McGill University, Faculty of Medicine

Curriculum Vitae for Promotions and Tenure Considerations

A. IDENTIFICATION

Name:	Simon Sipen Wing
Office Address:	Polypeptide Laboratory Strathcona Anatomy & Dentistry Building, Room W315 McGill University 3640 University St. Montreal, Quebec H3A 2B2
Telephone:	398-4101
Fax:	398-3923
Date of Birth:	July 22, 1955
Citizenship:	Canadian
Home Address:	46 Westland Drive Montreal Ouest, Quebec H4X 1M2
Telephone:	514-483-4803
Marital Status:	Married
Spouse's Name:	Mary Diovisalvi
Children:	Sara Lina Diovisalvi Wing, Emily Worjun Diovisalvi Wing
Place of Birth:	Montréal, Québec

B. EDUCATION

Undergraduate:	McGill University, Honours Biochemistry, BSc, 1977
Medical:	McGill University, Medicine, MDCM, 1981

Post-graduate training:

Clinical training:

Internship: Dept. of Medicine, Royal Victoria Hospital, July 1981 – June 1982

Residency: Junior and Senior Assistant Residents, Dept. of Medicine, Royal Victoria Hospital, July 1982 – June 1984

Chief Medical Resident: Dept. of Medicine, Royal Victoria Hospital, Jan.1986-June 1986

Sub-specialty fellow: Endocrinology & Metabolism, McGill University, July 1985-Dec. 1985, July 1986-June 1987.

Research training:

Post-doctoral fellow: Harvard Medical School, Dept. of Cellular and Molecular Physiology, July 1987 – Dec. 1989 - Supervisor: Dr. Alfred Goldberg; Topic: Regulation by glucocorticoids of ATP-dependent proteolysis in skeletal muscle

Post-doctoral fellow: National Research Council of Canada Biotechnology Research Institute, Jan. 1990 – Nov. 1992 - Supervisors: Dr. D. Banville, Dr. D. Thomas; Topic: Function and regulation of ubiquitin conjugating enzymes

Professional Certifications:

Licentiate of the Medical Council of Canada

Specialty certificates in internal medicine from:
Royal College of Physicians and Surgeons of Canada 1987
Corporation Professionelle des Médecins du Quebec 1987
American Board of Internal Medicine 1984

Specialty certificates in endocrinology and metabolism from:
Royal College of Physicians and Surgeons of Canada 1987
Corporation Professionelle des Médecins du Quebec 1987
American Board of Internal Medicine 1987

License to practice medicine in the province of Quebec

C. APPOINTMENTS

1. University:

Lecturer, Dept. of Medicine, McGill University, Montreal, Canada - July, 1992-March, 1993

Assistant Professor, Dept. of Medicine, McGill University - April, 1993-May, 1999

Associate Professor, Dept. of Medicine, McGill University – June,1999 to March, 2006

Professor, Dept. of Medicine, McGill University – April, 2006 to present

Associate Member, McGill Nutrition and Food Science Centre - January, 1993 to present

Associate Member, Dept. of Physiology, McGill University - December, 1993 to present

Associate Member, Dept. of Biochemistry, McGill University - June, 1998 to present

Director, Endocrinology and Metabolism Residency Training Program, McGill University, July, 2000 to March, 2002

Director of the McGill Clinical Investigator Training Program – January, 2003 to December, 2003

Director, Division of Endocrinology and Metabolism, McGill University - November, 2003 - present

2. Hospital:

Assistant Physician, Division of Endocrinology and Metabolism, Department of Medicine, Royal Victoria Hospital, Montreal, Canada - March, 1990-May, 1999

Associate Physician, Division of Endocrinology and Metabolism, Department of Medicine, Royal Victoria Hospital/McGill University Health Centre, Montreal, Canada – June,1999 to present

Director, Division of Endocrinology and Metabolism, McGill University Health Centre, Motnreal, Canada - November, 2003 - present

D. SPECIAL HONOURS, AWARDS, RECOGNITION

1. Undergraduate:

University Scholar
Sir Edward Beatty Memorial Scholarship
Graduated with first class honours in biochemistry

2. Medical School:
University Scholar

3. Residency Training:
Chief Medical Resident, Royal Victoria Hospital

4. Research Training:
Fellowship from the Fonds de la Recherche en Santé du Québec 1987-89
Fellowship from the Medical Research Council of Canada 1987-90
Clinician Scientist Award - Phase I from the Medical Research Council of Canada, 1990-93

5. Research Salary Awards
Clinician Scientist Award - Phase II from the Medical Research Council of Canada, 1993-1999
Senior Chercheur Boursier Award from the Fonds de Recherche en Santé du Québec, 1999-2003
Chercheur Nationaux Award from the Fonds de Recherche en Santé du Québec, 2003-2008

6. Research Awards
R. Howard Webster Foundation Grant for excellence in research in reproductive endocrinology from the Royal Victoria Hospital Foundation and Research Institute, November , 1999.

