD, Case Western Reserve University, Neurology  
Veronica Matthews (summer student 1996)  
Sheldon Joseph (summer student 1996), PhD, Dept. Physiology and Biophysics, Case Western Reserve University  
Patricia Lamont (summer student 1997), MD  
Veronica Matthews (summer student 1997), recipient Diabetes Found. Fellowship, currently MD, Sport Medicine, San Francisco, CA  
Lauri A. Leahy (summer student 1998), recipient Diabetes Found. Fellowship  
Julie E. Swindler (summer student 1998), MD, Neoucom  
Michael Kob (summer student 1998), MD, Graz, Austria  
Megan Howard (summer student 1999), PhD Microbiology, Colorado State University, Instructor  
Amy McKinnis (summer student 1999)  
Tiffani Humphries (summer student 2000), recipient Howard Hughes fellowship  
Faith Waldron (summer student 2000)  
Megan Riffle (summer student 2001)

Emily Riffle (summer student 2001)  
Ronya Emory (summer student 2001), recipient Howard Hughes fellowship  
Jonathan Youngner (summer student 2002), MD, Tufts University, Boston, MA  
Beverly Perry (summer student 2003), Res. Assistant, Yale  
B Dan Pipitone (summer student 2004), MO, Radiology, Metrohealth Hospital, Cleveland, OH  
Christopher Painter (summer student 2004), recipient Howard Hughes fellowship  
Christopher Painter (summer student 2005), MD, Yale  
Grant Reed (summer student 2005), recipient Howard Hughes fellowship  
Cleyton Pacheco (summer student 2005)  
Grant Reed (summer student 2006), MD, Univ. Toledo  
Deema Yousef (summer student 2006)  
Maria Avkshtol (summer student - 2007), BS, Case  
Mario Aragon (summer student – 2007), Master Bioengineering, New Mexico  
Misty Ahmed (summer 2007 through summer 2008), BS, Bioengineering, Case Western Reserve University  
Vera Avkshtol (summer student 2008), BS, Case  
Amy Jackobs – Harper (summer student 2008), SoM, Univ. of Toledo  
Huy Nguyen (summer student 2009)  
Dana Selle (summer student 2009), recipient of DAGC fellowship  
Steve Ewart (undergraduate, Senior Thesis 2009-2010, Physics major, CWRU), MS Biophysics, Ball Univ.  
Andrew Barfell (summer student 2010)  
Samantha Barclay (summer student 2010), NSF-REU training grant Recipient, currently SoM at CCF  
Jaclyn Sweetapple (summer student 2010), NSF-REU training grant Recipient  
Andrew Barfell (summer student 2011), NSF-REU training grant Recipient, currently SoM Cincinnati  
Christine Battis (summer student 2011), NSF-REU training grant Recipient  
Danial Amir Soltani (summer student 2011), Howard Hughes fellowship recipient  
Neal Dharmadhikari (summer student 2011), Undergraduate, Senior, Case Western Reserve University  
Elizabeth Learst (summer student 2012), NSF-REU training grant Recipient  
Neal Dharmadhikari (Jan 2012 – May 2012) CWRU Undergraduate, Graduated May 2012, Rutgers SoM (2013)  
Danial Amir Soltani (September 2011 – September 2012)  
Ali Azzam (September 2011 – May 2012)  
Kelly Keenan (summer student 2013)

## **Financial Supports**

### **Active - Research**

**Subcontract from UT-Houston:** *SLC polymorphism in hypertension*

**Principal Investigator:** Dr. Boron (Case Western Reserve University) Total Direct \$350,000

**Role:** Collaborator

**Effort:** 10%

**Aims:** To evaluate SLC polymorphism in hypertension

**March of Dimes:** *Magnesium Decreases Inflammatory Cytokine Production: A Novel, Important Innate Immunomodulatory Mechanism*

**Period:** 06-01-2013 – 05-31-2016

**Principal Investigator:** Dr. Bernstein (Case Western Reserve University) Total Direct \$400,000

**Role:** Collaborator

**Effort:** 10%

**Aims:** To evaluate the mechanism of action of Mg<sup>2+</sup> in modulating NFκB signaling in circulating monocytes

### **Pending**

**NSF-REU Award:** *Protein Dynamics* (Training Grant)

**Period:** 05.01.2014 – 08-31-2017

Total Direct Costs: \$220,000

**Role:** Director

**Effort:** 10%

**Aims:** To elucidate different mechanisms of protein dynamics

### **Completed**

**NSF-REU Award:** *Protein Dynamics* (Training Grant)

**Period:** 05.01.2009 – 08-31-2012

Total Direct Costs: \$197,440

**Role:** Director

**Effort:** 10%

**Aims:** To elucidate different mechanisms of protein dynamics

**NIH-AAA:** *Impairment of magnesium homeostasis in cardiac and liver cells by ethanol*

**Period:** 07.01.2005-06.30.2010: \$1,300,000

**Principal Investigator:** Dr. Andrea Romani **Effort:** 35%

**Aims:** To investigate the mechanisms by which acute and chronic ethanol administration result in an altered cellular Mg<sup>2+</sup> homeostasis and in a loss of Mg<sup>2+</sup> from liver and cardiac cells.

**NIDDK:** Continuous Oxalate treatment and nephrolithiasis (NIDDK-073730)

**Period:** 04/01/2006– 03/31/2009

**Aim:** To characterize the effect of continuous oxalate administration on calcium and phosphate transport in renal epithelium and their role in CaOx

**Role:** **Collaborator** (PI: Dr. Susan Marengo) **Effort:** 15%

**Case Center for Proteomics:** *Proteomic Identification of Proteins modified by HNE in the heart of type-I diabetic rats*

**Period:** 01.01.2008-12.31.2008: \$ 10,000

**Principal Investigator:** Dr. Andrea Romani

**Aims:** To identify mitochondrial proteins forming an adduct with HNE in the heart of type-I diabetic rats

**NIH:** *CARDIAC BIOENERGETICS* : HL 18708

**Period:** 01.01.2002-12.31.2006: \$ 1,410,143

**Principal Investigator:** Dr. Andrea Romani starting 07.01.2005



Aims: To understand the molecular mechanisms of heart bionergetics and function in normal and diseased states, with particular attention to the factors that govern tissue oxygen delivery and efficiency of ATP synthesis and utilization in the myocardium.

This project is Project 1 of the Program Project Grant “*ATP utilization and Ion Gradients in Myocardium*” coordinated by Dr. G. Dubyak

**NIH-AAA**: *Impairment of magnesium homeostasis in cardiac and liver cells by ethanol*

Period: 09.01.1998-08.31.2003: \$350.000

Principal Investigator: Dr. Andrea Romani      Effort: 50%

Aims: To investigate the mechanisms by which acute and chronic ethanol administration result in an altered cellular Mg<sup>2+</sup> homeostasis and in a loss of Mg<sup>2+</sup> from liver and cardiac cells.

**NIH**: *CARDIAC BIOENERGETICS* : HL 18708

Period: 04.01.1996-03.31.2001: \$ 1,107.404

Principal Investigator: Dr. Antonio Scarpa

Aims: To understand the molecular mechanisms of heart bionergetics and function in normal and diseased states, with particular attention to the factors that govern tissue oxygen delivery and efficiency of ATP synthesis and utilization in the myocardium.

Role: Collaborator (Effort: 40%)

**Diabetes Association** – Modulation of cellular magnesium by insulin in cardiac cells and its role on glucose transport regulation #397-A-97

Period: 07.01.1997 – 06.30.1999: \$40,000/year

Principal Investigator: Dr. Andrea Romani – Effort 15%

Aims: To elucidate the correlation between changes in cellular Mg<sup>2+</sup> homeostasis and glucose transport and utilization within cardiac myocytes under physiological and diabetic conditions.

**NIH**: *CARDIAC BIOENERGETICS* : HL 18708

Period: 04.01.1991-03.31.1996: \$ 987.000

Principal Investigator: Dr. Antonio Scarpa

Aims: To understand the molecular mechanisms of heart bionergetics and function in normal and diseased states, with particular attention to the factors that govern tissue oxygen delivery and efficiency of ATP synthesis and utilization in the myocardium.

