

PART I: General Information

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Phone: (617) 309-2635 **FAX:** (617) 309-2593
Place of Birth: Louisville, Kentucky

Education:

1964 B.A. University of Louisville (Chemistry, with highest honors)
1968 M.D. University of Louisville School of Medicine (with highest honors)
1984 M.S. University of Louisville (Chemistry)
1984 M.A. Harvard University (Honorary)
1984 D.Sc. University of Louisville (Honoris Causa)
1990 D.Sc. Université de Paris Pierre et Marie Curie (Honoris Causa)
2000 D.Sc. University of Geneva (Honoris Causa)
2008 D.Med. University of Copenhagen (Honoris Causa)
2012 D.Sc. Washington University in St. Louis (Honoris Causa)

Postdoctoral Training:

Internship/Residencies:

1968-1970 Intern and Resident, Ward Medicine, Barnes Hospital, St. Louis, MO

Research Fellowships:

1970-1973 Clinical Associate and Senior Clinical Associate, Clinical Endocrinology Branch, National Institutes of Arthritis, Metabolism and Digestive Diseases, NIH, Bethesda, MD

Licensure and Certification:

1968 Kentucky State Board of Medical Examiners, No. 15141
1973 American Board of Internal Medicine, No. 44765
1973 American Board of Internal Medicine, Subspecialty in Endocrinology and Metabolism, No. 44765
1981 Massachusetts State Medical Registration, No. 48036

Academic Appointments:

1980-1981 Adjunct Professor of Genetics, George Washington University, Washington, DC
1981-1984 Associate Professor of Medicine, Harvard Medical School, Boston, MA
1984-pres Professor of Medicine, Harvard Medical School, Boston, MA
1986-pres Mary K. Iacocca Professor of Medicine, Harvard Medical School, Boston, MA

Hospital or Affiliated Institution Appointments:

- 1972-1981 Admitting & Attending physician, National Institutes of Health, Clinical Center
- 1981-1991 Physician, Brigham and Women's Hospital, Boston, MA
- 1981-1992 Chief, Division of Diabetes and Metabolism, Department of Medicine, Brigham and Women's Hospital, Boston, MA
- 1985-pres Senior Staff, Joslin Clinic, Joslin Diabetes Center, Boston, MA
- 1981-1985 Associate Staff, Endocrinology/Internal Medicine, New England Deaconess Hospital, Boston, MA
- 1986-1995 Active Staff, Department of Medicine, Internal Medicine and Endocrinology, New England Deaconess Hospital, Boston, MA
- 1986-1992 Senior Physician, Brigham and Women's Hospital, Boston, MA
- 1993-pres Senior Consultant in Diabetes and Metabolism, Brigham and Women's Hospital, Boston, MA
- 1995-pres Active Staff, Department of Medicine, Beth Israel Deaconess Hospital, Boston, MA

Other Professional Positions and Major Visiting Appointments:

- 1973-1978 Senior Investigator, Diabetes Branch, National Institute of Arthritis, Metabolism and Digestive Diseases, NIH, Bethesda, MD
- 1979-1980 Visiting Scientist, Centre de Moleculaire, Centre National de la Recherche Scientifique, Gif-sur-Yvette, France
- 1979-1981 Chief, Section on Cellular and Molecular Physiology, Diabetes Branch, National Institute of Arthritis, Metabolism, and Digestive Disease, NIH, Bethesda, MD
- 1981 Clinical Associate Professor of Medicine, Uniformed Services University of Health Sciences, Bethesda, MD
- 1985 Overseas Visiting Professor, Royal Melbourne Hospital, Melbourne, Australia
- 1985 Visiting Professor, Royal Postgraduate Hospital, London, England
- 1985 Rosemary Sarver Visiting Professor in Endocrinology and Metabolism, The Hospital of the Good Samaritan, Los Angeles, CA
- 1990 Roerig Visiting Professorship in Diabetes, University of Colorado Health Sciences Center, Denver, CO
- 1990-1991 Visiting Scientist, Department of Cellular and Molecular Biology, Dana Farber Cancer Institute, Boston, MA
- 1998-2005 Visiting Research Scientist, Brandeis University, Waltham, MA
- 2005 Honorary Director and Professor of the Diabetes Center at Peking University, Beijing, China
- 2007 International Visiting Fellow, Garvan Institute, Sydney, Australia
- 2007-pres International Advisory Board, PhD School of Molecular Metabolism, University of Southern Denmark
- 2010-pres External Advisory Board, Life Sciences Institute, University of Michigan, Ann Arbor, MI
- 2012 External Advisory Board, Institute for Systems Biology, Seattle, WA