Elected to the American Society for Clinical Investigation, May 2000

Staff Award for Excellence in Research, Dept. of Medicine, McGill University Health Centre, May 2007

7. Teaching Awards:
Director's Award for best presentation at Endocrine Grand Rounds in 2000, Division of Endocrinology and Metabolism, McGill University Health Centre

E. TEACHING

1. McGill Courses:

Undergraduate:
Med I Molecules, Cells and Tissues Unit
Whole class lecturer 2 hrs/year, 2001 to present
Med I Gastrointestinal/Endocrinology & Metabolism Unit
Leader of a tutorial group, l4 hrs/year, 1993 to 2002
Coordinator of small group tutorials in endocrinology and metabolism, 2000 to

present
Whole class lecturer 4 hrs/year, 1998 to present
Med I Musculoskeletal System Unit, Leader of a tutorial group, 2 hrs, 2008
Med I Introduction to the Patient – Small group tutorial on Spirituality, Religious Adherence and Medicine, 2 hrs/year, 2003-2005
Med I Physicianship - Small group tutorial on Spirituality, Religious Adherence and Medicine, 2 hrs/year, 2006
Introduction to Clinical Medicine Part A 17 hrs, 1997, 2001
Med IV Back to Basics
Whole class lecturer 2 hrs/year, 2001 to 2003

Post-graduate:
Experimental Medicine 516-503B; Advanced Endocrinology, 3 hrs/year, 1993 - 1999
Physiology 552-618D; Reseach Topics in Physiology, 9 hrs/year, 1999-2000
Experimental Medicine 516-616A, Topics in Molecular and Cellular Biology, 2003-present, 3 hrs/year
Experimental Surgery 684A, Signal Transduction, 2007, 2 hrs

2. Research Trainees Supervised:

PhD Students:
Rose Oughtred, Experimental Medicine 1995 to 2000
Haijiang Lin, Experimental Medicine 1996 to 2000
Zhiqian Liu, Dept. of Biochemistry, 2000 to 2007
Zhiyu Pang, Experimental Medicine, 2001 to present
Yu Lu, Experimental Medicine, 2003 to present

M.Sc. Students:
Jon Koo, Dept. of Physiology, 1994 to 1995 (withdrew from program due to unsatisfactory performance in course work)
Jocelyn Reid, Dept. of Biochemistry, 2000 to 2003
Sylvia Lee, Experimental Medicine, 2002 to 2004
Priyanka Sundaram, Dept. of Biochemistry, 2006 to present
Miao Miao, Dept. of Biochemistry, 2008 to present

Summer Students:
Neelish Jain, Medicine, 1994.
Caroline Ng Cheong, Medicine, 1994
Yannick Amar, Medicine 1995
Miguel Chaput, Medicine 1996
Anne Keriel, Physiology 1997
Nicholas Marcotte, Medicine 1999
Alexandre Poppe, Medicine 1999
Christopher Ah-Lan, Medicine 2000 and 2001
Sigrid Witek, Dept. of Biochemistry 2002
Lauren Curtis, Dept. of Biochemistry 2002, 2003

Jing Wang, Medicine 2003
Siwen Sun, Medicine, 2006

Undergraduate Students:
Anne Keriel, Dept. of Physiology Sept. 1996-July 1997
Michael Smith, Dept. of Physiology Sept. 1997 –April 1998
Katia Zubkova, Dept. of Physiology Sept. 1998-April 1999
Sigrid Witek, Dept. of Biochemistry Jan 2002-April 2002
Xiyue (Michael) Chen, Dept. of Biochemistry Jan 2007-April 2007
Zhuo Shao, Dept. of Pharmacology Jan 2007-April 2007

Postdoctoral Fellows:
Pascal Hingamp 1995-1997
Venkatesh Rajapurohitem 1996-1998
Lydie Combaret 1997-1998
Olasunkanmi Adegoke 1999-2003

Endocrinology & Metabolism Residents:
Elmer Lee 2000-2001
Andy Suk 2001-2002

Visiting Professors:
Dr. Luiz Carlos Navegantes
Departamento de Biologia Molecular
Faculdade de Medicina de São José do Rio Preto, Brasil August-October, 2005

