CURRICULUM VITAE



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Education:

1986	B.S.	The Johns Hopkins University, Biomedical Engineering,
		Baltimore, MD
1990	M.D.	Harvard Medical School and Harvard-M.I.T., Division of
		Health, Sciences and Technology, Boston, MA

Postdoctoral Training:

Internship and Residencies:

1990-1991	Intern	Medicine	Massachusetts General Hospital, Boston, MA
1991-1993	Resident	Medicine	Massachusetts General Hospital, Boston, MA

Clinical and Research Fellowships:

1993-1996	Clinical & Research Fellow	Cardiology	Massachusetts General Hospital,
			Boston, MA
1993-1997	Clinical & Research Fellow	Medicine	Harvard Medical School, Boston, MA
8/94-12/94	Heart Failure Fellow	Cardiology	Brigham & Women's Hospital,
			Boston, MA

Licensure and Certification:

1991	Diplomate, National Board of Medical Examiners
1992	Massachusetts License Registration
1993	Diplomate, American Board of Internal Medicine, Internal Medicine
1997	Diplomate, American Board of Internal Medicine, Cardiovascular Disease

Academic Appointments:

1997-1998	Instructor in Medicine, Harvard Medical School, Boston, MA
7/98-12/02	Assistant Professor of Medicine, Harvard Medical School, Boston, MA
1/03-	Associate Professor of Medicine, Harvard Medical School, Boston, MA

Hospital or Affiliated Institution Appointments:

1997-1998	Clinical Assistant in Medicine, Massachusetts General Hospital, Boston, MA
1998-2002	Assistant in Medicine, Massachusetts General Hospital, Boston, MA
2002-	Director, Cardiovascular Laboratory of Integrative Physiology and Imaging,
	Massachusetts General Hospital, Boston, MA
2002-	Assistant Physician, Massachusetts General Hospital, Boston, MA

Other Professional Positions and Major Visiting Appointments:

2000	Visiting Professor, University of South Carolina, Division of Cardiology,
	Charleston, SC
2000	Visiting Professor, University of Miami, Department of Medicine, Miami, FL
2000	Visiting Professor, University of Cincinnati, Division of Cardiology and
	Department of Pharmacology, Cinicinnati, OH

Hospital and Health Care Organization Service Responsibilities:

1992-1996	Physician, Massachusetts Institute of Technology, Medical Department,
	Cambridge, MA
1002 1006	Devision Hanvard University Health Services Combridge MA

1993-1996 Physician, Harvard University Health Services, Cambridge, MA

Major Administrative Responsibilities:

1997- Principal Investigator, Cardiovascular Research Center, Massachusetts General Hospital, Boston, MA

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2002	Director, Cardiovascular Laboratory of Integrative Physiology and Imaging,
	Massachusetts General Hospital, Boston, MA

Major Committee Assignments:

Massachusetts General Hospital:

1997- Subcommittee on Research Animal Care, Member

Harvard Medical School:

1993-1995	Harvard-M.I.T Division of Health Sciences Subcommittee on Ethnic and Racial
	Sensitivities, Member
1998-	Harvard-M.I.T Division of Health Sciences & Technology, Board of Advisors,
	Member
1999-	Harvard-M.I.T Division of Health Sciences & Technology, Admission Committee,
	Member

<u>National:</u>

American Heart Association:

1996-	National Research Peer Review Committee, Member
1997	Affiliate Study Group Research Program & Evaluation Committee,
	Member
1997-1998	Northeast Peer Review Consortium, Member
	North East Research Peer Review Consortia, Member
2001-2004	North East Research Peer Review Committee, Member

National Institutes of Health/National Heart, Lung, and Blood Institute:

1998-	Research Training Review Special Emphasis Panel, Member
2001-	Committee for Program Project Grant, Member

National Academy of Sciences:

1999- Research Peer Review Committee, Member

Doris Duke Charitable Foundation:

1999- Annual Meeting Organization Committee, Member

Cardiovascular System Dynamics Society:

1999- Cardiovascular System Dynamic Society, Member-at-Large

Cardiovascular Cell and Gene Therapy Conference:

2002-2004 Director, Cardiovascular Cell & Gene Therapy Conference, Cambridge, MA

Professional Societies:

1982-1986	'Le Cercle Francais', Baltimore, MD, President
1993-1996	Tau Beta Pi, Engineering Honor Society, Johns Hopkins University,

- 1988- Biophysical Society, Member
- 1988- Massachusetts Medical Society, Member
- 1988-American Medical Association, Member
- 1991- American College of Physicians, Member
- 1993- American College of Cardiology, Member
- 1993- American Heart Association, Member
- 1997- Heart Failure Society of America, Member
- 1999- Cardiovascular System Dynamics Society, Member-at-Large
- 2000- American Society of Gene Therapy, Member
- 2001 Fellow of the American College of Cardiology
- 2001 Fellow of the American Heart Association

Editorial Boards:

- Circulation Research
- Journal of Molecular and Cellular Cardiology
- Contributing Editor for the Science of Aging Knowledge Environment (SAGE KE; http://sageke.sciencemag.org)

Reviewer:

- American Journal of Physiology
- Basic Research in Cardiology
- British Journal of Pharmacology
- Cardiovascular Research
- Circulation
- Circulation Research
- Developmental Biology
- Gene Therapy
- Journal of Clinical Investigation
- Journal of Clinical Therapeutics
- Journal of Molecular & Cellular Cardiology
- Journal of Cardiac Failure
- Metabolism
- Molecular Therapy
- New England Journal of Medicine
- Proceedings of the National Academy of Sciences
- Science

Awards and Honors:

- Premedical Honor Society, Alpha Delta Epsilon, The Johns Hopkins University, Baltimore, MD
 Engagering Honor Society, Tay Data Di, The Johns Honking University, Baltimore
- 1984 Engeering Honor Society, Tau Beta Pi, The Johns Hopkins University, Baltimore, MD
- 1983-1985 Dean's List, The Johns Hopkins University, Baltimore, MD

1986	General Academic Honors at Graduation, The Johns Hopkins University,
	Baltimore, MD
1986	Biomedical Engineering Departmental Honor, The Johns Hopkins
	University, Baltimore, MD
1986	Undergraduate Research Award in Biomedical Engineering, The Johns
	Hopkins University, Baltimore, MD
1990	Cum Laude (graduation), Harvard Medical School, Boston, MA
1993	Calderwood Manuscript Prize, Massachusetts General Hospital, Boston, MA
1995	DeSanctis Clinician Scholar Award, Massachusetts General Hospital,
	Boston, MA
1995	Astra Merck Young Cardiovascular Investigator Award, San Francisco, CA
1996	Bristol-Myers Squibb/American College of Cardiology Travel Award, Orlando, FL
1996-1997	Paul Dudley White Fellow of the American Heart Association, Massachusetts
	Affiliate
1996	New Investigator Award, American Heart Association, Scientific Conference on
	the Molecular Biology of the Normal, Hypertrophied, and Failing Heart
1996	Winner, Melvin Marcus Award for Integrative Physiology, American Heart
	Association, Council on Circulation, New Orleans, LA
1997	3 rd Place, AstraZeneca New England Cardiovascular Research Competition,
	Boston, MA
1998	Prize for Scientific Excellence, "Bold New Era for Cardiovascular Research",
	Boston, MA
1999	Doris Duke Clinical Scientist Award
1999	1 st Place, AstraZeneca Cardiovascular Young Investigators Forum, Banff, Alberta,
	Canada
2001	Beeson Scholar Award, American Federation for Aging Research
2003	Henry N Neufield Memorial Award, Israel
2005	American Society of Clinical Investigators, Member

Roger I Hajjar

Part II: Research, Teaching, and Clinical Contributions

A. Narrative Report

Congestive heart failure (CHF) represents an enormous clinical problem demanding effective therapeutic approaches. Despite advances in traditional approaches to its treatment, including pharmacologic management, myocardial revascularization, mechanical assist, and transplantation, CHF remains a leading cause of death worldwide. Even though new treatments for congestive heart failure have had a significant impact on mortality and the course of the disease, they do not reverse or cure the underlying pathological state of the heart. Our laboratory focuses on targeting molecular and cellular pathways to improve contractile function and survival in failing cardiac myocytes. We are targeting specific abnormalities that have been identified in failing hearts at the cellular level by gene transfer. These targets involve membrane channels, intracellular transporters involved in calcium homeostasis, intracellular pathways involved in cell survival.

1. Targeting calcium cycling proteins:

Contraction and relaxation in cardiac myocytes are tightly regulated by intrinsic mechanisms that govern the sequential rise and fall of cytosolic Ca^{2+} . During depolarization, Ca^{2+} entry through the L-type Ca^{2+} channels triggers the release of Ca^{2+} from the sarcoplasmic reticulum (SR) through ryanodine receptors resulting in activation of the contractile proteins. In human cardiomyocytes, the removal of Ca²⁺ from the cytoplasm is governed mainly by the SR Ca²⁺ ATPase (SERCA2a) pump and to a lesser extent the Na/Ca exchanger as shown. Cardiomyocytes isolated from failing human hearts are characterized by contractile dysfunction including prolonged relaxation, reduced systolic force and elevated diastolic force. These contractile abnormalities are paralleled by abnormal Ca²⁺ homeostasis such as reduced SR Ca²⁺ release, elevated diastolic Ca^{2+} and reduced rate of Ca^{2+} removal. In addition, failing human myocardium is characterized by a frequency-dependent decrease in systolic force and Ca^{2+} as opposed to normal myocardium where an increase in pacing rate results in potentiation of contractility and an increase in SR Ca^{2+} release. In the failing heart, the decrease in SR Ca^{2+} load has been linked to a decrease in SR Ca^{2+} ATPase function. We have recently shown that overexpression of SERCA2a by adenoviral gene transfer restores contractile function in cardiac myocytes from failing human hearts. In addition, we have shown that overexpression of SERCA2a in a model of pressure-overload hypertrophy in transition to failure improves contractile function and reserve in these animals. We are currently exploring the effect of longterm expression of SERCA2a in failing animals along with the energy cost of SERCA2a expression using NMR methods. We are also using a different strategy to improve SR Ca^{2+} ATPase activity, which involves decreasing the expression of phospholamban by antisense strategies to enhance SR Ca²⁺ ATPase activity. The Na/Ca exchanger is also being targeted to enhance calcium removal in failing hearts.

2. Clinical Trials in Gene Therapy for Heart Failure

Our laboratory has extended these studies in large animal models and is developing novel molecular imaging techniques to better track gene transfer. In addition, our laboratory is using both genomics and proteomics approaches to identify new targets based on the restoration of contractile function following SERCA2a gene transfer. The large body of data generated by our laboratory to establish SERCA2a as a key target for gene transfer in heart failure has culminated in the initiation of a NIH-funded clinical trial, "Gene Therapy with Adeno-associated Virus Carrying SERCA2a in Patients With Advanced Heart Failure Undergoing Ventricular Assist Device Placement". This trial will demonstrate the bench-to-bedside application of his research.

3. Targeting the Transient Outward Current:

Action potential prolongation is attributed to reductions in transient outward current (Ito) density in human heart failure. This prolongation can improve contractility but can also cause afte depolarization. Using gene transfer of various K channels responsible for Ito, we are investigating the molecular and the ionic basis of action potential prolongation in cardiac hypertrophy and failure and we are examining how intracellular calcium handling changes in response to alterations in action potential duration.

4. Gene Transfer in Aging Myocardium:

Gene therapy in heart failure has the biggest potential in the aging population where the disease is rampant. However adenoviral gene transfer is less effective in aging cardiac cells than in younger cells. We are examining the molecular mechanisms responsible for this decrease in infectivity.

5. Viral Vectors:

We are constructing viral vectors including adenoviruses (E1-E4 deleted), adeno-associated viruses, and lentiviruses with promoters that infer cardiac specificity and long-term expression.

6. Tracking stem cells in the cardiovascular system

Our laboratory is using newly developed molecular probes to track stem cells and to understand the biology of integration and the cellular fate of stem cells in large animal model of myocardial infarction and remodeling. These novel molecular probes generate contrast simultaneously for both magnetic resonance imaging (MRI) and near-infrared (NIR) fluorescent optical imaging. MRI permits stem cells to be identified in the normal and diseased hearts of large animals over time, non-invasively, and without sacrifice of the animal. NIR fluorescent optical imaging provides high sensitivity, and in some cases single cell sensitivity, which can be used for intraoperative physiological studies, and for histological correlation with other markers of cardiomyocyte function.

B. Funding Information (education and research)

<u>Past</u>						
1988-1989	Johnson & Johnson Fund Pre-Doctoral Student					
	Negative Tension Phenomena in Skeletal Muscle					
1996	AHA Massachusetts Affiliate PI					
	Gene Therapy in Heart Failure (Declined)					
1996-2001	NIH/K08 Mentored Clinician Scientist Development Award PI					
	Adenoviral Gene Transfer of Ca ²⁺ ATPase in Heart Failure					
1997-2001	NIH/R29 FIRST Award PI					
	Adenoviral Gene Transfer in Heart Failure					
1999-2000	American Federation for Aging Research PI					
	Restoration of Diastolic Function in Senescent Rats by Gene Transfer					
1998-2002	NIH/R01 Co-PI					
	Role of IGF-1 Receptor Signaling in Cardiocyte Apoptosis					
1998-2001	NIH/R01 Co-PI					
	Signaling Pathways, Apoptosis, and Heart Failure					
1999-2001	NIH/R01 Co-PI					
	NMR of Mitochondrial Transporter in Cardiac Hypertrophy					
1999-2001	NIH/R01 Co-PI					
	Signaling Pathways in Hypertrophy and Failure					
1999-2002	Doris Duke Clinical Scientist Award - PI					
	Targeting Signaling Pathways in Heart Failure					
1999-2003	NIH/NHLBI 2R01HL49574-05 - Co-PI					
	Heart Failure: Ca ²⁺ Homeostasis and Energy Reserve					
2001-2004	American Federation of Aging Research					
	Targeting Signaling Pathways in the Aging Heart by Gene Transfer					
2001-2002	Astra Zeneca - PI					
	Educational Grant					
2002-2003	NIH/NHLBI 1R13 HL71011-01					
	Conference Grant: Cardiovascular Cell & Gene Therapy Conference					

Active

4/01/02-3/31/06 - PI NIH/NHLBI R01 HL57263-05 Adenoviral Gene Transfer of Ca²⁺ ATPase in Heart Failure

7/15/03-6/30/07 - PI NIH/NHLBI R01 HL 71763-01 K and Ca Channels in Cardiac Hypertrophy and Failure

09/22/04-08/31/08-PI NIH/NHLBI R01 HL 078691 Optical & MRI Imaging of Stem Cells in Diseased Hearts

7/01/05-6/30/10-PI NIH/NHLBI R13 HL082354 Cardiovascular Cell & Gene Therapy Conference

12/01/05-11/30/10 NIH/NHLBI R01 HL080498 **PICOT & Cardiac Hypertrophy**

9/1/05-8/31/10-Co-PI Agency: Fondation LEDUCQ: Transatlantic Networks of Excellence Program Ca²⁺ cycling and novel therapeutic approaches for heart failure

7/15/03-6/30/07 - Co-PI NIH/NHLBI R01 HL733756-01 Tracking Stem Cells: Viability and Function in the Heart

9/1/03-8/31/07 - Co-PI NIH/NHLBI R01 HL67297-01 Regulation of Ca²⁺ Signaling in Myofilament by Troponin C

7/1/03-6/30/07 - Co-PI NIH/NHLBI R01 HL072265 Effect of Mitral Regurgitation on Ischemic Left Ventricular Remodeling

C. Report of Current Research Activities

<u>Principal Investigator, Cardiovascular Research Center, Massachusetts General Hospital</u> (see A):

- Gene Transfer in the Cardiovascular System

- Excitation-Contraction Coupling in Heart Failure
- Inotropic Mechanisms in Heart Failure
- Myofilament Regulation in Heart Failure
- Sarcoplasmic Reticulum Function in Heart Failure

D. Report of Teaching

1. Local Contributions

a. Johns Hopkins University:

1983-1986	Inorganic Chemistry Course, Teaching Assistant
1985	Organic Chemistry Course, Teaching Assistant

b. Harvard Medical School:

1990	Cardiovascular Pathophysiology, Harvard-MIT Division of Health Sciences and
	Technology, Teaching Assistant
1993-1996	Treatment of Heart Failure: Basic Science and Clinical Aspects, Lecturer.
	Fourth-year Harvard medical students, 10-20 students, one month/year,
	2-4 lectures on heart failure, 10 hrs/month
1994	Introduction to Clinical Medicine, Tutor. Second-year Harvard medical student,
	2 students, Spring term (Feb-May). Biweekly meeting: 2-4 hrs/week
1996-	Cardiovascular Pathophysiology (HT090), Harvard-MIT Division of Health
	Sciences and Technology, Core Faculty Lecturer. First-year Harvard medical
	students (HST program), 10 students/group, weekly meetings and 10 didactic
	lectures in the spring term (Feb-May), 5 hrs/week
1999-	Treatment of Heart Failure: Basic Science and Clinical Aspects (ME547.3),
	Co-Director. Fourth-year Harvard medical students, 10-14 students, one
	month/year and 8 didactic lectures on heart failure, 40 hrs/month

c. Harvard School of Public Health:

2000 *Frontiers in Cardiovascular Biology*, Lecturer to Harvard School of Public Health students, 20-30 students, one month/year and 1 didactic lecture on heart failure, 5 hrs/month

d. Graduate Medical Courses:

- 1999- *Molecular Medicine* (HT 140), Lecturer, MIT Graduate students and Second-year Harvard medical students, 20-30 students, one month/year and 2 didactic lectures on heart failure, 10 hrs/month
- 2000- *HST S11: The Art and Science of Medicine*, Lecturer: "Molecular Biology in Medicine," MIT, Undergraduate students, 2 hrs every semester

e. Local Invited Teaching Presentations (Lecturer) [e.g. grand rounds, seminars]:

- 1995 Colloquium, College of Pharmacy, Northeastern University, Boston, MA
- 1996 Cardiovascular Research Seminar, Brigham & Women's Hospital, Boston, MA
- 1997 Whitaker Research Seminar, Boston University, Boston, MA
- 1997 New England Cardiovascular Research Forum, Astra, Cambridge, MA
- 1998 Society of Fellows, Massachusetts General Hospital, Boston, MA

- 1998 Invited Speaker, Bold New Era for Cardiovascular Research, Boston, MA
- 1998 Medical Grand Rounds, Massachusetts General Hospital, Boston, MA
- 1998 Cardiovascular Research Seminar, Boston University, Boston, MA
- 1998 Heart Failure Symposium, Boston University Hospital, Boston, MA
- 1999 Cardiology Grand Rounds, Boston University School of Medicine, Boston, MA
- 1999 Cardiology Grand Rounds, Massachusetts General Hospital, Boston, MA
- 1999 Cardiovascular Seminar, Boston University School of Medicine, Boston, MA
- 1999 Cardiovascular Research Institute Seminar, New England Medical Center, Boston, MA
- 2000 Cardiovascular Research Seminar, Harvard School of Public Health, Boston, MA
- 2001 Heart Failure Research Seminar, Brigham & Women's Hospital, Boston, MA
- 2001 Gastrointestinal Unit Research Seminar, Massachusetts General Hospital, Boston, MA
- 2002 Clinical Pathological Conference, Case Records of the Massachusetts General Hospital, Boston, MA
- 2002 Medical Grand Rounds, Massachusetts General Hospital, Boston, MA

d. Continuing Medical Education Courses:

National:

- 1999 "New Treatment Modalities in Heart Failure", Buffalo, NY
- 2000 "Angiotension Receptor Blockade in Heart Failure", Miami, FL
- 2002 Pri-Med Symposia Beta Blockers in Heart Failure series, Washington, DC

Regional:

- 1998 "Angiotensin Receptor Blockers in Cardiovascular Disease", Portland, ME
- 1999 "Emerging Therapies in Heart Failure", Maine Medical Center, Portland, ME
- 2001 "Angiotensin Receptor Blockers in Cardiovascular Disease", Portland, ME
- 2002 Beta Blockers in Heart Failure, Providence, RI

Local:

- 1999 "Angiotensin and its Receptor's Impact on Cardiovascular Disease", Boston, MA
- 2001 "Angiotensin II and Cardiovascular Diseases", West Springfield, MA
- 2001 "National Initiative in Continuing Medical Education", Charlestown, MA
- 2002 Pri-Med Symposium on Beta Blockers in Heart Failure, Boston, MA

e. Advisory and Supervisory Responsibilities in Clinical or Laboratory Setting:

<u>Clinical</u>

- Two-three months/year Attending in the Heart Failure & Cardiac Transplantation Service. Supervision of one-two cardiology fellows. 40 hrs/week.
- One half day clinic every two weeks for general cardiology and evaluation of patients with severe heart failure. 4 hrs/2 weeks.
- One weekend per month covering Cardiac Transplantation and Heart Failure.
- Three weeks general cardiology consult per year. Supervision of two cardiology fellows. 20 hrs/week.
- Weekly cardiac transplantation meeting. 1 hr/week.
- Monthly Boston cardiac transplantation meeting. 3 hrs/month.
- Weekly heart failure meeting. 1 hr/week

Laboratory

- 1. 800 square feet at the Cardiovascular Research Center dedicated for gene transfer research in heart failure
- 2. Supervision of six postdoctoral fellows and one technician. 20 hrs/week
- 3. Supervision of of one-two undergraduate students from MIT. 5 hrs/week
- 4. Weekly laboratory meeting. 1 hr/week
- 5. Weekly cardiovascular gene therapy meeting. 1 hr/week
- 6. National/International meetings. 1/month

f. Teaching Leadership Roles in Department/Affiliated Institution:

1999- *Treatment of Heart Failure: Basic Science and Clinical Aspects (ME547.3)*, <u>Co-Director</u>. Fourth-year Harvard medical students, 10-14 students, one month/year and 8 didactic lectures on heart failure, 40 hrs/month

1999 Thesis advisor, director of the thesis committee for Gabriel Choukroun, Universite de Paris, France

g. Trainees (impact on career):

<u>Name</u>	<u>Type</u>	Dates	Degree	<u>Institution</u>	<u>Project</u>	Current Position
Balderas, Isabel	Pre-Doc	2002	BS	Harvard Medical School	Tissue specific promoter following gene transfer	American Federation of Aging Research-The John A. Hartford/AFAR Medical Student Geriatric Scholars Program
Beeri, Ronen	Post-Doc	2000-3	MD	Hebrew University, Jerusalem		US-Israel Binational Science Foundation, 2002
Bernecker, Oliver	Post-Doc	9/02-	MD	University of Innsbruck	Cardiac specific promoter for gene transfer	Max Kade Foundation for Research-Austria
Boecker, Wolfgang	Post doc	1998-00	MD	University of Berlin, Germany	Targeting the Heart with Tissue specific Promoters	Med. Internship, Johns Hopkins
Boelcke, Birgit	Post-doc	2002	PhD	University of Cologne, Cologne, Germany	Targeting sorcin in heart failure	Assistant in Medicine, Universitat Koln, Koln, Germany
Choukroun, Gabriel	Post-Doc	1996-99	MD, PhD	Universite de Paris Hopital Necker	SAPKinase and cardiac hypertrophy	Chief, Renal Unit Universite d'Amiens, France
Communal, Catherine	Post Doc	2000-2002	Ph.D	University of Fourier, Grenoble, France	P38 and Heart Failure CASPASE and heart failure	Research Scientist, Inserm, France
Dadfarmay, Sina	Med Student	6/25-9/30/01	BS		BNP Promoter for gene therapy	Medical Student, Royal College of Surgeons, Ireland
Dalal, Rishikesh	Pre-Doc	2002-3		Harvard University	Transcript Profiling following SERCA2a gene transfer	Departmental funds
Davia, Kerry	Post Doc	3/98-9/98	PhD	Imperial College School of Medicine	Isolation of Human Cardiomyocytes	Scientist, Glaxo-Welcome, UK
Grazette, Luanda	Post Doc	6/3/99-6/01	MD/MPH	Harvard/MGH	erb-B2 Receptors in Failing Hearts	Instructor in Medicine, Harvard Medical School
del Monte, Federica	Post Doc	2/98-03	MD/Ph.D	Univ."La Sapienza" of Rome, Imperial College, London	Targeted Gene Transfer in Failing Hearts	Assitant Professor of Medicine, Harvard Medical School Princip. Invest. Cardiovascular Res Center
Heist, Kevin	Post-Doc	7/02-	MD, PhD	Stanford University	Role of CAMkinase in heart failure	Cardiac Electrophysiology MGH

Hayase, Motoya	Instructor	2002-2005	MD	Toyoshima University, Japan	Guided delivery of genes	NHLBI (Hajjar)
Huq, Fawzia	Post-Doc	4/01-6/03	MD	University of Sydney	Gene Transfer in Failing Human Hearts	Resident, University of Texas, Southwestern
Iyer, Vivek	Pre-Doc		MS	Harvard	Excitation Contraction Coupling Modeling	
Jang, Monica	HS Stud.	7-9/00-01		Phillips Exeter Academy, New Hampshire	Viral gene transfer	Undergraduate, MIT
Kaprielian, Roger	Post Doc	9/1/99-2001	Ph.D	University of Toronto	Modulating Ito in Failing Hearts	Medical Information Scientist, Astra Zeneca
Kuri, Manuel	Visiting Scientist	Post-doc	PhD	Universidad Pan- Americana, Mexico City	Modulation of Ito current and Cardiac Hypertrophy by Ras	Instructor in Physiology,
Lamers, Frouke	Post Doc	1/7-31/98	MD	Erasmus University of Rotterdam	Adenoviral Vectors for gene transfer	Medical Resident, Erasmus University of Rotterdam

<u>Name</u>	<u>Type</u>	<u>Dates</u>	Degree	Institution	<u>Project</u>	Current Position
Mansour, Moussa	Post Doc	7/01-6/04	MD	Massachusetts General Hospital	Gene Transfer of the Na/Ca Exchanger in Atrial Fibrillation	Instructor in Medicine
Mestel, Celine	Pre-Doc	3/1-8/31/00	BS	Massachusetts Institute of Technology	CAR in Aging cardiomyocytes	Junior at MIT
Miyamoto, Michael	Post Doc	6/9/97-9/98	MD	Massachusetts General Hospital	Gene Transfer of SERCA in Aortic	Private practice, Cardiology, CA
Park, Woo Jin	Post Doc	2003	PhD		Proteomics in Heart Failure	
Perry, Curt	Student	7/17-8/17/01		Cambridge Rindge & Latin School (CRLS)	Infectivity in Aging Myocytes	Cambridge Rindge & Latin School (CRLS)
Ranu, Hardeep	Post Doc	11/15/98- 1/31/00	PhD	Imperial College School of Medicine	Na/Ca exchanger in Failing Hearts	Post-doctoral fellow, Renal Unit, MGH
Sakata, Naoya	Volunteer		Student	Kobe University of Commerce		
Sato, Takuya	Post-Doc	2002-2004	PhD	Mitsubishi Pharma	Effect of MCC 135 on Failing Cardiomyocyte Contractility	Mitsubishi Pharmaceuticals, Japan
Schmidt, Ulrich	Post Doc	1996-2001	MD/Ph.D	University of Munich	Gene Transfer of Bcl2 in Failing Hearts	NHLBI (K08) Mentored Clinical Scientist Award
Soltesz, Edward	Post Doc	2001-02	MD	Harvard Medical School	Gene Transfer in Porcine Model of Cardiomyopathy	Clinical Fellow, Harvard Medical School
			MD	American University of Beirut	Transcript Profiling analyses	Resident, Boston Medical Center
Tabchy, Adel	Post-Doc	2003-4				
Tsuji, Tsuyoshi	Post Doc	2001-03	M.D.	Nara University	Measurement of Metabolic Parameters in heart failure	Assistant Professor of Surgery, Nara University
Villa-Petroff, Martin	Visiting Scientist	2002	PhD	Centro de Investigaciones Cardiovasculares. Facultad de Medicina, Argentina	Gene Transfer of Na/Ca in Failing Hearts	Biologist, Centro de Investigaciones Cardiovasculares Facultad de Medicina, Argentina
Yerevanian, Armen	HS Student	2000		High school, Manoogian school, CA	Infectivity in Aging Cardiac Myocytes	High school, Manoogian school, CA

Yerevanian, Alex	HS Student	2004		High School, Demirdjian High School, CA		
Zhu, Xinsheng	Post-Doc	2002-4	Ph.D.	University of Wisconsin	Septic Shock and Heart Failure	Instructor, Dept of Anesthesia, MGH

PRESENT						
Name	<u>Type</u>	Dates	Degree	<u>Institution</u>	<u>Project</u>	<u>Funding</u>
Bukhari, Fariya	Post-Doc	2004-	MD	University of Arizona	Sarcoplasmic Reticulum Content in Heart Failure	NHLBI (Hajjar)
Chemaly, Elie	Post-Doc	2004-	MD	State University of NY	Zinc finger protein targeting calcium cvcling	NHLBI (Hajjar)
Hadri, Lahouaria	Post-Doc	2005-	MD MD	Universite de Paris Kyoto University	PICOT & Cardiac hypertrophy Gene & Cell Delivery to the Heart	NHLBI (Hajjar) Japanese Cardiology Fellowship
Hoshino, Kozo	Post-Doc	2003-	PhD	Chinese Academy of	K channels in heart failure	NHLBI (Hajjar)
Jin, Hongwei	Post-Doc	2005-		Medical Science & Peking Union Medical College		
Kawase Voshiaki	Post-doc	2003-	MD	Gifu University, Japan	Gene transfer in large animals	NHLBI (Hajjar)
Kuhn, Bernhard	Post-doc	2005-	MD	Boston Children's Hospital	Regenerative potential of the myocardium	NHLBI (Kuhn)
Lebeche, Djamel	Post Doc	8/1/99-	Ph.D.	Boston University	Kv Channels & hypertrophy	K01/NIH/NHLBI
Ly, Hung	Post-Doc	2005-	MD	Universite de Montreal	Cell delivery and MR tracking	Fonds de la Recherche-Quebec
Palomeque, Julieta	Post-Doc	9/1/2004-	MD, PhD	Faculty of Medical Siciences, La Plata, Argentina	AAV vectors in gene transfer	NHLBI(Hajjar)
Pomerantseva, Irina	Post-Doc	2002-	MD	Moscow Medical Academy	Stem cell therapy in heart failure	NHLBI (Hajjar)
	1000 200	2002	MD, PhD	Universite de Paris	Gene Therapy in Heart Failure	Societe Francaise de Cardiologie
Prunier, Fabrice	Post-Doc	2005-	MD	Tokyo University	MRI tagging of stem cells	Departmental Funds
Yoneyama, Ryuichi	Post-doc	2003-	PhD	Nara University	Energetics in the Failing Heart	Nara University Scholarship
Sakata, Susumu	Post-Doc	2003-				Г. Т. С. С. Т. С. С. Г. Г. Г. С. Г. Г. Г. С. Г.

Takewa, Yoshiaki Post-doc 2005-

PhD Nara University

Surgical gene transfer in large animals

Nara University Scholarship

Technicians:

- 1. Lifan Liang MD (2000-)
- 2. Cathy McMahon (2005-)
- 3. Jimmy Lough (2005-)

2. Regional, National, and International Contributions

a. Invited Presentations (Lecturer) [e.g. plenary presentations, visiting professorship]:

Local Presentation:

- 1999 Research Seminar in Aging, Institute of Aging, Harvard Medical School, Boston, MA
- 2000 Gordon Research Conference, Cardiac Regulatory Mechanisms, New London, NH
- 2000 "Improvement in Diastolic Function in Aging Hearts by Targeted Gene Transfer" American Federation of Aging, Boston, MA
- 2001 NASPE 22nd Annual Scientific Session, Boston, MA
- 2002 Cardiology Grand Rounds, Sturdy Memorial Hospital, Attleboro, MA
- 2002 Cardiology Grand Rounds, Beth Israel Hospital, Boston, MA
- 2002 Cardiology Grand Rounds, Brigham & Women's Hospital, Boston, MA
- 2003 Cardiac Grand Rounds, Union Hospital, Lynn, MA
- 2003 Harvard Medical School Division on Aging Research, Fellowship Review Meeting Boston, MA
- 2003 AstraZeneca: Toprol XL in Heart Failure, Framingham, MA
- 2003 AstraZeneca: Beta Blockers & Heart Failure, Plymouth, MA
- 2003 "Updates on new Dyslipidemia Therapies", AstraZeneca Crestor Program, Waltham, MA
- 2003 Grand Rounds Leonard Morse Hospital, Natick, MA
- 2003 Updates on Dyslipidemia, AstraZeneca, Springfield, MA
- 2003 ACCF: New Management of Advanced Heart Failure, Boston, MA

Regional Presentations:

- 1992 Cardiovascular Grand Rounds, Division of Cardiology, UCLA, Los Angeles, CA
- 1996 Cardiovascular Research Seminar, University of Cincinnati, OH
- 1996 Heart Failure Seminar, Columbia University, New York, NY
- 1997 Cardiovascular Grand Rounds, University of Maryland, Baltimore, MD
- 2000 Cardiology & Medical Grand Rounds, Piedmont Hospital, Atlanta, GA
- 2000 Medical Grand Rounds, Charlotte Hospital, Torrington, CT
- 2001 Invited Distinguished Faculty, Cardiovascular Center, University of Illinois, Chicago, IL
- 2000 Visiting Professor, University of Miami, Department of Medicine, Miami, FL
- 2000 Visiting Professor, University of Cincinnati, Division of Cardiology and Department of Pharmacology, Cincinnati, OH
- 2000 BWH Cardiac Center Nursing Symposium: Cardiovascular Care 2000, Bartlett, NH
- 2002 Cardiology Grand Rounds, University of California at San Diego, San Diego, CA
- 2001 Research Seminar, University of California at San Diego, San Diego, CA
- 2001 Medical Grand Rounds, Gene Therapy in Cardiovascular Disease, Roger Williams Medical Center, Providence, RI
- 2001 Cardiology Grand Rounds, Ohio State University Medical Center, Columbus, OH
- 2001 Cardiology Grand Rounds, Hanhnemann Hospital/Penn State, Philadelphia, PA
- 2001 Medical Cardiac Grand Rounds, Emory University Hospital, Atlanta, GA
- 2001 Vascular Biology Seminar, Emory University Hospital, Atlanta, GA
- 2001 Medical Grand Rounds, Washington University, St Louis, MO
- 2001 Cardiology Grand Rounds, Washington University, St Louis, MO
- 2001 Biomedical Engineering Seminar, Johns Hopkins University, Baltimore, MD

- 2002 Cardiovascular Seminar, Albert Einstein Medical Center, Bronx, NY
- 2002 Guest Speaker, 10th Annual Cardiovascular Symposium, Bradley Memorial Hospital, CT
- 2002 Gordon Research Conference, Cardiac Regulatory Mechanisms, CT
- 2002 Gordon Research Conference, "Cardiac Regulatory Mechansisms." "Mechanisms for rescue of the failing Heart", New London, CT
- 2003 "Under the Microscope: Attacking Heart Failure on the Cellular level" St. Vincent's Catholic Medical Center, Manhatten, New York, NY
- 2004 Invited Speaker "Angiotension Receptor Antagonist in Heart Failure", Cardiovascular Continuing Education Symposium, Providence, RI
- 2004 Invited Speaker "Hypertension and Heart Failure", NAMCP Continuing Medical Education, Norwalk, CT

National Presentations:

- 1995 Forum of Young Cardiovascular Investigators, Astra Merck, San Francisco, CA
- 1995 "Molecular Mechanisms of Cellular Dysfunction in Heart Failure", American Heart Association, Basic Science Council, Anaheim, CA
- 1998 "Gene Transfer of SERCA", American Heart Association, Basic Science Council, Dallas, TX
- 1999 "Gene Transfer of SERCA2a" Heart Failure Society of America, "Late Breaking Science", San Francisco, CA
- 2000 "Experimental Models of Cardiovascular Disease", Society of Toxicology, Philadelphia, PA
- 2001 "Improving Contractile Function by Gene Transfer in Human Heart Cells" Doris Duke Yearly Scientific Meeting, VA
- 2000 "The Future of Gene Therapy for Heart Failure", North American Society of Pacing and Electrophysiology (NASPE), Washington, DC
- 2000 "Gene Transfer in Heart Failure", Heart Lung, and Blood Diseases, National Institutes of Health, Baltimore, MD
- 2000 Enhancing Contractile Function by Gene Transfer in Failing Human Hearts" Heart Failure Society of America, "Late Breaking Science", Boca Raton, FL
- 2000 American Heart Association (AHA) 73rd Scientific Sessions, New Orleans, LA
- 2001 Satelite Symposium, Cardiac Remodeling, Minneapolis, MN
- 2001 Heart Failure Society of America, Washington, DC
- 2001 American College of Cardiology (ACC) 50th Scientific Sessions, Orlando, FL
- 2001 Experimental Biology 2001 Symposium, Orlando, FL
- 2001 The First Annual Fall Cardiovascular Symposium, Maui, Hawai
- 2001 American Heart Association, Anaheim, CA
- 2001 "Gene Therapy in Heart Failure", Symposium, Avigen Inc., Alameda, CA
- 2002 Clinical Course, Gene Therapy, North American Society of Pacing & Electrophysiology 23rd Annual Session, San Diego, CA
- 2002 International Society for Heart Research, Madison, WI
- 2002 Invited Speaker, "Gene Therapy in Heart Failure" Medtronic Symposium, Keystone, CO
- 2002 Invited Speaker, "Techniques in Gene Transfer in Rodent Models of Heart Disease." AHA, Snowbird, CO
- 2002 Invited Speaker, "Targeting Signaling Pathways in the Failing Heart." Symposium, Bristol Myers Squibb, NJ
- 2002 Invited Speaker, Therapeutics Horizon in Heart Failure, San Diego, CA
- 2003 Invited Speaker, Division of Cardiology, University of Minnesota, Minneapolis, MN
- 2003 Seminar, Dept of Physiology & BioPhysics, Case Western University, Cleveland, OH

- 2003 "Beta Blockers: Standard of Care in Heart Failure" Grand Round, Div.of Cardiology, University of Michigan, Ann Arbor, MI
- 2003 FASEB Summer Research Conference on: "Transport ATPases: Genomics, Mechanisms and Targeting the ATPase Pump". "Rescuing Diseased Myocardium by Relevance to Diseases". Vermont Academy, Saxton, VT
- 2003 "Disease Interrupted: Using Beta Blockers in the Treatment of Heart Failure": Olean General Hospital, Olean, NY
- 2003 "Gene Therapy for Heart Failure", GUIDANT Biologics Advisory Board Meeting for Heart Failure, Minneapolis, MN
- 2003 "New Developments in Gene Therapy". 7th Annual Scientific Meeting, Heart Failure Society of America, Las Vegas, NV
- 2003 "Maximizing Approaches in the Evaluation and Management of Patients with Dyslipidemia". APOLLO Dyslipidemia Grand Rounds: a CME Grand Rounds Series, San Francisco, CA
- 2003 "Under the Microscope: Attacking Heart Failure on the Cellular Level", Newark Beth Israel Medical Center, Newark, NJ
- 2003 "Gene Therapy in Medical Rx Session", No Boundaries: State-of-the-Art Medical/Surgical Approaches to Advanced Heart Failure, Mohegan Sun Casino, Unkersville, CT
- 2003 "Gene Therapy in Heart Failure", Medical Grand Rounds at Geisinger, Harrisburg, PA
- 2004 Invited Speaker "Gene Therapy for Heart Failure", Cardiology Colloquim on Heart Failure, Dayton,OH
- 2004 Invited Speaker "Genetic Editing of Dysfunctional Myocardium: Mechanistics Insights" Orlando, FL
- 2004 Speaker "Targeted Cardiac Gene Transfer"-The American Society of Gene Therapy Minneapolis, MN
- 2004 Speaker "Targeted Gene Transfer for Diastolic Dysfunction"—American Federation of Aging Research, Beeson Award, Park City, Utah
- 2004 "Rescuing the Failing Heart with Gene Transfer". Invited Speaker Cardiology Grand
- Rounds University of Virginia, Charlottesville, VA
- 2004 "Targeting Calcium cycling in Failing Heart with Gene Transfer". Invited Speaker Cardiology Grand Rounds, University of Louisville, KY
- 2005 "Targeted Gene Transfer in Heart Failure" Invited Speaker Cardiology Grand Rounds, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, OH
- 2005 "Calcium cycling in heart failure" Heart & Vascular Center for the MetroHealth System and Director, Heart & Vascular Research Center, MetroHealth Campus, Case Western Reserve University
- 2005 "Gene Therapy in Heart Failure" Cardiology Division, Dartmouth Medical Center, NH

2005 "From basic Mechanisms to Targeted Gene Therapy in Heart Failure" Cardiology Division, Mount Sinai Medical Center, NY

International Presentations:

- 1991 Gargellen Conference, Cellular and Molecular Alterations in the Failing Human Heart, Gargellen, Austria
- 1996 American Lebanese Medical Association, Beirut, Lebanon
- 1996 Cardiovascular Grand Rounds, American University of Beirut, Beirut, Lebanon

- 1997 "Gene Transfer in Myocardium", European Society of Cardiology, Heart Failure '97, Cologne, Germany
- 1997 Transition from Cardiac Hypertrophy to Failure, Cologne, Germany
- 1999 Gene Transfer of Calcium Cycling Proteins in Heart Failure, Toronto Heart Failure Summit, American College of Cardiology, Toronto, Canada
- 1999 Manipulation of SERCA2a in the Heart by Gene Transfer, International Symposium on Molecular Approaches to the Therapy of Heart Failure, Gottingen, Germany
- 1999 Fifth Annual AstraZeneca Cardiovascular Young Investigators Forum, Banff, Alberta. Canada
- 1999 "Therapie Genique de l"insuffisance Cardiaque" Institut de Myologie, Hopital de la Salpetriere, Paris, France
- 1999 "Therapie Genique de l'insuffisance Cardiaque" Hopital Necker, Paris, France
- 2000 IV International Conference on Myocardial Function, Padova, Italy
- 2000 Expert Meeting on New Targets in Congestive Heart Failure, Boehringer Ingelheim, Frankfurt, Germany
- 2001 International Symposium: Cardiac Function: Improving Function in Failing Hearts by Targeted Gene Transfer, Osaka, Japan
- 2001 "Heart Failure: From Molecular Mechanisms to Targeted Gene Transfer", Nara University, Nara Japan
- 2001 "Basic Mechanisms of why the heart fails", Fu Wai Hospital, Beijing, China
- 2001 "New Therapeutic Approaches in Heart Failure", Beida Hospital, Beijing, China
- 2001 "Basic Mechanisms of why the heart fails", Union Hospital, Beijing, China
- 2001 "Targeting apoptic pathways by gene transfer in cardiac muscle", "Cardiac transplantation in the year 2000," Fu Wai Hospital, Beijing, China
- 2001 XVII ISHR World Congress, Winnipeg, Canada
- 2001 "Gene Therapy for Heart Failure", 50th Anniversary of the Egyptian Society of Cardiology, American College of Cardiology, Cairo, Egypt
- 2001 "SERCA2a gene transfer in Heart Failure", 3rd Cologne Conference on Heart Failure, Cologne, Germany
- 2001 "Gene transfer in animals in vivo," European Heart Failure 2001, Barcelona, Spain
- 2001 "Novel Treatments for Heart Failure", Japanese Heart Failure Society, Sendai, Japan
- 2001 Gene Transfer of SERCA2a in Heart Failure, Toronto Heart Failure Summit, American College of Cardiology, Toronto, Canada
- 2001 "Targeting SERCA2a in Heart Failure", Mitsubishi Chemicals, Tokyo, Japan
- 2002 "Targeting Signaling Pathways in Heart Failure" Department of Pharmacology, University of Wurzburg, Wurzburg, Germany
- 2002 Targeting calcium cycling proteins by gene transfer "*in vivo* and *in vitro*" The Journal of Physiology Symposium at the joint meeting of the UK, German and Scandinavian Physiological Societies, Tübingen, Germany.
- 2002 Gene Transfer of calcium cycling proteins in heart failure, Toronto Heart Failure Summit, American College of Cardiology, Toronto, Canada
- 2002 Targeting signaling pathways in hypertrophy and heart failure. Xth Annual Meeting of the International Society of Heart Research (ISHR), La Plata, Argentina
- 2000 Gene Therapy for Heart Failure. Xth Anual meeting of the International Society of Heart Research (ISHR), La Plata, Argentina
- 2002 "Gene Therapy for Heart Failure." Molecular Mechanisms in Heart Failure. Tokyo,

Japan

- 2002 "Molecular Mechanisms of Heart Failure and Novel Therapeutic Strategies", Keynote Speaker, Japanese Heart Failure Society, Tokyo, Japan
- 2002 "Rescuing the Failing Heart by Targeted Gene Transfer." Symposium, Yokohama City University, Yokohama, Japan.
- 2002 "Gene Therapy for Heart Failure." Samsung Symposium in Cardiac and Vascular Disease. Seoul, Korea
- 2003 "Improving Deficit Calcium Regulation in Heart Failure" European Society of Cardiology (ESC) Congress, Vienna, Austria
- 2004 "Gene Therapy for Heart Failure", International Society for Heart Research-Latin American Section, Iguazu Falls, Argentina
- 2004 "Targeted Gene Therapy in Heart Failure", 8th Annual Scientific Meeting of the Japanese Heart Failure Society, Gifu, Japan
- 2004 "Gene Therapy in Heart Failure", The International Congress of Cardiology of the Lebanese Society of Cardiology, Beirut, Lebanon
- 2004 "Program in Cardiovascular Gene Therapy". Xinjiang Medical University, Uruqmi, China
- 2004 "Gene Therapy for Heart Failure", 3rd International Congress of the Helleric College of Cardiology & Cardiac Surgery, Athens, Greece.
- 2004 "Therapie Genique pour l'Insuffisance Cardiaque" Hopital Pitie-Salpetriere, Paris, France
- 2005 "Towards Clinical Gene Therapy in Heart Failure" Keynote Speaker, German Society of Cardiology, Mannheim, Germany

2005 "From Basic Mechanisms to Clinical Trials in Heart Failure." 7th Cologne Conference on Heart Failure.

2005 "In vivo Tracking of Stem cells" Ernst Schering Research Foundation Workshop 60, Kobe, Japan

- 2005 "Gene therapy for heart failure" Gwangju Institute, Gwangju Korea
- 2005 "Cibles Genetiques dans l'Insuffisance cardiaque" Hopital Lemoyne, Montreal, Canada

2005 "Insuffisance Diastolique" Hopital Notre-Dame, Montreal, Canada

2005 "Therapie Genique pour l'Insuffisance cardiaque" Hopital L'Enfant Jesus, Quebec, Canada

2005 "Cible Genique pour l'Insuffisance cardiaque" Hopital L'Hotel Dieu, Quebec, Canada 2005 "Targeting Signaling Pathways in Heart Failure" Queen Victoria Hospital, Montreal,

Canada

2005 "Therapie Genique pour l'Insuffisance cardiaque" Montreal Heart Institute, Montreal, Canada

2006 "Gene Transfer of SERCA2a and phospholamban: preclinical results and current clinical studies" New Frontiers in Cardiology, Munich

b Professional and Educational Leadership Roles:

National:

Chair, Scientific Session, "Models of Heart Failure", American Heart Association
Chair, Scientific Session, "Contractile Mechanisms", European Society of Cardiology

1999	Chair, Scientific Session, "Gene Therapy in Experimental Models", American
	Heart Association
2000	Faculty at National Consultant Meeting, β-blockers in Heart Failure, Astra Zeneca,
	Atlanta, GA
2000	Faculty at National Consultant Meeting, β-blockers in Heart Failure, Astra Zeneca,
	New Jersey
2001	Chair, "Gene Therapy in Experimental Models", American Heart Association
2001	Faculty at National Consultant Meeting, Astra Zeneca, Miami, FL
2000-	Chair, North American Society of Pacing & Electrophysiology. "Arrhythmias and
	Calcium Homeostasis" and "Basic Science V: Remodeling: Good or Bad
	Memories", San Diego, CA
Regional :	
1999	Novartis New England Cardiology Panel Meeting, Boston, MA
2000	Editorial Board, Journal of Molecular & Cellular Cardiology
2001	Faculty at National Consultant Meeting, β -blockers in Heart Failure, Astra Zeneca,
	Boston, MA

2001- Editorial Board, Circulation Research

3. Description of Teaching Awards

None

4. <u>Major Curriculm Offerings, Teaching Cases or Innovative Educational Programs</u> <u>Developed</u>

- Institute of Continuing Healthcare Education: β-Blockers: Standard of care in heart failure, Atlanta, GA
 Helped organize the curriculum on beta blockers in heart failure with the relevant slides and clinical material for national presentations with 40 other leading specialists in heart failure .
- 2000 ASTRAZENECA National Consultant Meeting on Heart Failure, Phoenix, AZ Helped organize the curriculum on beta blockers in heart failure with the relevant slides and clinical material for national presentations with 100 other leading specialists in heart failure.
- 2000 Novartis New England Cardiology Panel Meeting, Boston, MA Organized the molecular gene therapy part for this one day course on heart failure. Forty cardiologists from the Boston area attended the conference.
- 2002 Director, "Cardiovascular Cell & Gene Therapy Conference", Cambridge, MA Organized all the scientific sessions and the invitation of 40 speakers worldwide on the topic of gene and cell therapies in cardiovascular diseases for the two and half day conference. Two hundred attendees who were cardiologists, scientists from universities and biotechnology firms and medical students.
- 2004 Director, "Cardiovascular Cell & Gene Therapy Conference II", Cambridge, MA

Organized all the scientific sessions and the invitation of 50 speakers worldwide on the topic of gene and cell therapies in cardiovascular diseases for the two and half day conference. Two hundred attendees who were cardiologists, scientists from universities and biotechnology firms and medical students.

E. Report of Clinical Activities -- Massachusetts General Hospital

1. <u>Practice</u>: Heart Failure and Cardiac Transplantation.

2. <u>Patient Load</u>: 150-200 mainly post-cardiac transplantation patients with complex medical issues and patients with end-stage heart failure.

3. <u>Time Commitment:</u>

- Two months a year attending in the Heart Failure & Cardiac Transplantation Service. Supervision of one cardiology fellow. 40 hrs/week.
- One half day clinic every two weeks for general cardiology and evaluation of patients with severe heart failure. 5 hrs/2 weeks.
- One weekend per month covering Cardiac Transplantation.
- Three weeks general cardiology consult per year. Supervision of two cardiology fellows. 20 hrs/week.
- Weekly cardiac transplantation meeting. 1 hr/week.
- Monthly Boston cardiac transplantation meeting. 3 hrs/month.
- Weekly heart failure meeting. 1 hr/week.

PART III: Bibliography

Original Reports

- 1. **Hajjar RJ**, Gwathmey JK, Briggs GM, Morgan JP. Differential effects of DPI 201-106 on the sensitivity of them Myofilaments to Ca²⁺ in iIntact and skinned trabeculae from control and myopathic human hearts. J Clin Invest 1988; 85: 1578-1584.
- 2. Gwathmey JK, Slawsky MT, **Hajjar RJ**, Briggs GM, Morgan JP. Role of intracellular calcium handling in force interval relationships of human ventricular myocardium. J Clin Invest 1990; 85(5): 1599-1628.
- 3. Gwathmey JK, **Hajjar RJ**. Effect of protein kinase C activation on sarcoplasmic reticulum function and apparent myofibrillar Ca²⁺ sensitivity in intact and skinned muscles from normal and diseased human myocardium. Circ Res 1990; 67: 744-752.
- 4. **Hajjar RJ**, Gwathmey JK. Direct evidence of changes in responsiveness of the myofilaments to calcium during hypoxia and reoxygenation in mammalian myocardium. Am J Physiol 1990; 259 (Heart Circ Physiol 28): H784-H795.
- Gwathmey JK, Hajjar RJ. Relationship between steady-state force and intracellular calcium in intact human myocardium: Index of myofibrillar responsiveness to Ca²⁺. Circulation 1990; 82: 1266-1278.
- 6. Force T, Hyman G, **Hajjar RJ**, Sellmayer A, Bonventre JV. Non-cyclooxygenase metabolites of arachidonate amplify the Ca²⁺ signal of a phospholipase C-linked vasoconstrictor by releasing Ca²⁺ from iIntracellular stores. J Biol Chem 1991; 266: 4295-4302.
- Hajjar RJ, Gwathmey JK. Modulation of calcium-activation in control and pressureoverload hypertrophied ferret hearts: Effect of DPI 201-106 on myofilament calcium responsiveness. J Mol Cell Cardiol 1991; 23: 65-75.
- 8. Gwathmey JK, **Hajjar RJ**. Intracellular calcium related to force development in twitch contraction of mammalian myocardium. Cell Calcium 1991; 11: 531-538.
- 9. Gwathmey JK, **Hajjar RJ**. Protein kinase C activation in human ventricular myocardium. Biorheology 1991; 28: 151-160.
- 10. **Hajjar RJ**, Bonventre JV. Oscillations of intracellular calcium induced by vasopressin in individual fura-2-loaded mesangialcCells. J Biol Chem 1991; 266: 21589-21594.
- Gwathmey JK, Hajjar RJ, Solaro RJ. Contractile activation and uncoupling of crossbridges: Effects of 2,3-butanedione-monoxime on mammalian myocardium. Circ Res 1991; 69: 1280-1292.
- 12. **Hajjar RJ**, Gwathmey JK. Calcium sensitizing inotropic agents in the treatment of heart failure: A critical view. Cardiovascular Drugs and Therapy 1991; 5(6): 751-756.
- Hajjar RJ, Gwathmey JK. Cross-bridge dynamics in human ventricular myocardium: Regulatory properties of contractility in the failing heart. Circulation 1992; 86: 1819-1826.
- Gwathmey, JK, Hajjar RJ. Calcium-activated force in a turkey model of spontaneous dilated cardiomyopathy: Adaptive changes in thin myofilament Ca²⁺ regulation with resultant implications on contractile performance. J Mol Cell Cardiol 1992; 24: 1459-1470.
- 15. **Hajjar RJ**, Liao R, Young JB, Fuleihan F, Glass MG, Gwathmey JK. Physiological and biochemical characterization of an avian model of dilated cardiomyopathy: Comparison to findings in human dilated cardiomyopathy. Cardiovas Res 1993; 27: 2212-2221

- 16. Glass, MG, Fuleihan F, Liao R, Lincoff AM, Chapados R, Hamlin R, Apstein CS, Allen PD, Ingwall JS, Hajjar RJ, Cory CR, O'Brien PJ, Gwathmey, JK. Differences in cardioprotective efficacy of adrenergic receptor antagonists and calcium channel antagonists in an animal model of dilated cardiomyopathy: Effects on gross morphology, global cardiac function, and twitch force. Circ Res 1993; 73: 1077-1089.
- Hajjar RJ, Ingwall JS, Gwathmey JK. Mechanism of action of 2,3 butanedione monoxime on contracture during metabolic inhibition. Am J Physiol 1994; 267 (Heart Circ Physiol 36): H100-H108.
- 18. **Hajjar RJ**, Rose G, Madsen J, Levine R, DeSanctis RW. Extrapericardial hematoma resulting in tamponnade. Am Heart J 1995; 130: 620-621.
- 19. Paige JA, Liao R, **Hajjar RJ**, Foisy RL, Cory CR, O'Brien PJ, Gwathmey JK. Effect of a high omega-3 fatty acid diet on cardiac contractile performance in Oncorhynchus Mykiss. Cardiovasc Res 1996; 31: 249-262.
- 20. Narula J, Haider N, Virmani R, DiSalvo TG, **Hajjar RJ**, Kolodgie F, Schmidt U, Semigran MJ, Dec GW, Khaw B-A. Programmed cardiomyocyte death is present in end-stage dilated cardiomyopathy. New Enl. J Med 1996; 335: 1182-1189.
- Kagaya Y, Hajjar RJ, Gwathmey JK, Barry WH, Lorell BH. Long-term angiotensin converting enzyme inhibition with fosinopril improves depressed responsiveness to Ca²⁺ in myocytes from aortic-banded rats. Circulation 1996; 94: 2915-2922.
- 22. **Hajjar RJ**, Schmidt U, Helm P, Gwathmey JK. Ca²⁺ sensitizers impair cardiac relaxation in failing human myocardium. J Pharm Exp Ther 1997; 280: 247-254.
- Hajjar RJ, Kang JX, Gwathmey JK, Rosenzweig A. Physiological effects of adenoviral gene transfer of sarcoplasmic reticulum Ca²⁺ ATPase in isolated myocytes. Circulation 1997; 95: 423-429.
- 24. **Hajjar RJ**, Schmidt U, Kang JX, Matsui T, Rosenzweig A. Adenoviral gene transfer of phospholamban in isolated rat cardiomyocytes. Circ Res 1997; 81: 145-153.
- 25. **Hajjar RJ**, DiSalvo TG, Schmidt U, Thaiyananthan G, Semigran MJ, Dec GW, Gwathmey JK. Clinical correlates of the myocardial force-frequency relationship in patient with end-stage heart failure. J Heart & Lung Transplant 1997; 8: 1157-1167.
- 26. **Hajjar RJ**, Schmidt U, Matsui T, Guerrero JL, Lee K-H, Gwathmey JK, Dec GW, Semigran MJ, Rosenzweig A. Modulation of ventricular function through gene transfer in vivo. Proc Natl Acad Sci 1998; 95: 5251-5256.
- Choukroun G, Hajjar RJ, Kyrakis J, Bonventre JV, Rosenzweig A, Force T. Role of stress-activated protein kinases in endothelin-induced hypertrophy in cardiac myocytes. J Clin Inv 1998; 102: 1311-1320.
- 28. Meadows KN, **Hajjar RJ**, Gwathmey JK. Effects of pH and temperature on myocardial calcium-activation in Pterygoplichthys (Catfish). J Compar Physiol 1998; 168: 526-532.
- 29. Schmidt U, **Hajjar RJ**, Helm PA, Kim C, Doye AA, Gwathmey JK. Contributions of abnormal sarcoplasmic reticulum ATPase activity to systolic and diastolic dysfunction in human heart failure. J Mol Cell Cardiol 1998; 30: 1929-1937.
- Miyamoto MI, Kim CS, Guerrero JL, Rosenzweig A, Gwathmey JK, Hajjar RJ. Ventricular pressure and dimension measurements in mice. Lab Animal Sci 1999; 49: 305-307.
- 31. Force T, Rosenzweig A, Choukroun G, **Hajjar RJ**. Calcineurin inhibitors and hypertrophy. Lancet 1999; 353: 1290-1292.

- 32. Gwathmey JK, Kim CS, **Hajjar RJ**, Khan F, DiSalvo TG, Matsumori A, Bristow MR. Cellular and molecular remodeling in an animal model of dilated cardiomyopathy treated with the β-blocker carteolol. Am J Physiol 1999; 276: H1678-1690
- 33. Schmidt U, Hajjar RJ, Kim C, Lebeche D, Doye AA, Gwathmey JK. CAMP dependent stimulation of sarcoplasmic reticulum Ca²⁺ ATPase and phosphorylation level of phospholamban. Am J Physiol 1999; 277: H474-480.
- Choukroun G, Hajjar RJ, Fry S, del Monte, F, Guerrero JL, Picard MH, Rosenzweig A, Force TL. Regulation of cardiac hypertrophy in vivo by the stress-activated protein kinase/c-jun N-terminal kinases. J Clin Invest 1999; 104: 391-398.
- 35. Matsui T, del Monte F, Li L, Fukui Y, Franke TF, **Hajjar RJ**, Rosenzweig A. Adenoviral gene transfer of activated PI3-kinase and akt inhibits apoptosis of hypoxic cardiocytes. Circulation 1999; 100: 2373-2379.
- 36. Morris N, Kim CS, Doye AA, **Hajjar RJ**, Laste N, Gwathmey JK. A pilot study: A new chicken model of alcohol-induced cardiomyopathy alcoholism: Clinical and experimental research, 1999; 23: 1668-1672.
- Davia K, Hajjar RJ, Terracciano CMN, Kent NS, Ranu HK, OGara P, Rosenzweig A, Harding SE. Functional alterations in adult rat myocytes following overexpression of phospholamban using adenovirus. Physiologic. Genomics 1999; 1: 41-50.
- 38. del Monte F, Harding S, Schmidt U, Matsui T, Kang ZB, Dec GW, Gwathmey JK Rosenzweig A, Hajjar RJ. Restoration of contractile function in isolated cardiomyocytes from failing human hearts by gene transfer of SERCA2a. Circulation 1999; 100: 2308-2311.
- 39. Schmidt U, del Monte F, Miyamoto MI, Matsui T, Gwathmey JK, Rosenzweig A, Hajjar RJ. Restoration of diastolic function in senescent rat hearts by adenoviral gene transfer of sarcoplasmic reticulum Ca²⁺ ATPase. Circulation 2000; 101: 790-796.
- **40. Hajjar RJ**, Schwinger RHG, Schmidt U, Kim CS, Lebeche D, Doye AA, Gwathmey JK. Myofilament calcium regulation in human myocardium: Effects of pH and inorganic phosphate. Circulation 2000; 101: 1679-1685.
- 41. Miyamoto MI, del Monte F, Schmidt U, Matsui T, Guerrero JL, DiSalvo, T, Gwathmey JK, Rosenzweig A, Hajjar RJ. Adenoviral gene transfer of SERCA2a improves left ventricular function in aortic-banded rats in transition to heart failure. Proc Natl Acad Sci 2000; 97: 793-798.
- **42.** Pereira N, Parisi A, Dec GW, Choo J, **Hajjar RJ**, Gordon PC. Myocardial stunning in hyperthyroidism. Clin Cardio 2000; 23: 298-300.
- 43. Griffin JJ, O'Donnell JM, White LT, **Hajjar RJ**, Lewandowski ED. Developmental expression and activity of mitochondrial 2-oxoglutarate malate carriers in intact hearts. Am J Physiol 2000; 279: C1704-C1709
- 44. Haq S, Choukroun G, Lim HW, Tymitz KM, del Monte F, Gwathmey JK, Grazette L, Michael A, Hajjar RJ, Force TL, Molkentin J. Differential activation of signal transduction pathways in human hearts during hypertrophy and failure. Circulation 2001; 103: 670 - 677.
- 45. Haq S, Choukroun G, Kang ZB, Ranu H, Matsui, Rosenzweig A, Alessandrini A, Molkentin JD, Woodgett J, Hajjar RJ, Michael A, Force T. Glycogen synthase kinase 3-β is a negative regulator of cardiomyocyte hypertrophy. J. Cell Biol. 2000; 151: 117-130.
- 46. Choukroun GJ, Marchanski V, Gustafson CE, McKee M, **Hajjar RJ**, Rosenzweig A, Brown D, Bonventre JV. Cytosolic phospholipase A2 alters golgi apparatus

organization and intracellular trafficking of membrane proteins. J Clin Invest 2000; 106: 983-993.

- 47. DeWindt LJD, Lim HW, Bueno OF, Tymititz KM, Braz JC, Glascock BJ, Kimball TF, del Monte F, **Hajjar RJ**, Molkentin JD. Targeted inhibition of calcineurin attenuates cardiac hypertrophy in vivo. Proc Natl Acad Sci 2001; 98: 3322-3327.
- 48. Davia K, Bernobich E, Ranu HK, del Monte F, Terracciano CM, MacLeod KT, Adamson DL, Chaudhri B, Hajjar RJ, Harding SE. SERCA2a overexpression decreases the incidence of aftercontractions in adult rabbit ventricular myocytes. Journal of Molecular & Cellular Cardiology. 33(5):1005-15, 2001 May.
- 49. Lebeche D, Kang B and **Hajjar RJ**. Candesartan abrogates G-protein coupled receptors agonist-induced MAPK activation and cardiac myocyte hypertrophy. Journal of Renin-Angiotensin-Aldosterone System . JRAAS, 2001 2:154-62
- 50. Kuhlencordt PJ, Gyurko R, Han F, Scherre-Crosbie M, Aretz TH, **Hajjar RJ**, Picard MH, Huang PL. Accelerated atherosclerosis, aortic aneurysm formation and ischemic heart disease in apoE/eNOS double knockout mice. Circulation, 2001; 104:448-54
- 51. Matsui T, Tao J, Lee K-H, Li L, delMonte F, Picard M, Franke TF, **Hajjar RJ**, Rosenzweig A. Akt activation preserves cardiac function and prevents injury after transient cardiac ischemia. Circulation 2001; 104: 330-335
- 52. del Monte F, Williams E, Lebeche D, Schmidt U, Rosenzweig A, Gwathmey JK, Lewandowski D, Hajjar RJ. Improvement in Survival and Cardiac Metabolism Following Gene Transfer of SERCA2a in an Animal Model of Heart Failure. Circulation; 2001; 104:1424-9
- 53. Washington, B. Butler K, Jang M, Doye AA, Hajjar RJ, Gwathmey JK. Heart Function Challenged With β-receptor Agonism or Antagonism in a Heart Failure Model. Cardiovascular Drugs and Therapy 2001; 15:479-86.
- 54. del Monte F, Harding S, Dec GW, Gwathmey JK, **Hajjar RJ**. Targeting phospholamban in human heart failure by gene transfer. Circulation 2002; 104: 1424-1429
- 55. Communal C, Sumandea M, Narula, Solaro RJ, **Hajjar RJ**. Functional consequences of apoptosis in cardiac myocytes: Myofibrillar proteins are targets for Caspase-3. Proc. National Acad Sci. 2002; 99: 6252-6256
- 56. del Monte F, Butler K, Boecker W, Gwathmey JK, Lewandowski D, **Hajjar RJ**. Novel Technique of Aortic Banding Followed by Gene Transfer during Hypertrophy and Heart Failure. Physiologic Genomics, 2002 9: 49-56
- 57. **Hajjar RJ**, Kradin RL. A 55-Year-Old Man with Second-Degree Atrioventricular and chest pain New Engl. J. Med 2002; 346:1732-1738,
- 58. Ranu H, Terracciano CMN, Davia K, Bernobich E, Chaudhri B, Robinson SE., Kang ZB, Hajjar RJ, MacLeod K, Harding SE. Effects of Na⁺/Ca²⁺-exchanger overexpression on excitation-contraction coupling in adult rabbit ventricular myocytes. J Mol Cell Cardiol. 2002; 34:389-400
- 59. Carr A, Schmidt AG, Suzuki Y, del Monte F, Sato Y, Lanner C, Breeden K, Gerst M, Allen PB, Greengard P, Yatani, A, Hoit B, Grupp I, Hajjar RJ, dePaoli-Roach A, Kranias E. Type 1 phosphatase A negative regulator of cardiac function. Mol. Cell. Biol. 2002 22: 4124-4135.
- 60. Terracciano CMN, **Hajjar RJ**, Harding SE. Overexpression of SERCA2a accelerates repolarisation in rabbit ventricular myocytes. Cell Calcium 2002; 31:299-305
- 61. Neagoe C, Kulke M, del Monte F, Gwathmey JK, de Tombe P, **Hajjar RJ**, Linke M. Titin isoform switch in ischemic human heart disease. Circulation 2002 106: 1327 1332

- 62. Beeri R, Guerrero JL, Supple G, Sullivan S, Levine RA, **Hajjar RJ**. New Efficient Catheter-Based System for Myocardial Gene Delivery. Circulation 2002; 106:1756-59
- **63.** Chaudhri B, del Monte F, **Hajjar RJ**, Harding SE. Interaction between increased SERCA2a activity and β-adrenoceptor stimulation in adult rabbit myocytes. Am J. Physiol 2002; 283: H2450-H2457
- 64. Nakayama A, del Monte F, **Hajjar RJ**, Frangioni JV. Functional Imaging for Cardiac Surgery and Targeted Gene Therapy. Molecular Imaging 2002; 1(4): 1-13
- **65.** Chaudhri B, del Monte F, **Hajjar RJ**, Harding SE. Contractile effects of adenovirallymediated increases in SERCA2a activity: a comparison between adult rat and rabbit ventricular myocytes. Molecular and Cellular Biochemistry 2003; 251:103-9
- **66.** Communal C, Huq F, Lebeche D, Mestel C, Gwathmey JK, **Hajjar RJ**. Decreased efficiency of adenovirus-mediated gene transfer in aging cardiomyocytes. Circulation 2003; 107: 1170 1175
- **67.** Okafor CC, Saunders L, Li X, Ito T, Dixon M, Stepenek A, **Hajjar R J,** Wood JR, Doye A, Gwathmey JK. Myofibrillar responsiveness to cAMP, PKA, and caffeine in an animal model of heart failure. Biochem Biophys Res Commun 2003; 300:592-9.
- 68. Okafor CC, Perreault-Micale C, Lebeche D, Skiroman K, Jabbour G, Doye AA, Hajjar RJ, Lee MX, Laste N, Gwathmey JK. Chronic Treatment with Carvedilol Improves Ventricular Function and Reduces Myocyte Apoptosis in an Animal Model of Heart Failure. Biomed Central 2003.
- **69.** Opitz CA, Kulke M, Leake MC, Neagoe C, Hinssen H, **Hajjar RJ**, and Linke WA Damped elastic recoil of the titin spring in myofibrils of human myocardium . PNAS 2003, 100: 12688-93
- **70.** del Monte F, Lebeche D, Guerrero JL, Tsuji T, Doye A, Gwathmey JK, **Hajjar RJ**. Abrogation of Ventricular Arrhythmias in a Model of Ischemia and Reperfusion by Targeting Myocardial Calcium Cycling. PNAS 2004; 101:5622-5627.
- 71. Huq F, Lebeche D, Iyer V, Liao R, **Hajjar RJ.** Gene Transfer of Parvalbumin Improves Diastolic Dysfunction in Senescent Myocytes. Circulation 2004; 109: 2780-5
- 72. Boecker W, Bernecker OY, Wu JC, Zhu X, Sawa T, Grazette L, Rosenzweig A, del Monte F, Schmidt U, Hajjar RJ. Cardiac specific Gene Expression Facilitated by an Enhanced Myosin Light Chain Promoter Cardiac specific Gene Expression Facilitated by an Enhanced Myosin Light Chain Promoter. Molecular Imaging 2004; 3:69-75
- 73. del Monte F, Dalal R, Tabchy A, Couget J, Bloch KD, Peterson R, Hajjar RJ. Transcriptional Changes Following Restoration of SERCA2a Levels in Failing Rat Hearts FASEB J. 2004; 1096
- 74. Makarenko I, Opitz CA, Leake MC, Neagoe C, Kulke M, Gwathmey JK, del Monte F, Hajjar RJ. Linke W. Passive stiffness change sdue to upregulation of compliant titin isoforms in human dilated cardiomyopathy hearts. Circ Res 2004; 95; 708-16
- 75. Lebeche D, Kaprielian R, del Monte F, Tomaselli G, Gwathmey JK, Schwartz A, Hajjar RJ. In Vivo Cardiac Gene Transfer of Kv4.3 Abrogates the Hypertrophic Response in Rats Following Aortic Stenosis. Circulation 2004; 110:3435-43
- **76.** Frangioni, JV, **Hajjar RJ**. *In Vivo* Tracking of Stem Cells for Clinical Trials in Cardiovascular Disease. Circulation 2004; 110:3378-84
- 77. Grazette L, Boecker W, Matsui T, Semigran MJ, Force TL, **Hajjar RJ**, Rosenzweig A. Inhibition of erbB2 causes mitochondrial dysfunction in cardiomyocytes. J Amer Coll Cardiol 2004; 44:2231-8
- 78. Grazette LP, Boecker W, Matsui T, Semigran M, Force TL, Hajjar RJ, Rosenzweig A.

Inhibition of ErbB2 causes mitochondrial dysfunction in cardiomyocytes: implications for herceptin-induced cardiomyopathy. J Am Coll Cardiol. 2004;44:2231-8.

- 79. Zhu X, Bernecker OY, Manohar N, Hajjar RJ, Hellman J, Ichinose F, Valdivia H, Schmidt U. Increased leakage of sarcoplasmic reticulum Ca²⁺ contributes to abnormal Ca²⁺ handling and contractility in sepsis. *Critical Care Medicine* 2005; 33:598-604
- Schmidt U, Zhu X, Lebeche D, Huq F, Guerrero JL, Hajjar RJ. In Vivo Gene Transfer of Parvalbumin Improves Diastolic Function in Aged Rat Hearts. Cardiovasc. Res. 2005; 66: 318-23.
- **81.** Frank K, Bolck B, Ding Z, Krause, Hattebuhr N, Mailk A, Brixius K, **Hajjar RJ**, Schrader J, Schwinger RHG. Overexpression of sorcin enhances contractility in vivo and in vitro. J Mol Cell Cardiol 2005; 38(4):607-15.
- 82. Hayase M, del Monte F, Kawase Y, MacNeill BD, McGregor J, Yoneyama R, Hoshino K, Tsuji T, De Grand AM, Gwathmey JK, Frangioni JV, Hajjar RJ. Catheter-Based Antegrade Intracoronary Viral Gene Delivery with Coronary Venous Blockade. Am J Physiol 2005; H2995-3000.
- 83. Hayase M, Kawase Y, Yoneyama R, Hoshino K, MacNeill BD, McGregor J, Lowe H, Burkhoff D, Boeckstegers P, **Hajjar RJ.** Catheter based ventricle coronary vein bypass. *Catheterization and Cardiovascular Interventions* 2005; 65:394-404
- 84. Zhu X, Olbinski B, Hajjar RJ, Valdivia H, Schmidt U. Altered Ca²⁺ Sparks and Gating Properties of Ryanodine Receptors in Aging Cardiomyocytes. *Cell Calcium* 2005; 37:583-91
- 85. Pathak A, del Monte F, Zhao W, Carr A, Weiser D, Shultz J, Bodi I, Hahn H, Syed F, Mavila M, Jha L O'Neal E, Qian J, Marreez Y, Mitton B, Fan F, McGraw D, Heist EK, Guerrero JL, DePaoli-Roach A, Hajjar RJ, Kranias, E. Enhancement of Cardiac Function and Suppression of Heart Failure Progression By Inhibition of Protein Phosphatase 1. Circ Res 2005; 96:756-66
- 86. Lipskaia L, del Monte F, Capiod T, Yacoubi S, Hadri L, Hours M, Hajjar RJ, Lompré AM.Sarco/endoplasmic reticulum Ca²⁺-ATPase gene transfer reduces VSMC proliferation and neointima formation in the rat. Circ Res 2005; 97:488-95
- 87. Kawase Y, Hoshino K, Yoneyama Y, McGregor J, **Hajjar R**, Jang IK, Hayase M. In vivo volumetric analysis of coronary stent using optical computed tomography with a novel balloon occlusion-flushing catheter: a comparison with intravascular ultrasound. Ultrasound in Med & Biol. 2005; 1343-9
- 88. Yoneyama R, Kawase Y, Hoshino K, McGregor J, Mac Neill BD, Lowe HC, Burkhoff D, Boekstegers P, Hajjar RJ, Hayase M. Magnetic resonance assessment of myocardial perfusion via catheter-based ventricle-coronary vein bypass in porcine myocardial infarction model. Catheter Cardiovasc Interv. 2006; 67:58-67.
- 89. Chemaly ER, Yoneyama R, Frangioni JV, **Hajjar RJ**. Tracking stem cells in the cardiovascular system. Trends Cardiovasc Med. 2005 Nov;15(8):297-302.
- 90. Palomeque J, Sapia J, **Hajjar RJ**, Mattiazzi A, Vila Petroff MG. Angiotensin II-induced negative inotropy in rat ventricular myocytes: Role of Reactive oxygen species and p38 MAPK. Am J Physiol 2006;290:H96-106.
- 91. Sakata S, Lebeche D, Sakata Y, Sakata N, Chemaly ER, Liang L, Padmanabhan P, Konishi N, Takaki M, del Monte F, and Hajjar RJ. Mechanical & Metabolic Rescue in a Type II Diabetes Model of Cardiomyopathy by Targeted Gene Transfer. Molecular Therapy, 2006; 13(5):987-996.
- 92. Dally S, Bredoux R, Corvazier E, Andersen JP, Clausen JD, Dode L, Fanchaouy M,

Gelebart P, Monceau V, del Monte F, Gwathmey JK, **Hajjar RJ**, Chaabane C, Bobe R, Aly Raies, Enouf J. Ca²⁺-ATPases in non-failing and failing heart: evidence for a novel cardiac sarco/endoplasmic reticulum Ca²⁺ATPase 2 isoform (SERCA2c). Biochem J. 2006;395(2):249-58

- 93. Lebeche D, Kaprielian R, Hajjar RJ. Modulation of action potential duration on myocyte hypertrophic pathways. Journal Mol Cell Cardiol 2006; 40(5):725-735
- 94. Hoshino K, Kimura T, De Grand AM, Yoneyama R, Kawase Y, Houser S, Kushibiki, T, Furukawa Y, Ono K, Tabata Y, Frangioni JV, Kita T, Hajjar RJ, Hayase M. Three catheter-based strategies for cardiac delivery of therapeutic gelatin microspheres. Gene Therapy 2006;
- 95. Jeong D, Cha H, Kim E, Kang M, Yang D, Kim JM, Yoon PO, Oh JG, Bernecker OY, Sakata S, Thu LT, Cui L, Lee Y-H, Kim D-H, Woo S-H, Liao R, Hajjar RJ, Park WJ. PICOT (PKC-interacting cousin of thioredoxin) inhibits cardiac hypertrophy and enhances ventricular function and cardiomyocyte contractility. Circ Res 2006; 99:

<u>Editorials</u>

- **1.** Hajjar RJ, Macrae CA. α/β Adrenoreceptor Polymorphisms in Heart Failure. *New England Journal of Medicine* 2002; 347: 1196-1199
- 2. Huq F, Heist KE, **Hajjar RJ.** Titin-Springing back to youth. *Science of Aging Knowledge Environment*, 2002; 49:20.
- 3. Heist EK, Huq F, **Hajjar RJ**. Telomerase and the Aging Heart. *Science of Aging Knowledge Environment*, 2003; pe11.
- 4. Hajjar RJ. Kick starting calcium cycling in the rat. Gene Therapy; 2005; 12:730-2
- 5. Hajjar RJ, Samulski RJ. A silver bullet to treat Heart Failure. Gene Therapy; 2006;
- 6. Hajjar RJ, Leopold JA. Xanthine Oxidase Inhibition and Heart Failure: Novel Therapeutic Strategy for Ventricular Dysfunction? Circ Res 2006; 98:169-71

Guest Editor:

Hajjar RJ, del Monte F. Pathogenesis of Heart Failure. *Heart Failure Clinics*. 2005; 1 (2)

Proceedings of Meetings

- 1. **Hajjar RJ,** Morgan JP. Calcium-activation in myopathic human and pressure-overload hypertrophied ferret hearts. In: *Annual Harvard-MIT Health Sciences & Technology Forum*. Cambridge, MA: MIT Press; 1987, p. 32-41.
- Hajjar RJ. Gene Therapy in Heart Failure. In New Advances in the treatment of Cardiac and Vascular Diseases. Samsung Symposium in cardiac and Vascular Disesae; 2002; p.137-141
- 3. Hajjar RJ. Rescuing the Failing Heart by Targeted Gene Transfer. Cardiology Rounds 2003.