Major Administrative Responsibilities:

1981-2000 Director, Elliott P. Joslin Research Laboratory, Joslin Diabetes Center
 1981-2002 Head, Section on Cellular and Molecular Physiology, Joslin Diabetes Center
 1997-2000 Executive Vice President and Director, Joslin Diabetes Center
 2000-2007 President and Director, Joslin Diabetes Center
 2000-2003 Member, Board of Directors, Care Group, Health Care System
 2000-2007 Member, Board of Directors, Medical Academic and Scientific Community Organization (MASCO)
 2002-2009 Head, Section of Obesity and Hormone Action Research, Joslin Diabetes Center
 2007-2010 Vice Chair, Board of Trustees, Joslin Diabetes Center
 2008-pres Warren Alpert Award Committee, Harvard Medical School
 2010-pres Head, Section of Integrative Physiology and Metabolism, Joslin Diabetes Center
 2012-pres Chief Academic Officer, Joslin Diabetes Center

Major Committee Assignments:

Medical School:

1985-1988 Member, Committee on Promotions and Appointments, Harvard Medical School
 1987-1990 Member, Standing Committee on Faculty Fellowships, Harvard Medical School
 1989-1994 Member, Appeals Board, Student Promotion Board, Faculty of Medicine, Harvard Medical School
 1997-1998 Member, Faculty Council, Harvard Medical School
 2005- Member, Glenn Laboratories on Aging Research, Scientific Advisory Board

Affiliated Institutions:

1996- Member, Scientific Advisory Committee, Boston Obesity Center, New England Medical Center, Boston, MA
 2009-2011 Member, Scientific Advisory Committee, Geroscience Program, Buck Institute, Novato, CA
 2011-pres Member, iPS Cell Core Advisory Committee, Harvard Stem Cell Institute
 2012-pres Member, Promotion Committee of the Department of Medicine, Brigham and Women's Hospital, Boston, MA

Regional, National and International:

1977-1981 Quality Assurance Committee, National Institute of Health
 1978 Co-Chairman, Organizing Committee, Fogarty International Conference on Hormones and Cancer, Bethesda, MD, (March 29-31)
 1978-1980 Postgraduate Committee, Endocrine Society
 1979-1982 Medical Science Advisory Board, Juvenile Diabetes Foundation
 1981-1984 Nominating Committee, Endocrine Society
 1982-1985 Research Committee, American Diabetes Association
 1983 Vice Chairman, Organizing Committee, Hormone Action, Gordon Conference, Meriden, NH (August 7-12)
 1983 Scientific Committee, Second International Symposium on Insulin Receptors and Insulin Action, Rome, Italy (August 31-September 3)
 1983-1986 Medical Science Advisory Committee, Juvenile Diabetes Foundation
 1984 Co-Chairman, Organizing Committee, UCLA Symposia on Molecular and

- Cellular Biology Membrane Receptors and Cellular Recognition, Park City, UT (March 25-30)
- 1984 Chairman, Organizing Committee, Gordon Conference on Hormone Action, Meriden, NH (August 5-10)
- 1985 Scientific Committee, Third International Symposium on Insulin Receptors and Insulin Action
- 1985 Chairman, Organizing Committee, Gordon Conference on Hormone Action, Meriden, NH (August 4-9)
- 1985 Organizing Committee, JDFI World Conference on Diabetes Research - Current Status and Future Directions, Monaco (November 4-6)
- 1986 Organizing Committee, Immunology of Diabetes - Immunity to Insulin and the Insulin Receptor, Edmonton, Canada (June 26-28)
- 1987-1988 Countdown Editorial Advisory Board, Juvenile Diabetes Foundation
- 1988 Chairman, Organizing Committee, Insulin and The Cell Membrane, Smolenine Castle, Czechoslovakia (June 27-30)
- 1988 Chairman, Organizing Committee, The Action of Insulin and Related Growth Factors in Diabetes Mellitus, Joslin Diabetes Center's 90th Anniversary Symposium, Boston, MA (October 10-13)
- 1988-1990 Medical Science Advisory Committee, Juvenile Diabetes Foundation
- 1990-1993 Council Member, Endocrine Society
- 1991 Organizing Committee, Keystone Symposia on Diabetes and Insulin Action, Park City, UT (January 18-24)
- 1992 Organizing Committee, FASEB Summer Conference on Receptors and Signal Transduction, Copper Mountain, CO (July 12-17)
- 1992-2000 Central Committee of International Society of Endocrinology
- 1992-1996 National Institutes of Health Reviewer's Reserve
- 1993-1994 Chair, Council on Molecular, Cellular and Biochemical Aspects of Diabetes, American Diabetes Association
- 1996 Organizing Committee, VIth International Symposium on Insulin Receptors and Insulin Action, Copenhagen, Denmark (May 6-10)
- 1996 Organizing Committee, 75th Anniversary of the Discovery of Insulin, Toronto, Canada (October 6-9)
- 1997 Member, Cardiovascular Advisory Board, Monsanto/Searle
- 1997 Organizing Committee, 16th International Diabetes Federation Congress, Helsinki, Finland (July 20-25)
- 1997-2000 Member, International Endocrine Society Steering Committee
- 1998 Co-Chair, Organizing Committee, Diabetes Mellitus: From Patients to Genes and Back, A symposium on the 100th Anniversary of the Joslin Diabetes Center, Boston, MA (October 21-23)
- 1998- Member, External Advisory Committee, JDFI Program Project, Mount Sinai School of Medicine, New York, NY
- 1998- Advisory Board, NRSA Training Grant, State University New York at Stony Brook
- 2000 Co-Chair, Organizer of Keystone Symposium on Diabetes, Taos, NM (February 16-22)
- 2003 Co-Chair, Proteomics in Diabetes Meeting, Bethesda, MD (April 24-25)
- 2003 Fellow, American Academy of Microbiology, Recognizing Scientific Excellence
- 2004- Member, External Scientific Advisory Board, University of Geneva

- 2006- Selection Committee, Luft Prize, Karolinska Institute, Stockholm, Sweden
- 2008 Co-Chair, NIDDK Workshop on Adipose Development, Bethesda, MD
- 2008- Member, Scientific Advisory Board, Cologne Cluster of Excellence on Cellular Stress Responses in Aging-associated Diseases (CECAD)
- 2008 Member, External Advisory Board, Life Sciences Institute, University of Michigan
- 2009-2011 Member, Geroscience Program, Buck Institute, Novato, CA
- 2011 Co-Chair, Cell Symposium on Aging and Metabolism, Hyannis, MA
- 2011 Co-Chair, NIDDK Workshop on Drug Response - A Tool for Understanding the Systems Biology of Type 2 Diabetes, Bethesda, MD
- 2013 Chair, Keystone Symposium on Diabetes, Keystone, CO

Assignments on National Commissions:

- 1981-1985 National Diabetes Advisory Board
- 1982-1985 Co-Chairman, Research Committee, National Diabetes Advisory Board
- 1995-1998 Member on the Endocrinology Study Section, Division of Research Grants, National Institutes of Health
- 1998-2002 NIDDK Board of Scientific Counselors
- 1998 Co-Chair, Workshop on Diabetes Research: Challenges and Opportunities, National Institutes of Health
- 1998-1999 Chair, Congressionally-mandated Diabetes Research Working Group (DRWG)
- 1998-2002 Member, National Diabetes and Digestive and Kidney Diseases Advisory Council, National Institutes of Health
- 2002-2007 Awards Committee, Endocrine Society, Bethesda, Maryland
- 2007-2010 Chair, Class IV (Biomedical Sciences), National Academy of Science
- 2007-2009 Finance Committee, American Diabetes Association
- 2008-2009 NIDDK Diabetes Research Strategic Plan, Chair, Systems Biology Committee
- 2010-2012 Research Policy Committee, American Diabetes Association

Professional Societies:

- 1963- Member, Alpha Epsilon Delta
- 1964- Member, Phi Kappa Phi
- 1965- Member, Alpha Omega Alpha
- 1966- Member, Sigma Xi
- 1972- Member, American Federation for Clinical Research
- 1975- Member, The Endocrine Society
- 1976- Member, American Diabetes Association
- 1979- Member, American Society for Clinical Investigation
- 1982- Member, American Society of Biological Chemistry
- 1983- Member, Association of American Physicians
- 1986- Member, National Council, American Society of Clinical Investigation
- 1987-1988 President-Elect, American Society of Clinical Investigation
- 1988-1989 President, American Society of Clinical Investigation
- 1991- Member, American Academy of Arts and Sciences
- 1994- Fellow, American Association for the Advancement of Science
- 1999- Member, National Academy of Science
- 1999- Member, Institute of Medicine