3. Invited Lectures:

Within the Dept. of Medicine

I usually give Endocrine Grand Rounds at the Royal Victoria Hospital/MUHC once per year. The most recent ones were "Ubiquitin – Does it cause any endocrine disease? Will it cure anything?" January 26, 2006; "A day in the life of the Endorine Division at the MUHC" October, 2003 and "Hyperglycemia in Acute Strokes – Should We Care?" May 1, 2003 given in conjunction with Dr. Liam Durcan. I have also presented at Endocrine Rounds at the Montreal General Hospital and the Sir Mortimer B. Davis Jewish General Hospital, the Lady Davis Institute and at Medical Grand Rounds at the Royal Victoria Hospital.

McGill Departments (other than in Endocrinology):

Dept. of Physiology, Regulation of ubiquitin dependant proteolysis in atrophying skeletal muscle, October, 1993

Dept. of Anatomy, Cloning and characterization of ubiquitin conjugating enzymes

induced in atrophying skeletal muscle and in testis maturation. February 8, 1995

Dept. of Biochemistry, Role of ubiquitin dependent proteolysis during spermatogenesis. Oct. 2, 1997.

Dept. of Anatomy, Role of ubiquitin dependent proteolysis during spermatogenesis, Nov. 19, 1997.

Dept. of Pediatrics, Function of the ubiquitin system during spermatogenesis. March 8, 1999

Dept. of Obstetrics & Gynecology, MUHC. Ubiquitin-dependent proteolysis – roles in muscle protein turnover and spermatogenesis. October 7, 1999.

Division of Geriatrics, Dept. of Medicine, MUHC. Ubiquitin-dependent proteolysis – roles in muscle protein turnover and spermatogenesis. April 17, 2000.

Dept. of Animal Science, Macdonald Campus. Ubiquitin-dependent proteolysis - roles in muscle protein turnover and spermatogenesis. October 26, 2000

Dept. of Anatomy and Cell Biology. Function and regulation of ubiquitin-dependent proteolysis during spermatogenesis. November 15, 2000

Division of Nephrology, MUHC. Ubiquitin and the nephrologist. September 20, 2001

Dept. of Pharmacology & Therapeutics. McGill University. Ubiquitin dependent proteolysis and spermatogenesis. October 8, 2002

Dept. of Physiology, McGill University. Ubiquitination – Structure and function of enzymes in the testis. January 20, 2004

Meakins-Christie Laboratories, McGill University. Ubiquitin and Muscle Wasting. March 27, 2006.

Dept. of Physiology, McGill University. Role of the USP 19 deubiquitinating enzyme in cell growth and muscle wasting. November 3, 2006.

Critical Care Division, McGill University Health Centre. Role of the USP19 deubiquitinating enzyme in muscle wasting. December 21, 2006.

Dept. of Anatomy and Cell Biology, McGill University. Role of the USP19 deubiquitinating enzyme in cell proliferation. November 7, 2007.

<u>Outside McGill</u>:

Institut Nationale de la Recherche Agronomique, Centre de Theix, France. Regulation of ubiquitin conjugation in skeletal muscle. March 5, 1993

Myogenics, Boston, USA. Regulation of ubiquitin conjugation in skeletal muscle. April 3,1993

Institut Nationale de la Recherche Agronomique, Centre de Theix, France. Regulation of conjugation of ubiquitin to proteins in skeletal muscle by insulin and IGF-1. Oct.5, 1995.

Dept. of Biochemistry, University of Alberta. Function and regulation of ubiquitin dependent proteolysis during spermatogenesis. July 8, 1997.

FASEB Summer Research Conference on Ubiquitin and Intracellular Protein Degradation, Saxtons River, Vermont, USA. Regulation and roles of a UBC-4 dependent pathway of conjugation in the testis. August 1, 1999

Division of Endocrinology and Metabolism, Dept. of Medicine, Medical College of Vermont, Burlington, Vermont, USA. Ubiquitin-dependent proteolysis – roles in muscle protein turnover and spermatogenesis. March 13, 2000.

Canadian International Workshop on Anorexia Cachexia Syndrome. Montreal, Canada. The ubiquitin-proteasome system and muscle protein wasting. October 2, 2002

Dept. of Pathology, Université de Montréal. Role of ubiquitin dependent proteolysis during spermatogenesis. October 27, 2003

Alberta Cancer Board Annual Research Meeting, Banff, Alberta. