

BIOGRAPHICAL SKETCH

NAME	Amira KLIP	POSITION TITLE	• Senior Scientist, Cell Biology Program, Research Institute, The Hospital for Sick Children, Toronto, Ontario, Canada
eRA COMMONS USER NAME	• AMIRAKLIP		• Professor of Paediatrics, Biochemistry & Physiology, University of Toronto • Canada Research Chair in Cell Biology of Insulin Action, Tier I

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
• Centre for Research and Advanced Studies (CINVESTAV-IPN), Mexico City, Mexico	• BSc/MSc	• 09/1970–01/1974	• Biochemistry
• Centre for Research and Advanced Studies (CINVESTAV-IPN), Mexico City, Mexico	• PhD	• 01/1974–07/1976	• Biochemistry
• Postdoctoral Fellow, Banting and Best Department of Medical Research, University of Toronto, Ontario, Canada		• 09/1976–08/1978	• Biochemistry
• Research Associate, Laboratorium fur Biochemie ETH-Zentrum, Zurich, Switzerland		• 09/1978–08/1979	• Biochemistry

A. Personal Statement

The goal of our research is to understand the molecular and cellular basis of the regulation of glucose transport into muscle cells, with emphasis on how insulin and contraction signal to intracellular traffic events. In parallel, we study how insulin crosses the microvasculature to reach tissues, and establish cellular paradigms and animal models to investigate the contribution by immune cells to insulin resistance and type 2 diabetes.

B. Positions and Honors**Positions and Employment:**

- 2014 Visiting Professor – Cell Biology Department, Institut Curie, Paris, France
 2007–2010 Editor-in-Chief – American Journal of Physiology–Endocrinology and Metabolism
1992–current Professor – Departments of Paediatrics, Biochemistry, & Physiology, University of Toronto
1992–current Senior Scientist – Cell Biology Program, Research Institute, The Hospital for Sick Children, Toronto
 1991–2008 Associate Chief of Research – Research Institute, The Hospital for Sick Children, Toronto
 1986–2009 Founder & Director – Research Training Centre, Research Institute, The Hospital for Sick Children
 1985–1992 Associate Professor – Departments of Paediatrics, & Biochemistry, University of Toronto
 1980–1985 Assistant Professor – Departments of Paediatrics, & Biochemistry, University of Toronto
 1980–1992 Scientist – Cell Biology Program, Research Institute, The Hospital for Sick Children, Toronto

Honors and Distinctions:

- 1990 Young Scientist Award, Canadian Diabetes Association
 1992 Pharmacia Award for Excellence in Biomedical Research, Canadian Biochemical Society
 1998 PMAC Award, Canadian Federation of Biological Societies
 2000 Jeanne Manery Fisher Memorial Award, CSBMCB
 2000 Elected Fellow, Royal Society of Canada
 2002 Dales Award for Medical Research, Life Sciences Committee, University of Toronto
 2004 G. Malcolm Brown Award, Canadian Federation of Biological Societies
 2004–2011 Canada Research Chair in Cell Biology of Insulin Action, Tier I
 2005 Solomon A. Berson Distinguished Award, APS, Endocrinology & Metabolism Section
 2009 Honorary Professor, Tianjin Medical University, Tianjin, China
 2011 Elected Fellow, Canadian Academy of Health Sciences
 2011–2018 Canada Research Chair in Cell Biology of Insulin Action, Tier I
 2013 Peter F. Curran Lecture Award, Yale University, New Haven, CT
 2013 Hugh Davson Distinguished Award, APS, Cell Biology Section
 2015 Elected Fellow, American Physiological Society, San Diego, CA
 2015 Honorary Doctorate, University of Copenhagen, Copenhagen, Denmark
 2016 Walter B. Cannon Memorial Award, American Physiological Society, San Diego, CA

Fellowships, Scholarships, and Career Awards:

- 1972–1976 Graduate Studentship, National Council of Science and Technology, Mexico
1976–1978 Postdoctoral Award, Medical Research Council of Canada
1980–1985 Scholar Award, Medical Research Council of Canada
1985–1990 MRC Scientist Award, Medical Research Council of Canada
1991, 2008 Glassman Lecturer, Hebrew University of Jerusalem, Israel
1999–2004 MRC Distinguished Scientist Award, Medical Research Council of Canada
2006 Dozor Visiting Scholar, Ben Gurion University of the Negev, Israel
2014 Rothschild-Yvette Mayent-Institut Curie Award, Paris, France

Other Experience and Professional Memberships:

Editorial Board Member

- 1987–2001 American Journal of Physiology–Cell Physiology
1988–2000 American Journal of Physiology–Endocrinology and Metabolism (Editor-in-Chief, 2007–2010)
1989–1992 Endocrinology
1991-94, 2014–Diabetes
2001–2006 Journal of Biological Chemistry
2003– Physiology (Associate Editor, 2017–current)
2007– Faculty of 1000, Endocrinology Section

Academic National and International Boards, Committees, and Panels (Last 5 years)

- 2004-06, 2011–Cell Biology and Mechanisms of Disease Grants Committee, Canadian Institutes of Health Research
2005–2011 Advisory Panel, Latin American Fellows Program, PEW Charitable Trusts
2010–2011 Chair, External Research Evaluation (Endocrinology/Metabolism programs), Karolinska Institute and Hospital, Stockholm, Sweden
2010–2014 Scientific Advisory Board, Diabetes Strategic Research Program, Karolinska Institutet, Stockholm, Sweden
2011 Steering Committee and Session Chair, Inflammation in Chronic Disease Consensus Conference, organized by Canadian Institutes of Health Research
2014– Advisory Board, Instituto Leloir de la Investigacion Cientifica, Buenos Aires, Argentina
2015– External Evaluation Committee, Instituto Leloir de la Investigacion Cientifica, Buenos Aires, Argentina
2015 External Reviewer, Cellular and Physiological Sciences Dept., UBC, Vancouver, BC
2015– Member, Nominating Committee, Royal Society of Canada
2016 Alberta Innovates Health Science, postdoctoral fellowships, Edmonton, AL
2016– CIHR Foundation College of Reviewers
2017–2019 Selection Committee, John Charles Polanyi Prizes, Council of Ontario Universities

Activities at The Hospital for Sick Children Research Institute and University of Toronto (Last 5 years)

- 2010–2012 Steering Group and Lecturer, Integrity in Research, SickKids
2012–2014 Board Member, The Dr. Charles H. Best Foundation, University of Toronto
Annual courses taught at the University of Toronto: Signal Transduction (4th year Biochemistry), Endocytosis (3rd year Physiology), Selected Topics (Graduate level, Biochemistry)

C. Contributions to Science

Peer-Reviewed Publications (Selected from last 5 years) (from total of 287; H index 89; citations 23,109):

- Niu W, Bilan PJ, Yu J, Gao J, Boguslavsky S, Schertzer JD, Chu G, Yao Z, Klip A. (2011) PKC ϵ Regulates contraction-stimulated GLUT4 traffic in skeletal muscle cells. *J. Cell. Physiol.* 226: 173-80.
- Schertzer JD, Tamrakar AK, Magalhães JG, Pereira S, Bilan PJ, Fullerton MD, Liu Z, Steinberg GR, Giacca A, Philpott DJ, Klip A. (2011) NOD1 Activators Link Innate Immunity to Insulin Resistance. *Diabetes* 60: 2206-15.
- Yu J, Shi L, Wang H, Bilan PJ, Yao Z, Samaan MC, He Q, Klip A, Niu W. (2011) Conditioned medium from hypoxia-treated adipocytes renders muscle cells insulin resistant. *Eur. J. Cell Biol.* 90: 1000-15.
- Kewalramani G, Fink LN, Asadi F, Klip A. (2011) Palmitate-activated macrophages confer insulin resistance to muscle cells by a mechanism involving Protein Kinase C θ and ϵ . *PLoS One* 6: e26947.
- Boguslavsky S, Chiu T, Foley KP, Osorio-Fuentealba C, Antonescu CN, Bayer KU, Bilan PJ, Klip A. (2012) Myo1c