- 2005- Fellow, American College of Physicians
- 2005- Honorary Member, British Society for Endocrinology
- 2008-2011 Chair, Class IV Medical Sciences, National Academy of Science

Editorial Boards:

- 1977-1980 Journal of Clinical Endocrinology and Metabolism
- 1977-1984 Diabetes
- 1979-1984 American Journal of Medicine
- 1979-1984 Journal of Clinical Investigation
- 1980-1983 Journal Receptor Research
- 1980-1983 Hormone and Metabolic Research
- 1981-1985 Endocrinology
- 1983-1988 Journal of Biological Chemistry
- 1984-2002 Diabetes and Metabolism Reviews
- 1987-1990 ISI Atlas of Science Editorial Advisory Board
- 1989- Receptor
- 1989-1990 Executive Editor, Trends in Endocrinology and Metabolism
- 1991-1996 Editorial Advisory Council, Journal of Endocrinological Investigation
- 1991-1995 Trends in Endocrinology and Metabolism
- 1992-1996 Consulting Editor, The Journal of Clinical Investigation
- 1992-2002 Journal of Receptor Research
- 1993-1994 Member, Board of Editors, Endocrine
- 1996-2001 Associate Editor, Diabetes
- 1996-1997 Member, Endocrine Reviews Advisory Board
- 1997-2002 Editorial Board, Proceedings of the Association of American Physicians
- 1998-2003 Consulting Editor, Journal of Clinical Investigation
- 1998-2003 Member, Editorial Board, American Journal of Medicine
- 2000-2005 Associate Editor, Endocrine Reviews
- 2001-2006 Editorial Board, American Journal of Physiology
- 2002- Editorial Board, Diabetes/Metabolism Research and Reviews
- 2004- Associate Editor, Cell Metabolism
- 2008- Associate Editor, BMC Endocrine Disorders
- 2008- Editorial Board, Journal of Clinical Endocrinology & Metabolism
- 2009- Editorial Board, Journal of Diabetes Investigation
- 2010- Editorial Board, Diabetology International
- 2011- Consulting Editor, Metabolism

Awards and Honors:

- Undergraduate: Woodcock Honor Society; Phi Lambda Upsilon; Alpha Epsilon Delta; Phi Kappa Phi Honor Society; Graduate with Highest Honors
- Medical School: Saunder's Award for Biochemistry; Mosby Award; Upjohn Award for Medicine; Alpha Omega Alpha; Sigma Xi; Vice President, Junior Class; President Senior Class; Graduate with Highest Honors
- Professional:
 - 1977 David Rumbough Memorial Award for Scientific Achievement, Juvenile Diabetes Foundation
 - 1978 Laurentian Hormone Conference

1981 Eli Lilly Award for Research, American Diabetes Association
 1981 CIBA-Geigy Drew Award for Biochemical Research
 1982 Mary Jane Kugel Award, Juvenile Diabetes Foundation
 1983 American Federation for Clinical Research (AFCR) Award for Outstanding
 Clinical Research Under Age 40
 1983 Sol Berson Memorial Lectureship, National Institutes of Health
 1984 Hahnemann Lecture in Pharmacology, University of California, San
 Francisco
 1984 Artium Magistrum (Honorary), Harvard University
 1984 Doctor of Science (Honoris Causa), University of Louisville
 1984 Rachmiel Levine Lectureship, New York Medical College
 1985 Carl V. Moore Memorial Lecture, Washington University School of
 Medicine
 1986 Kelly West Lecture, University of Oklahoma School of Medicine
 1986- Mary K. Iacocca Professor of Medicine, Harvard Medical School
 1986 Pfizer Biomedical Research Award, Pfizer, Inc., Groton, Connecticut
 1987 Sixty-Eighth Mellon Lecture, University of Pittsburgh School of Medicine,
 Pittsburgh, Pennsylvania
 1987 Ninth Annual Steve Broidy Lectureship in Diabetes, Cedars-Sinai Medical
 Center, Los Angeles, California
 1987 Edwin B. Astwood Lecturer, The Endocrine Society
 1987 McGill Novo Nordisk Lecturer, McGill University, Montreal, Canada
 1988 Gifford Lectureship, Southwestern Medical Center, Dallas, Texas
 1988 Cristobal Diaz Award, International Diabetes Federation
 1989 Otto Brandman Award, American Diabetes Association New Jersey Affiliate
 1989 Elliott P. Joslin Medal, American Diabetes Association, Massachusetts
 Affiliate
 1990 Doctor of Science (Honoris Causa), Universite de Paris Pierre et Marie
 Curie, Paris, France
 1990 Top 100 Most-Cited Scientists for 1973-1984 and 1981-1988, The Scientist,
 March 19 and October 1, 1990
 1991- Fellow, American Academy of Arts and Sciences
 1993- Alumni Fellow, University of Louisville
 1993 Banting Medal for Distinguished Scientific Achievement, American Diabetes
 Association
 1994 Edwin Krebs Lecture, University of Washington
 1994 Pincus Taft Lecturer in Clinical Endocrinology, Australian Endocrine
 Society
 1995 Fellow, American Association for the Advancement of Science
 1995 Kroc Lecturer, University of California, Irvine
 1995 Bates Lecturer, State University of New York, Syracuse
 1996 Invited Lecturer, Symposium in Honor of the 100th Birthday of Carl Cori and
 Gerty Cori, Harvard Medical School, Boston, MA
 1997 Distinguished Scientist Award, Clinical Ligand Assay Society
 1997 Solomon Berson Distinguished Lecture, American Physiological Society
 1998 Albert Renold Award, American Diabetes Association
 1998 Lewis Memorial Lecture, Mount Sinai School of Medicine
 1998 209th Eli Lilly Lecturer, Eli Lilly Company
 1999 Dorothy Hodgkin Award, British Diabetes Association