Role: Collaborator (Effort: 40% from 01.01.1993 to 03.31.1996)

## **LIST OF PUBLICATIONS**

### **1. Full Papers**

- 1) **Romani A** (1984) Perdita della reazione di perossidazione lipidica come marker istochimico in isole preneoplastiche di epatociti di ratto trattato con cancerogeni, *Atti Accademia dei Fisiocritici*, Siena Serie XV, Tomo III, 365-369.  
[Loss of lipid peroxidation as an early histochemical marker for neoplastic foci in hepatocytes from carcinogen-treated rats]
- 2) Benedetti A, Pompella A, Fulceri R, **Romani A**, Comporti M (1986) Detection of 4-hydroxynonenal and other lipid peroxidation products in the liver of bromobenzene-poisoned mice, *Biochimica Biophysica Acta* 876: 658-666.
- 3) A Benedetti, A Pompella, R Fulceri, **A Romani**, M Comporti (1986), 4-Hydroxynonenal and other aldehydes produced in the liver in vivo after bromobenzene intoxication, *Toxicological Pathology* 14: 457-461.
- 4) Benedetti A, Fulceri R, **Romani A**, Comporti M (1987) Stimulatory effect of glucose 6-phosphate on the non-mitochondrial  $\text{Ca}^{2+}$  uptake in permeabilized hepatocytes and  $\text{Ca}^{2+}$  release by inositol trisphosphate, *Biochimica Biophysica Acta* 928: 282-286.
- 5) Benedetti A, Fulceri R, **Romani A**, Comporti M (1988) MgATP -dependent glucose 6-phosphate-stimulated  $\text{Ca}^{2+}$  accumulation in liver microsomal fractions. Effects of inositol 1,4,5-trisphosphate and GTP, *Journal of Biological Chemistry* 263: 3466-3473.
- 6) Pompella A, **Romani A**, Fulceri R, Benedetti A, Comporti M (1988) 4-hydroxynonenal and other lipid peroxidation products are formed in mouse liver following intoxication with allyl alcohol, *Biochimica Biophysica Acta* 961: 293-298.
- 7) **Romani A**, Fulceri R, Pompella A, Benedetti A (1988) MgATP -dependent, glucose 6-phosphate-stimulated liver microsomal  $\text{Ca}^{2+}$  accumulation: difference between rough and smooth microsomes, *Archives of Biochemistry and Biophysics* 266: 1-9.
- 8) **Romani A**, Fulceri R, Pompella A, Ferro M, Benedetti A (1988) Active  $\text{Ca}^{2+}$  accumulation in the endoplasmic reticulum of different hepatomas: stimulation by phosphates and  $\text{Ca}^{2+}$ -releasing effect of IP3, *Annals of New York Academy of Science* 551: 249-252.
- 9) Benedetti A, Graf P, Fulceri R, **Romani A**, Sies H (1989)  $\text{Ca}^{2+}$  mobilization by vasopressin and glucagon in perfused livers. Effects of prior intoxication with bromotrichloromethane, *Biochemical Pharmacology* 38: 1799-1805.
- 10) Fulceri R, **Romani A**, Bellomo G, Benedetti A (1989) Liver cytosolic non-dialysable factor(s) can counteract GTP-dependent  $\text{Ca}^{2+}$  release in rat liver microsomal fractions, *Biochemical and Biophysical Research Communications* 163: 823-829.
- 11) Fulceri R, **Romani A**, Pompella A, Benedetti A (1990) Glucose 6-phosphate stimulation of MgATP-dependent  $\text{Ca}^{2+}$  uptake by rat kidney microsomes, *Biochimica Biophysica Acta* 1022: 129-133.
- 12) Fulceri R, Bellomo G, **Romani A**, Mirabelli F, Benedetti A (1990) Concerted operation of GTP, phosphates, glucose 6-phosphate and cytosol in regulating  $\text{Ca}^{2+}$  distribution among different 'microsomal' pools in rat liver, *Journal of Physiology* (London), 424: 41P.
- 13) **Romani A**, Scarpa A (1990) Hormonal control of  $\text{Mg}^{2+}$  transport in heart, *Nature* 346: 841-844.