- binding to submembranous actin mediates insulin-induced tethering of GLUT4 vesicles. *Mol. Biol. Cell* 23: 4065-78.
- Pillon NJ, Arane K, Bilan PJ, Chiu TT, Klip A. (2012) Muscle cells challenged with saturated fatty acids mount an autonomous inflammatory response that activates macrophages. *Cell Commun. Signal.* 10: 1: 30.
 - Osorio-Fuentealba C, Contreras-Ferrat AE, Altamirano F, Espinosa A, Li Q, Niu W, Lavandero S, Klip A, Jaimovich E. (2013) Electrical Stimuli Release ATP to Increase GLUT4 Translocation and Glucose Uptake via PI3K γ -Akt-AS160 in Skeletal Muscle Cells. *Diabetes* 62: 5: 1519-26.
 - Fink LN, Oberbach A, Costford SR, Chan KL, Sams A, Blüher M, Klip A. (2013) Expression of anti-inflammatory macrophage genes within skeletal muscle correlates with insulin sensitivity in human obesity and type 2 diabetes. *Diabetologia* 56: 7: 1623-8.
 - Chiu TT, Sun Y, Koshkina A, Klip A. (2013) Rac-1 Superactivation Triggers Insulin-independent Glucose Transporter 4 (GLUT4) Translocation That Bypasses Signaling Defects Exerted by c-Jun N-terminal kinase (JNK)- and Ceramide-induced Insulin Resistance. *J. Biol. Chem.* 288: 24: 17520-31.
 - Fink LN, Costford SR, Lee YS, Jensen TE, Bilan PB, Oberbach A, Blüher M, Olefsky JM, Sams A, Klip A. (2014) Pro-inflammatory macrophages increase in skeletal muscle of high fat-fed mice and correlate with metabolic risk markers in humans. *Obesity* 22: 3: 747-57.
 - Sun Y, Chiu TT, Foley KP, Bilan PJ, Klip A. (2014) Myosin Va mediates Rab8A-regulated GLUT4 vesicle exocytosis in insulin-stimulated muscle cells. *Mol. Biol. Cell* 25: 7: 1159-70.
 - Foley KP, Klip A. (2014) Dynamic GLUT4 sorting through a syntaxin-6 compartment in muscle cells is derailed by insulin resistance-causing ceramide. *Biol. Open* 3: 5: 314-25.
 - Costford SR, Castro-Alves J, Chan KL, Bailey LJ, Woo M, Belsham DD, Brumell JH, Klip A. (2014) Mice lacking NOX2 are hyperphagic and store fat preferentially in the liver. *Am. J. Physiol. Endocrinol. Metab.* 306: 12: E1341-53.
 - Li Q, Zhu X, Ishikura S, Zhang D, Gao J, Sun Y, Contreras-Ferrat A, Foley KP, Lavandero S, Yao Z, Bilan PJ, Klip A, Niu W. (2014) Ca²⁺ signals promote GLUT4 exocytosis and reduce its endocytosis in muscle cells. *Am. J. Physiol. Endocrinol. Metab.* 307: 2: E209-24.
 - Pillon NJ, Li YE, Fink LN, Brozinick JT, Nikolayev A, Kuo MS, Bilan PJ, Klip A. (2014) Nucleotides Released from Palmitate-Challenged Muscle Cells Through Pannexin-3 Attract Monocytes. *Diabetes* 63: 11: 3815-26.