1999- Elected Member, National Academy of Sciences

1999- Elected Member, Institutes of Medicine, National Academy of Sciences

1999 Nelson Medical Lectureship, University of California Davis School of Medicine

2000 MERIT Award, National Institutes of Diabetes, Digestive and Kidney Diseases

2000 Fred Conrad Koch Award for Distinguished Contributions to Endocrinology, Endocrine Society

2000 Hamden Award for Medical Research, United Arab Emirates

2001 Lawson Wilkins Lecture, Pediatric Endocrine Society and International Pediatric Endocrine Society, Toronto, Canada

2001 Donald W. Seldin Lecture, American Society of Nephrology and International Society of Nephrology, San Francisco, CA

2001 Rolf Luft Award Lecture, Karolinska Institute, Stockholm, Sweden

2001 Naomi Berrie Award for Outstanding Achievement in Diabetes Research, Columbia University, New York, NY

2002 Societa' Italiana Di Diabetologia Mentor Award, Italy

2002 Steven C. Beering Award for Advancement of Biomedical Science

2002 J. Allyn Taylor International Prize in Medicine for Diabetes

2002 Jacobeus Prize, Novo-Nordisk Foundation, Lund, Sweden

2002 Dean's Distinguished Lecture, University of Colorado School of Medicine

2002 Fellow American Academy of Microbiology

2002 Fast Breaking Paper in the field of Multidisciplinary as determined by the Thompson-ISI Web of Science database

2003 Gordon Wilson Lecture, Transactions of the American Clinical and Climatological Association

2003 Stapleton Lecture, University of Colorado School of Medicine

2004 9th Annual Dundee Signaling Lecture, Scotland

2004 Claude Bernard Medal awarded by the European Association for the Study of Diabetes (EASD), Munich, Germany

2004 Bristol Myers Squibb Award for Distinguished Achievement in Metabolic Research

2005 Dale Medal Lecture, British Society for Endocrinology

2005 Honorary Director and Professor of the Diabetes Center of Peking University, Beijing, China

2005 Dean's Lecture, Mount Sinai School of Medicine, New York, NY

2006 Heskett Lecture, Northwestern University Feinberg School of Medicine

2006 Honorary Member, British Society for Endocrinology

2006 Banting Memorial Lecture, British Diabetic Association, Birmingham, UK

2006 Baxter Lecture, Yale University School of Medicine

2006 Best Doctors in America and Best Doctors in Boston for 2005-2006

2007 Best Doctors in American 2006-2007

2007 International Visiting Fellow, Garvan Institute, Sydney, Australia

2008 Mary Shorb Lecture, University of Maryland

2008 Robert B. Greenblatt Distinguished Lecture, Medical College of Georgia

2008 Louis-Jeantet Foundation 25th Anniversary Symposium, Geneva, Switzerland

2008 Banting and Best Lecture, Canadian Diabetes Association, Montreal, Canada

2008 Johns Hopkins 100th Anniversary Symposium for Department of Biochemistry, Baltimore, Maryland

- 2008 Honorary Doctor in Medicine, University of Copenhagen, Denmark
- 2008 Presidential Distinguished Lecture, University of San Antonio Health Science Center, San Antonio, Texas
- 2008 Dewitt Goodman Lecture, Columbia University School of Medicine, New York, NY
- 2009 Lydia J. Roberts Lecture, University of Chicago and Chicago Nutrition Society, Chicago, IL
- 2009 Inaugural Recipient Manpei Suzuki International Prize, Tokyo, Japan
- 2009 Distinguished Visiting International Lecturer, University of Toronto
- 2009 Hans Falk Memorial Lecture, National Institute of Environmental Health Science, Research Triangle Park, NC
- 2010 Inaugural Beutler Visiting Professor, The Scripps Research Institute, San Diego, CA
- 2010 Presidential Lecture, Memorial Sloan Kettering Cancer Institute, New York
- 2010 David Seegal Alpha Omega Alpha Visiting Professor, Columbia University Medical School, New York, NY