- 14) **Romani A**, Scarpa A (1990) Norepinephrine evokes a marked  $Mg^{2+}$  efflux from liver cells, *FEBS Letters* 269: 37-40.
- 15) Pompella A, **Romani A**, Benedetti A, Comporti M (1991) Loss of membrane protein thiols and lipid peroxidation in allyl alcohol hepatotoxicity, *Biochemical Pharmacology* 41: 1255-1259.
- 16) Bãnhegyí G, Fulceri R, Bellomo G, **Romani A**, Pompella A, Benedetti A (1991) Role of a non-mitochondrial  $Ca^{2+}$  pool in the synergistic stimulation by cyclic AMP and vasopressin of  $Ca^{2+}$  uptake in isolated rat hepatocytes, *Archives of Biochemistry and Biophysics* 287: 320-328.
- 17) **Romani A**, Marfella C, Scarpa A (1991) Hormonal regulation of magnesium transport in cardiac and liver cells, *Acta Medica Romana* 29: 267-276.
- 18) **Romani A**, Dowell E, Scarpa A (1991) cyclic AMP-induced  $Mg^{2+}$  release from rat liver hepatocytes, permeabilized hepatocytes and isolated mitochondria, *Journal of Biological Chemistry* 266: 24376-24384.
- 19) **Romani A**, Marfella C, Scarpa A (1992) Regulation of  $Mg^{2+}$  uptake in isolated rat myocytes and hepatocytes by protein kinase C, *FEBS Letters* 296: 135-140.
- 20) **Romani A**, Scarpa A (1992) cAMP Control of  $Mg^{2+}$  homeostasis in heart and liver cells, *Magnesium Research* 5: 131-137.
- 21) Fulceri R, Bellomo G, Gamberucci A, **Romani A**, Benedetti A (1993) Physiological concentrations of inorganic phosphate enhance  $MgATP$ -dependent  $Ca^{2+}$  uptake and  $IP_3$ -induced  $Ca^{2+}$  release in microsomal fractions from non-hepatic cells, *Biochemical Journal* 289: 299-306.
- 22) **Romani A**, Marfella C, Scarpa A (1993) Regulation of magnesium uptake and release in the heart and in isolated rat ventricular myocytes, *Circulation Research* 72: 1139-1148.
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### **In Preparation**

\*Nguyen H, DiNuoscio G, **Romani A**, Effect of acute and chronic EtOH exposure on cardiac myocytes and H9C2 cells

Voma C, \*Barfell A, Croniger C, **Romani A**, Magnesium deficiency results in increased G6PD activity and NADPH production within the endoplasmic reticulum of liver cells

\*Soltani DA, Etwebi Z, Croniger C, **Romani A**, Magnesium deficiency results in decreased glucose uptake and utilization in liver cells: Involvement of mitochondrial pyruvate dehydrogenase

\*Soltani DA, Etwebi Z, Croniger C, Prosdocimo DA, Mukesh J, **Romani A**, Decreased glucose uptake and increased fatty acid metabolism in the liver of Mg<sup>2+</sup>-deficient rats and mice.

Voma C, **Romani A**, Magnesium deficiency results in increased cortisol production via hepatic 11-β-OHSD: Implications for metabolic syndrome.

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Shafqat A, Dharmadhikari N, Azeem A, Bernstein HB, Nagy L, **Romani A**, Loss of cellular Mg<sup>2+</sup> results in increased production of proinflammatory cytokines in Kupffer cells

Dharmadhikari N, Azeem A, Bernstein HB, **Romani A**, Loss of cellular Mg<sup>2+</sup> results in increased production of ROS in Kupffer cells

\*Barfell A, DiNuoscio G, **Romani A**, Identification of HNE-modified protein in the endoplasmic reticulum of hepatocytes from animals exposed to ethanol.