Reviews, Chapters

- 1. Gwathmey JK, **Hajjar RJ**. The complexity of simplicity: The pathophysiology of heart Failure. Hype or hope? *Resident & Staff Physician* 1993; 39: 45-59.
- 2. Schmidt U, **Hajjar RJ**, Gwathmey JK. The force-frequency relationship in humans. *J Cardiac Failure* 1995; 1:311-321.

- 3. Gwathmey JK, Liao R, Helm R, Thaiyananthan G, **Hajjar RJ**. Is contractility depressed in heart failure? *Cardiovascular Drugs & Therapy* 1995; 247-263.
- 4. **Hajjar RJ**, Grossman W, Gwathmey JK. Responsiveness of the myofilaments to Ca²⁺ in human heart failure: Implications for Ca²⁺ and force regulation. *Basic Research in Cardiology* 1992; 87:143-159.
- 5. Liao R, Helm PA, **Hajjar RJ**, Saha C, Gwathmey JK. [Ca²⁺]_i in human heart failure. *Yale Journal of Biology and Medicine* 1995; 67: 247-264.
- 6. Schmidt U, **Hajjar RJ**, Gwathmey JK. The force-interval relationship in human myocardium. *Journal of Cardiac Failure* 1995; 1(4): 311-321.
- 7. **Hajjar RJ**, Müller FU, Schmitz W, Schnabel P, Böhm M. Molecular aspects of adrenergic signal transduction in cardiac failure. *J Molecular Medicine*; 1998: 76:747-755.
- 8. Narula J, **Hajjar RJ**, Dec GW. New insights into dilated cardiomyopathy: Apoptosis in the failing Heart. *Cardiology Clinics* 1998; 16: 691-710.
- 9. Force TL, **Hajjar RJ**, del Monte F, Rosenzweig A, Choukroun G. Signaling pathways mediating the response to hpertrophic stress in the heart. *Gene Expression* 1999; 7: 337-348.
- Lee K-H, Hajjar RJ, Matsui T, Choukroun G, Force T, Rosenzweig A. Cardiac intracellular signaling pathways and their potential as imaging targets. *J Nuc Cardiol* 2000: 7:63-71
- 11. **Hajjar RJ**, del Monte F, Matsui T, Rosenzweig A. Prospects for gene therapy for heart failure. *Circ Res* 2000; 86: 616-621.
- 12. Hajjar RJ. Gene therapy for heart failure. Lebanese Medical Journal 2000; 48:
- 13. del Monte F, **Hajjar RJ**, Harding SE, Inesi G. Overwhelming Evidence of the Beneficial Effects of SERCA Gene Transfer in Heart Failure . *Circ Res* 2001 88: e66-e67.
- Kaprielian R, del Monte F, Hajjar RJ. Targeting Ca²⁺ Cycling Proteins and the Action Potential in Heart Failure by Gene Transfer. Basic Research in Cardiology (supplement) 2002; 97:136-145.
- 15. Kaprielian R, del Monte F, **Hajjar RJ**. Targeting Calcium Cycling Proteins and the action potential in Heart Failure by Gene Transfer. *Basic Res. Cardiol* 2002; 97: 136-145
- 16. Kassiri K, **Hajjar RJ**, Backx PH. Molecular components of transient outward potassium current in cultured neonatal rat ventricular myocytes *J Mol Med*; 2002; 80: 351-358
- 17. Huq F, del Monte F, **Hajjar RJ**. Modulating Signaling pathways in Hypertrophy and Heart Failure by Gene Transfer. *Journal of Cardiac Failure* 2002 (Suppl 6); S389-400.
- 18. **Hajjar RJ,** Huq F, Matsui T, Rosenzweig A. Targeting Cardiac Dysfunction Through Gene Transfer. *Medical Clinics* 2003; 87:553-67.
- 19. del Monte F, **Hajjar RJ**. Targeting Calcium Cycling Proteins in Heart Failure Through Gene Transfer. J. Physiol (Lond) 2003; 546:49-61.
- 20. MacNeill BD, Hayase M, **Hajjar RJ**. Targeting signaling pathways in heart failure by gene transfer. Curr Atherosclerosis Reports 2003; 5:178-85
- 21. **Hajjar RJ**, Huq F, Matsui T, Rosenzweig A. Genetic editing of dysfunctional myocardium. Med Clin North America; 2003; 87:553-67
- 22. Bernecker O, del Monte F, **Hajjar RJ**. Gene Therapy for the Treatment of Heart Failure Calcium Signaling. *Seminars in Thoracic and Cardiovascular Surgery 2003*;15 (3):268-276
- 23. Chaudri B, del Monte F, Harding SE, & Hajjar RJ. Targeting Failing Cardiomyocytes by Gene Transfer. *Surgical Clinics of North America*; 2004: 84:141-59
- 24. Bernecker O, Huq F, Heist EK, Podesser BK, **Hajjar RJ**. Apoptosis in heart failure and the senescent heart. Cardiovasc. Toxicol. 2003; 3:183-90

- 25. del Monte F, Kizana E, Tabchy A, **Hajjar R.** Targeted gene transfer in heart failure: Implications for novel gene identification. Curr Opin Mol Ther. 2004; 6(4):381-94.
- 26. Bukhari, F, del Monte F, **Hajjar RJ**. Genetic maneuvers to ameliorate ventricular function in heart failure: therapeutic potential and future potentials. *Expert Review of Cardiovascular Therapy; 2005; 3:85-97*.
- 27. Lebeche D, Dalal R, Jang M, del Monte F, **Hajjar RJ.** Transgenic models of heart failure: Elucidation of the molecular mechanisms of heart disease. Heart Failure Clinics 2005; 1(2): 219-236.
- 28. Sato M, Fuller S, **Hajjar RJ**, Harding SE. Targeting genes and cells in the progression to heart failure. Heart Failure Clinics 2005; 1(2): 287-302
- Antoun JG, Hajjar RJ. Gene and cell therapy in heart failure. J Med Liban. 2005; 53(1):28-38.
- 30. Gianni D, Chan J, Gwathmey JK, del Monte F, Hajjar RJ. SERCA2a in heart failure: role and therapeutic prospects.J Bioenerg Biomembr. 2005 Dec;37(6):375-80.

Books, Monographs, and Text Books

- Gwathmey JK, Hajjar RJ. Abnormal calcium metabolism in heart muscle dysfunction. In: Figulla HR, Kandolf R, McManus B, editors. *Idiopathic Dilated Cardiomyopathy, Cellular and Molecular Mechanisms, Clinical Consequence*. Berlin Heidelberg New York: Springer Verlag; 1993, p 132-144.
- 2. Gwathmey JK, **Hajjar RJ**, Allen PD. Analysis of excitation-contraction coupling in human ventricular myocardium: Relationship to the pathohysiology of heart failure. In: Gwathmey JK, Briggs GM, Allen PD, editors. *Treatment of Heart Failure: Basic Research and Clinical Practice*. New York: Marcel Dekker; 1993, p. 121-144.
- Gwathmey JK, Liao R, Hajjar RJ. Intracellular free calcium in hypertrophy and failure. In: Lorell BH, Grossman W, editors. *Diastolic Relaxation*. Boston: Kluwer Academic Publishers; 1994, p. 55-56.
- 4. **Hajjar RJ**, Schmidt U, Gwathmey JK. Calcium cycling dependent and independentmechanisms of relaxation in mammalian ventricular myocardium. In: Ingels N, editor. *Systolic and Diastolic Function*. Kluwer; 1996, p. 201-210.
- 5. Schmidt U, **Hajjar RJ**, Carles M, Gwathmey JK. Calcium homeostasis in human heart failure. In: Altschuld R, Hayworth RA. *Advances in Organ Biology: Heart Metabolism in Failure*. London: JAI Press Inc.; 1998; volume 4A, p. 63-79.
- del Monte, Harding SE, Hajjar RJ. Manipulation of SERCA2a in the heart by gene transfer. In: Hasensfus G, Marban E. *Molecular Strategy to the Therapy of Heart Failure*; Springer 2000, pp 53-68
- Hajjar RJ, Force TL, Rosenzweig A. Targeting genes and modulating signal transduction in cardiomyopathies. In: Willerson JT, editor. *Pathogenic Basis of Myocardial Diseases*. Kluwer Publiahers; 2002, in press.
- Gwathmey JK, del Monte F, Kaprielian R, Hajjar RJ. Abnormalities of calcium homeostasis and defective excitation-contraction coupling in cardiomyopathy. In: Willerson JT. *Pathogenic Basis of Myocardial Diseases*. Kluwer Publishers; 2002, in press.
- 9. Schmidt U, **Hajjar RJ**. Gene therapy in heart failure. Best Practice & Research : Clinical Anaesthesiology. Genetic Basis of Cardiovasclar Diseases and Perioperative Pain. Guest editors: SC Brody and SK Sherman. Vol.15 No.2, 2001. pages 301-12

- del Monte F, Hajjar RJ. Efficient viral gene transfer to rodent hearts in vivo. In *Methods in Molecular Biology: Cardiac Cell & Gene Transfer*. Editor: Joseph Metzger. Vol. 219; chapter 14. Humana Press. Totowa, NJ, pages 179-95
- 11. Harding SE, del Monte F, **Hajjar RJ**. Antisense Strategies for the Treatment of Heart Failure. Editor: Ian Phillips *Antisense Therapeutics*, 2nd edition;2004 pages 69-82.
- Hajjar RJ, Rosenzweig A. Targeted Gene Transfer in Heart Failure. Heart Failure (editors G. William Dec, Thomas Disalvo, Roger J. Hajjar, Marc J Semigran). Heart Failure 2005: A Comprehensive Guide to Diagnosis and Treatment, p.527-545.
- del Monte F, Hajjar RJ. Excitation-Contraction Coupling Mechanisms in Heart Failure. (editors G. William Dec, Thomas Disalvo, Roger J. Hajjar, Marc J Semigran) Heart Failure 2005: A Comprehensive Guide to Diagnosis and Treatment p. 61-75.
- 14. Kizana, E. del Monte F, Harding SE, **Hajjar RJ**. Cardiovascular Gene & Cell Therapy. Essential Cardiology (Editor: Clive Rosendorf); 2005; pages: 763-788
- Yoneyama R, Chemaly ER, Hajjar RJ. Tracking stem cells in vivo. Stem Cells in Reproduction and in the Brain. Ernst Schering Research Foundation Workshop 60. (Editors: J. Morser, SI Nishikawa, and HR Scholer). Pages: 99-109

Patents:

1. Evaluation of Delivery of and Use of Agents to Treat Heart Disorder"

2. Reduction of Vascular Restenosis and Smooth Muscle Proliferation by Gene Transfer of SERCA"

3. Anti-hypertrophic effects and inotropic effects of PICOT