- 2010 Pfizer Visiting Professor in Obesity, Northwestern Medical School, Chicago, IL
- 2010 Frontiers in Science Award, American Association of Clinical Endocrinologists, Boston, MA
- 2010 John B. Hickam Endowed Lecture, Central Society for Clinical Research, Chicago, IL
- 2010 NIDDK 60th Anniversary Scientific Symposium, Bethesda, MD
- 2010 Washington University School of Medicine 100th Anniversary, St. Louis, MO
- 2010 Cockrell Foundation Award in Basic and Clinical Research, Houston, TX
- 2010 Glenn Distinguished Lecture, Massachusetts Institute of Technology, Cambridge, MA
- 2010 Distinguished Leader in Insulin Resistance, World Congress of Insulin Resistance in Diabetes & Cardiovascular Disease, Los Angeles, CA
- 2011 Ray A. and Robert L. Kroc Lecture, University of Massachusetts Medical School, Worcester, MA
- 2011 Invited Lecturer, Fourth Annual Pfizer Frontiers in Human Disease Symposium, New York, NY
- 2011 Invited Lecturer, Cell Symposia 2011, Cape Cod, MA
- 2011 Invited Lecturer, 4th International Congress on Prediabetes and Metabolic Syndrome, Madrid, Spain
- 2011 Roslyn Yalow Lecture, Mount Sinai School of Medicine, 4th New York Skeletal Biology and Medicine Conference, New York, NY
- 2011 Distinguished Biomedical Scholar Lecturer, University of Iowa, Iowa City, IA
- 2011 Gairdner Symposium on the 90th Anniversary of Insulin, Toronto, Canada
- 2011 David Murdock Dole Honorary Lecture, Mayo Clinic-Karolinska, Nobel Forum, Stockholm, Sweden
- 2012 Stanley Mirsky Memorial Lecture, Mount Sinai School of Medicine, New York, NY
- 2012 16th Annual Carl W. Gottschalk Lecture, University of North Carolina School of Medicine, Chapel Hill, NC
- 2012 Del Fisher Visiting Professor and Distinguished Lecturer, University of

- California, Los Angeles, CA
- 2012 Keynote Speaker, Ben May Department for Cancer Research, University of Chicago, Chicago, IL
- 2012 Doctor of Science (Honoris Causa), Washington University, St. Louis, MO
- 2012 Maurice Visscher Lectureship, University of Minnesota, Minneapolis, MN
- 2012 George Randolph and Patricia Scott Lecturer, Mayo Clinic, Rochester, MN
- 2012 Dean's Distinguished Lecture, Virginia Commonwealth University School of Medicine, Richmond, VA

PART II: Research, Teaching and Clinical Contributions

A. Narrative report of Research, Teaching and Clinical Contributions.

My laboratory is focused in four highly related and integrated areas: 1) mechanisms of insulin receptor signaling in control of metabolism and growth; 2) how insulin signaling is altered in insulin resistant states such as type 2 diabetes and obesity; 3) the development of adipose tissue and its relationship to insulin resistance; and 4) what is the impact of genetics, environment and aging on these processes.

In early work, we discovered that the insulin receptor is an insulin-stimulated receptor tyrosine kinase which initiates a complex intracellular network leading to the multiple actions of insulin on the cell. Following activation of the receptor kinase, several intracellular substrates become tyrosine phosphorylated, the best studied of which are termed insulin receptor substrates-1, 2, 3 and 4 (IRS-1 thru -4). These phosphorylated IRS proteins serve as intracellular messengers by docking to other intracellular signaling proteins that contain SH2 domains. This links insulin to two major intracellular cascades - one mediated by the enzyme phosphatidylinositol 3-kinase (PI 3-kinase) and the other mediated by the Ras-MAP kinase pathway. These form a series of critical nodes in the insulin signaling network and are important points of diversion in insulin signaling. We have shown that both the receptor itself and many of its downstream signaling events are important points of regulation in normal physiology and disease states.