*Invited Speaker in International Meetings*

- \* Regulation of intracellular magnesium in heart and liver cells, in *First Italian-German "Villa Vigoni" Conference on Ion and Cell Regulation*, Lovenno di Menaggio, Como (Italy), Oct. 20-23, 1991.
- \* Regulation of magnesium efflux and influx in cardiac and liver cells by cAMP and PKC and requirement of intra- and extracellular cations, in *XXXII International Congress of Physiology (IUPS)* - Glasgow (UK), Aug. 1-6, 1993.
- \* cAMP Binds to the Adenine Nucleotide Translocase of Mitochondria and Induces a Sizable Magnesium Efflux, in *2nd International Congress of Biochemistry and Molecular Biology (IUBMB)* - Bari (Italy), Sept. 29-Oct. 3, 1993.
- \* Regulation hormonal del eflujo e influjo celular de  $Mg^{2+}$ , *II Congreso Iberoamericano de Biofísica*, Puebla, Mexico, October 3-7, 1993.
- \* Cellular  $Mg^{2+}$  fluxes, in *Second Italian-German "Villa Vigoni" Conference on Ion and Cell Regulation*, Lovenno di Menaggio, Como (Italy), Oct. 10-13, 1993.
- \* Direct effect of thyroid hormone on mitochondrial ATP translocase, in *Novel Action of Thyroid Hormone*, satellite meeting of the 1995 International Thyroid Congress, Toronto, Ontario (Canada), Sept. 10, 1995.
- \* Increase of plasma  $Mg^{2+}$  level by selective stimulation of  $\beta_2$ -adrenergic receptors in anesthetized rats, in *Third Italian-German "Villa Vigoni" Conference on Ion and Cell Regulation*, Lovenno di Menaggio, Como (Italy), Oct. 8-11, 1995.
- \* Hormonal control of Magnesium in Heart and Liver, in *Magnesium in Biochemical Processes*, Gordon Research Conference, Oxnard, CA, Jan. 29-Febr. 2, 1996.
- \* Role of PKC in ethanol-induced inhibition of magnesium accumulation in liver cells, in *Magnesium in Biochemical Processes*, Gordon Research Conference, Oxnard, CA, March 3 – 6, 2008.
- \* Isoproterenol and insulin: the ying-yang of regulation of  $Mg^{2+}$  homeostasis in mammalian cells, Ehrlich 2008 International Symposium, Nurnberg, Germany, Oct. 3-5, 2008.
- \* Magnesium deficiency results in increased conversion of cortisone to cortisol in the hepatocyte: Implications for metabolic syndrome, CBB Symposium, Toronto, Sept 16-18, 2013.

Seminars

- \*\*\*) Regolazione del trasporto di magnesio in cellule cardiache ed epatiche, held at the Istituto di Patologia Generale, Università Cattolica del Sacro Cuore, Rome (Italy), November 13, 1991  
[Regulation of Magnesium Transport in cardiac and liver cells]
- \*\*\*)  $\beta$ -adrenergic stimulation and role of cellular cAMP in mediating  $Mg^{2+}$  extrusion from cardiac and liver cells, held at Department of Nutrition and Metabolism, University of Montreal, Montreal, Quebec (Canada), August 24, 1992.
- \*\*\*) Controllo ormonale del trasporto di magnesio in cellule cardiache ed epatiche, held at the Istituto di Fisiopatologia Clinica, Divisione di Endocrinologia, Università di Firenze, Florence (Italy), September 16, 1992.  
[Hormonal regulation of Magnesium handling in cardiac and liver cells]
- \*\*\*) cAMP mediated  $Mg^{2+}$  efflux from cardiac ventricular myocytes, held at Merck Sharp & Dome, West Point, PA, February 18, 1994.
- \*\*\*) Regolazione ormonale dei livelli plasmatici e cellulari di magnesio: Implicazioni fisiopatologiche e farmacologiche, held at the Istituto di Clinica Medica II, Università di Firenze, Florence (Italy), October 20, 1995.  
[Hormonal regulation of serum and cellular Magnesium levels: Physio-Pathological and Pharmacological implications]
- \*\*\*) Role of  $\alpha$ - and  $\beta$ -adrenergic receptors and insulin in the regulation of cellular magnesium in cardiac and liver cells, held at the Istituto di Patologia Generale, Università di Siena, Siena (Italy), January 10, 1998.
- \*\*\*) Impairment of  $Mg^{2+}$  homeostasis in liver cells following acute administration of ethanol, Department of Biological Sciences, University of Novara, Novara (Italy), October 28, 1998.
- \*\*\*) Hormonal regulation of cellular  $Mg^{2+}$  in cardiac myocytes and hepatocytes: Physiological and pathological implications, held at Endocrine Grand Rounds, Division of Endocrinology, Case Western Reserve University, Cleveland, Febr. 3, 1999
- \*\*\*) Hormonal regulation of cellular  $Mg^{2+}$  content under physiological and pathological conditions, held at Department of Nutrition, University of Montreal, Montreal, Canada, March 17, 1999.
- \*\*\*) Hormonal regulation of cellular and plasma  $Mg^{2+}$  content under physiological and pathological conditions, held at Institute of General Pathology, Università di Ferrara, Ferrara, Italy, Oct. 27, 1999.
- \*\*\*) Hormonal Regulation of cellular and plasma  $Mg^{2+}$  content under physiological and pathological conditions, held at Department of Pharmacological Science, Università di Siena, Siena, Italy, Nov. 5, 1999.
- \*\*\*) Physio-pathology of magnesium, an overlooked ion, held at Department of Pharmacological Science, Università di Siena, Siena, Italy, Nov.16, 2000.
- \*\*\*) Alteration of  $Mg^{2+}$  homeostasis in liver cells following acute and chronic EtOH administration: Implications for liver metabolism, held at Department of Nutrition, Case Western Reserve Univ., Cleveland, Oct. 19, 2001.
- \*\*\*) Regulation of Calcium homeostasis, Endocrinology Division, Cleveland Clinic Foundation, September 13, 2002.
- \*\*\*) Regulation of cellular magnesium and its alteration under pathological conditions, Center for Anesthesiology Research, Cleveland Clinic Foundation, October 1, 2002.