 - Azizi PM, Zyla RE, Guan S, Wang C, Liu J, Bolz S-S, Heit B, Klip A, Lee WL. (2015) Clathrin-dependent entry and vesicle-mediated exocytosis define insulin transcytosis across microvascular endothelial cells. *Mol. Biol. Cell* 26: 4: 740-50.
 - Pillon NJ, Azizi PM, Li YE, Liu J, Wang C, Chan KL, Hopperton KE, Bazinet RP, Heit B, Bilan PJ, Lee WL, Klip A. (2015) Palmitate-induced inflammatory pathways in human adipose microvascular endothelial cells promotes monocyte adhesion and impair insulin transcytosis. *Am. J. Physiol. Endocrinol. Metab.* 309: 1: E35-44.
 - Chan KL, Pillon NJ, Sivaloganathan DM, Costford SR, Liu Z, Théret M, Chazaud B, Klip A. (2015) Palmitoleate Reverses High Fat-induced Proinflammatory Macrophage Polarization via AMP-activated Protein Kinase (AMPK). *J. Biol. Chem.* 290: 27: 16979-88.
 - Sorge RE, Mapplebeck JC, Rosen S, Beggs S, Taves S, Alexander JK, Martin LJ, Austin JS, Sotocinal SG, Chen D, Yang M, Shi XQ, Huang H, Pillon NJ, Bilan PJ, Tu Y, Klip A, Ji RR, Zhang J, Salter MW, Mogil JS. (2015) Different immune cells mediate mechanical pain hypersensitivity in male and female mice. *Nat. Neurosci.* 18: 1081-5.
 - Chang Y-J, Pownall S, Jensen TE, Mouaaz S, Foltz W, Zhou L, Liadis N, Woo M, Hao Z, Dutt P, Bilan PJ, Klip A, Mak T, Stambolic V. (2015) The Rho-guanine nucleotide exchange factor PDZ-RhoGEF governs susceptibility to diet-induced obesity and type 2 diabetes. *eLife* 4: e06011: 1-24.
 - Sun Y, Jaldin-Fincati J, Liu Z, Bilan PJ, Klip A. (2016) A complex of Rab13 with MICAL-L2 and α -actinin-4 is essential for insulin-dependent GLUT4 exocytosis. *Mol. Biol. Cell* 27: 1: 75-89.
 - Miyatake S, Bilan PJ, Pillon NJ, Klip A. (2016) Contracting C₂C₁₂ myotubes release CCL2 in an NF- κ B-dependent manner to induce monocyte chemoattraction. *Am. J. Physiol. Endocrinol. Metab.* 310: 2: E160-70.
 - Sylow L, Nielsen IL, Kleinert M, Møller LLV, Ploug T, Schjerling P, Bilan PJ, Klip A, Jensen TE, Richter EA. (2016) Rac1 governs exercise-stimulated glucose uptake in skeletal muscle through regulation of GLUT4 translocation in mice. *J. Physiol.* 594: 17: 4997-5008.
 - Pillon NJ, Chan KL, Zhang S, Mejdani M, Jacobson MR, Ducos A, Bilan PJ, Niu W, Klip A. (2016) Saturated fatty acids activate caspase-4/-5 in human monocytes, triggering IL-1 β and IL-18 release. *Am. J. Physiol. Endocrinol. Metab.* 311: E825-35.