Using a wide range of genetic and biochemical approaches, as well as cellular, animal and human systems, my laboratory is working to define the specific pathways that lead to each of insulin's actions and how they are modified in insulin resistant states. This includes defining the roles of each of the IRS-proteins, isoforms of PI 3-kinase and their downstream kinases (Akt and atypical PKCs), in insulin signaling and insulin resistance through the creation of cell lines and animal models in which these proteins are either eliminated by a genetic "knock-out" or knocked-down using RNAi. This also includes studies utilizing the technique of tissue specific gene inactivation to determine the role of insulin in various tissues of the body, including classical target tissues for insulin action such as liver, muscle and fat, as well as non-classical targets such as the brain, endothelial cell and beta cell. We also study mechanisms of insulin resistance, including the role of regulation of insulin receptor, IRS proteins, different catalytic and regulatory subunits of PI 3-kinase, as well as other molecules that can act directly or indirectly as inhibitors of insulin action, such as some forms of protein kinase C and the sirtuin protein deacetylases.

To identify genetic alterations that might contribute to the development of type 2 diabetes in humans and rodents, we have assessed gene expression and function using microarray analysis, proteomics and other techniques. This has allowed us to answer questions about which components of the insulin signaling cascade are involved in regulation of different pathways and to dissect insulin vs. diabetes regulated events. More recently, we have added the study of microRNAs as targets and regulators of insulin action.

The biology of adipocytes and their special role in insulin resistance is another major area of interest. Here we are focused on understanding the role of various fat depots in insulin resistance, and what determines fat distribution and the nature of adipocyte lineages, including the formation of brown vs. white fat and subcutaneous vs. intra-abdominal fat. We have found

important roles for a variety of fundamental developmental genes, and are exploring these through the creation of knockout and knockdown mouse and cellular models.

Finally, we are also interested in the problem of aging and the relationship between insulin action, obesity and lifespan. Again we have taken advantage of some of our genetic models to define better the physiological connections between these events. We are now studying several pathways involved in the connection between aging and metabolism at the molecular level. In this area, we also have been studying the role of sirtuins, especially Sirt2 and Sirt3, in aging and metabolic control.

B. Funding Information (present and recent past)

Present:

1980-2015	National Institutes of Health	Prin. Invest.	Insulin Receptor Structure and Turnover
1988-2013	National Institutes of Health	Prin. Invest.	Insulin Receptor Phosphorylation and Insulin Action
1992-2011	American Diabetes Association	Prog. Dir.	ADA Mentor-based Grant
1999-2012	National Institutes of Health	Prin. Invest.	Role of PI 3-kinase Isoforms in Insulin Action
2002-2009	National Institutes of Health	Prin. Invest.	Diabetes Genome Anatomy Project (DGAP)
2009-2014	National Institutes of Health	Prin. Invest.	Developmental Genes and the Origin of Fat
2009-2011	National Institutes of Health	Prin. Invest.	Imaging Strategies to Measure Brown Fat and its Activity
1996-2001	National Institutes of Health	Prog. Dir.	Diabetes and Endocrinology Research Center
1981-2001	National Institutes of Health	Prog. Dir.	Training in Diabetes and Metabolism
1998-2003	Juvenile Diabetes Foundation (JDF Center for Islet Transplantation at HMS)	Investigator	Search for Islet Growth Factors in Animal Models of Insulin Resistance

C. Report of Teaching Experience:

1976-1978	Course director, "Correlations between the basic sciences and internal medicine," Foundation for Advanced Education in the Sciences, NIH
1967-1981	Lecturer, Courses in Internal Medicine and Endocrinology, Foundation for Advanced Education in Sciences, NIH
1977-1979	Course developer and coordinator, "Endocrinology Board Review Course," Foundation for Advanced Education in the Sciences, NIH
1978-1981	Thesis supervisor for Ph.D. in genetics for J.M. Podskalny, George Washington University
1974	Participation in a variety of CME courses throughout the U.S.
1984	Research Supervisor, Cell and Developmental Biology Program, Harvard Medical School
1987	Thesis Committee for Ph.D. in Cell Biology, Laird D. Madison, Yale University
1981-present	Physiology, Cell Biology and Human Systems Courses at Harvard Medical School and MIT