- \*\* Alteration of  $Mg^{2+}$  homeostasis in liver cells following acute and chronic EtOH administration: Implication for liver metabolism, held at Division of Gynecology, University Hospital, Cleveland, April 9, 2003.
- \*\* Functional modification of cardiac mitochondrial proteins by 4-HNE in streptozotocin diabetic rats. Cardiovascular Seminar, School of Medicine, Case Western Reserve University, December 3, 2004
- \*\* How is cellular magnesium regulated? And why should we care?, MetroHealth Medical Center, Cleveland, OH, February 5, 2008.
- \*\* Functional modification of cardiac mitochondrial proteins by 4-HNE in streptozotocin diabetic rats. Case Center for Proteomics, Cleveland, OH, April 24, 2008.
- \*\* Alteration of  $Mg^{2+}$  homeostasis in liver cells following acute and chronic EtOH administration: Implication for liver metabolism, held at Department of PathoBiology, Cleveland, Clinic Foundation, Cleveland, March 20, 2009.
- \*\* Effect of acute and Chronic EtOH administration on Hepatic  $Mg^{2+}$  homeostasis, College of Wooster, Sept, 11, 2009.
- \*\* Role of  $Mg^{2+}$  in Liver metabolism, Cedarville University, Dec. 5, 2011.
- \*\* Cellular  $Mg^{2+}$  Homeostasis: Physiological and Pathological Implications, Cleveland State University, Center for Gene Regulation in Health & Disease, April 5, 2012
- \*\*  $Mg^{2+}$  Homeostasis and Regulation of Glucose Metabolism in Liver cells, Cleveland State University, Dept. Clinical Chemistry, Sept, 7, 2012.

## Fields of Interest

1) Magnesium homeostasis, transport and redistribution in cardiac and liver cells under physiological (i.e. stimulation by catecholamines and insulin) and pathological (i.e. following acute and chronic ethanol administration and under diabetic conditions) conditions. Role of magnesium homeostasis on hepatic glucose and fatty acid metabolism.

2) Calcium homeostasis in liver cells: role of smooth and rough endoplasmic reticulum of liver cells in maintaining a physiological level of cytosolic free  $\text{Ca}^{2+}$  using glucose 6-phosphate or inorganic phosphates to enlarge the reticular pool of  $\text{Ca}^{2+}$  mobilizable by inositol 1,4,5-trisphosphate and GTP.

3) Identification of proteins forming stable adducts with 4-hydroxynonenal (4-HNE) in diabetes and alcoholism or following lipid peroxidation induced by halo-alkenals, bromo-benzene and allyl alcohol in liver cells and under diabetic conditions: thiols groups in membranes of subcellular compartments (i.e. mitochondria, endoplasmic reticulum, etc.) and in the cytoplasm.

(Identification of proteins forming stable adducts with 4-hydroxynonenal (4-HNE) under various conditions and its implications for mitochondria and ER functions)

### Key-Works:

- $\text{Mg}^{2+}$  homeostasis
- liver toxicology,
- Alcohol
- Diabetes
- 4-HNE/protein adducts

Signaling: cAMP, protein kinase C, insulin, glucose 6-phosphate, glucose, inorganic phosphate.

Experimental Models: perfused heart; perfused livers, cell isolation, cell in culture, plasma membrane vesicles, mitochondria, endoplasmic reticulum vesicles (microsomes), protein purification.

Techniques: organ perfusion, cell isolation, organelle isolation, TLC, HPLC, fluorimetry, spectroscopy, biochemical assay, antisense technique, radioisotope distribution, protein purification, gel electrophoresis, WB analysis, mRNA isolation.