Invited Lectures and Presentations (Selected from last 5 years) (from total of 305):

2012 • 12th Annual Rachmiel Levine Symposium on Diabetes, Pasadena, CA

- Endocrine Grand Rounds, Yale University, New Haven, CT
- 15th International Biochemistry of Exercise Congress (IBEC Satellite Symposium), Copenhagen, Denmark
- Remi Savioz Glut1 Foundation of Greater Pittsburgh, 1st Annual Conference for Glucose Transporter, Orlando, FL
- School of Life Sciences, Xiamen University, Xiamen, China
- Insulin Resistance Symposium, 50th Anniversary celebration, Dept. of Biochem., CINVESTAV, Mexico City, Mexico
- Molecular and Biochemical Aspects of Cardiovascular Pathology, ITESM Symposium, Monterrey, Mexico
- 48th Annual Meeting of the Argentinian Society of Investigation in Biochemi & Mol Biol, Mendoza, Argentina
- 2013** • Institute of Biomedical Research (Neurobiology), National University of Mexico, Queretaro, Mexico
- Leica Scientific Forum, lectures in Melbourne, Sydney, and Brisbane – declined due to family emergency
- Hugh Davson Distinguished Lecture APS, Experimental Biology 2013 Meeting, Boston, MA (Keynote Lecture)
- IFNH Laboratory of Translational Nutrition Biology, ETH Zurich, Switzerland
- Symposium on Diabetic Models Across Species, 2nd Meeting of the NASCE, Juriquilla, Queretaro, Mexico
- Cell Symposia Immunometabolism: from Mechanisms to Therapy, Toronto, ON
- FASEB Summer Conference on Glucose Transport: Gateway for Metabolic Systems Biology, Snowmass, CO
- Institute de Recherches Cliniques de Montréal (IRCM) Lecture Series, Montreal, QC
- 27th Peter F. Curran Lecture in Physiology, Yale University School of Medicine, New Haven, CT (Keynote Lecture)
- JDRF Symposium on World Diabetes Day, Mississauga, ON
- 2014** • Membrane Trafficking Club, Seminar Series, McGill University, Montreal, QC
- Cedars-Sinai Medical Center, Diabetes and Obesity Research Institute, Lecture Series, Los Angeles, CA
- First Tel Aviv University/U of T Joint Workshop on Membrane Traffic & Biophysics, Tel Aviv, Israel
- Section of Molecular Physiology, August Krogh Center, University of Copenhagen, Copenhagen, Denmark
- Strategic Research Program in Diabetes Symposium, Karolinska Institute, Stockholm, Sweden
- Institut Curie, Paris, France
- Rothschild-Yvette Mayent-Institut Curie Lecture, Institut Curie, Paris, France
- Institut des Maladies Metaboliques et Cardiovasculaires, Universite Paul Sabatier, Toulouse, France
- 1st PanAmerican Congress of Physiological Sciences, Physiology without Borders, Iguassu Falls, Brazil
- Cytoskeleton Support Group, University of Toronto, Toronto, ON
- Dept. of Pharmacology and Physiology, Schulich School of Medicine & Dentistry, Western University London, ON
- 2015** • FASEB Conference on Glucose Transport: Gateway for Metabolic Systems Biology, Big Sky, MT
- 23rd International Union of Biochemistry and Molecular Biology (IUBMB) Congress, Foz do Iguacu, Brazil
- Summer School on Diabetes and Metabolism, Danish Diabetes Academy, Copenhagen, Denmark
- ACCDiS International Theoretical & Practical Course & Symposium on Metabolic Cell Signaling & Chronic Diseases, Santiago, Chile
- 4^o Certamen Latinoamericano de Investigacion Bioquimica, Toluca, Mexico
- August Krogh Institute, University of Copenhagen, Copenhagen, Denmark
- 2016** • Department of Biochemistry, The University of Texas Health Science Center, San Antonio, TX
- Translational Research Inst. for Metabolism & Diabetes, Florida Hospital & Sanford-Burnham-Prebys, Orlando, FL
- Keystone Symposia, Immunometabolism in Immune Function and Inflammatory Disease, Banff, AB
- National Institute for Biotechnology in the Negev Ltd., Ben-Gurion University of the Negev, Beer-Sheva, Israel
- Tel Aviv University Mini Symposium on Membrane Transport and Remodeling, Tel Aviv, Israel
- Walter B. Cannon Memorial Award Lecture, Experimental Biology meeting 2016, San Diego, CA
- Einstein Diabetes Research Center Grand Rounds, Albert Einstein College of Medicine, Bronx, NY
- Department of Biochemistry, Weill Cornell Medical College, New York, NY
- 7th Annual Muscle Health Awareness Day (MHAD7), York University, Toronto, ON
- Gordon Research Conference on Lysosomes and Endocytosis, Andover, NH
- 16th IUBMB Conference on Signalling Pathways in Development, Disease and Aging, Vancouver, BC
- Department of Pharmacology, College of Medicine, University of Illinois, Chicago, IL
- 3rd BBDC-Joslin-UCPH Conference on Cellular Mechanisms and Cell-Based Therapies of Diabetes, Boston, MA
- 2017 (accepted)**
- Canada-France Symposium on Diabetes, Toronto, Canada
- Ulrich Hopfer Lecture, Case School of Medicine, Cleveland, OH
- Metabolism and Childhood Obesity Research Program, McMaster University, Hamilton, ON

- McGill University Health Center Research Institute, Experimental Therapeutics and Metabolism program, Montreal, QUE
- Cold Spring Harbor meeting on Mechanisms of Metabolic Signaling, Cold Spring Harbor, NY
- FASEB Summer Conference on Glucose Transport: Gateway for Metabolic Systems Biology, Snowmass, CO
- International Society of Exercise Immunology, 13th Symposium, Coimbra, Portugal

Organization of Symposia:

- 1995 FASEB Annual Meeting, Mini-symposium: Regulation of Glucose Transport By Exercise, Stress & Growth Factors, Atlanta, GA (Organizer and Chair)
- 1997 FASEB Research Conference on Glucose Transporter Biology, Copper Mountain, CO (Organizer and Co-chair)
- 1999 FASEB Research Conference on Glucose Transporter Biology, Snowmass Village, CO (Organizer and Chair)
- 2014 1st PanAmerican Congress of Physiological Sciences, Physiology without Borders, Iguassu Falls, Brazil (Symposium: Inflammation and Metabolic Disease: the Physiological Crossway) (Organizer and Chair)
- 2016 Keystone Symposia, Immunometabolism in Immune Function and Inflammatory Disease, Banff, AB (Organizer and Co-chair)

Intellectual Property – Patents & Licenses:

- Co-applicant: German Patent #: 42 18 572 A1; European Patent #: EP 0 958 816 A2; US Patent #: 5,948,810
Use of R-(+)-alpha-Lipoic Acid, R-(-)-Dihydrolipoic Acid and Metabolites in the Form of Free Acid or Salts or Esters or Amides for the Preparation of Drugs for the Treatment of Diabetes Mellitus as well as of its Sequelae
- Licensing Opportunity # 429 (held in conjunction with The Hospital for Sick Children)
Immortalized L6 Rat Skeletal Muscle Cells of High Fusion Capacity and Insulin-Responsive Glucose Uptake
- Licensing Opportunity # 437 (held in conjunction with The Hospital for Sick Children)
Immortalized Rat Skeletal Muscle Cells (L6) Expressing GLUT4myc Glucose Transporter
- Licensing Opportunity # 687 (held in conjunction with The Hospital for Sick Children)
Transgenic Mouse Model to Study Glucose Transporter 4myc Regulation in Skeletal Muscle

D. Research Support

Ongoing Research Support:

- 07/15–06/22; PA; CIHR Foundation Grant; *Cell biology & physiology of muscle insulin delivery, action & resistance leading to diabetes*

Completed Research Support (last 5 years):

- 10/07–09/12; PA; CIHR Grant; *The GLUT4 interactomes and metabolic implications*
- 07/09–06/12; PA; CDA Grant; *Interplay between fatty acids and macrophages in the genesis and relief of muscle cell insulin resistance*
- 10/10–06/15; PA; CIHR Grant; *Regulation of muscle glucose transporters by Rac and Rabs during insulin action and lipotoxicity*
- 01/12–12/14; NPA; China-Canada JHRI, CIHR & NSFC Grant; *Molecular convergence of insulin and muscle contraction signalling at Rab proteins: Implications for type 2 diabetes*
- 07/12–06/15; PA; CDA Grant; *Endothelial and transendothelial events underlying immune cell infiltration of metabolic tissues in pre-diabetes*
- 10/13–06/15; PA; CIHR Grant; *Macrophage lipotoxic inflammation: Its mechanism, impact on insulin delivery and interplay with muscle*