1985-present HST-060/061 Endocrinology Course, Massachusetts Institute of Technology
1986-present HST-140/141 Molecular Medicine Course
1989-1994 Thesis supervisor, Harvard Cell and Developmental Biology Program
1989-1992 Appeals Board, Student Promotions Board, Faculty of Medicine, Harvard Medical School
1994- present Graduate Faculty of BBS, Harvard Medical School
2002-2006 Thesis supervisor for Ph.D. in Cell Biology C. Taniguchi, Harvard Medical School
2009-2011 Chair, Dissertation Advisory Committee, Mandrita Datta, Harvard Medical School
2009-2011 Chair, Dissertation Advisory Committee, Xun Wang, Harvard Medical School

D. Report of Clinical Activities:

1981-1990 Chief, Division of Diabetes and Metabolism, Brigham and Women's Hospital, Boston, MA
-one month per year attending on Endocrine service
1987- Active Staff, Beth Israel Deaconess Medical Center, Boston, MA

PART III: Bibliography

Original Reports:

1. Kahn CR, Huseby RM, Murray M. The use of infrared dichronic absorption spectra in the study of the structure of bovine fibrinogen and fibrin. *Life Sci.* 1970; 9:1125-1132.
2. Freychet P, Kahn CR, Roth J, Neville DM, Jr. Insulin interactions with liver plasma membranes: Independence of binding and degradation. *J Biol Chem.* 1972; 247:3953-3961.
3. Kahn CR, Neville DM, Jr., Gorden P, Freychet P, Roth J. Insulin receptor defect in insulin resistance: Studies in the obese hyperglycemic mouse. *Biophys Biochem Res Commun.* 1972; 48:135-142.
4. Freychet P, Laudat MH, Laudat P, Rosselin G, Kahn CR, Gorden P, Roth J. Impairment of insulin binding to the fat cell membrane in the obese hyperglycemic mouse. *FEBS Lett.* 1972; 25:339-342.
5. Kahn CR, Neville DM, Jr., Roth J. Insulin-receptor interactions in the obese-hyperglycemic mouse: A model for insulin resistance. *J Biol Chem.* 1973; 248:244-250.
6. Freychet P, Kahn CR, Roth J, Neville DM, Jr. Insulin receptor in liver cell plasma membranes. In: Scow R, ed. *Endocrinology: Proceedings of the IV International Congress of Endocrinology.* New York: Excerpta Medica (ICS #273). NY, 1973:335-340.
7. Schein P, Kahn CR, Gorden P, Wells S, DeVita V. Streptozotocin therapy of malignant insulinoma and carcinoid tumor. *Arch Intern Med.* 1973; 132:555-561.
8. Pilch B, Kahn CR, Ketcham A, Henson D. Thyroid cancer after radioactive iodine diagnostic procedures in childhood. *Pediatrics.* 1973; 51:898-902.
9. Schein PS, DeLellis RA, Kahn CR, Gorden P, Kraft AR. Islet cell tumors: Current concepts and management. *Ann Intern Med.* 1973; 79:239-257.
10. Goldfine ID, Kahn CR, Neville DM, Jr., Roth J, Garrison MM, Bates RW. Decreased binding of insulin to its receptors in rats with hormone induced insulin resistance. *Biochem Biophys Res Commun.* 1973; 53:852-857.
11. Butcher RW, Crofford OB, Gammeltoft S, Gliemann J, Gavin JR III, Goldfine ID, Kahn CR, Rodbell M, Roth J. Insulin activity: The solid matrix. *Science.* 1973; 182:396-397.
12. Kahn CR, Freychet P, Neville DM, Jr., Roth J. Quantitative aspects of the insulin-receptor interaction in liver plasma membranes. *J Biol Chem.* 1974; 249:2249-2257.
13. Gorden P, Roth J, Hendricks CM, Kahn CR. The plasma proinsulin-like components. *Isr J Med Sci.* 1974; 10:1212-1221.

14. Megyesi K, Kahn CR, Roth J, Froesch ER, Humbel RE, Zapf J, Neville DM, Jr. Insulin and non-suppressible insulin-like activity (NSILA-s): Evidence for separate plasma membrane receptor sites. *Biochem Biophys Res Commun.* 1974; 57:307-315.
15. Megyesi I, Kahn CR, Roth J, Gorden P. Hypoglycemia in association with extrapancreatic tumors: Demonstration of elevated plasma NSILA-s by a new radio-receptor assay. *J Clin Endocrinol Metab.* 1974; 38:931-934.
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REVIEWS, CHAPTERS, EDITORIALS

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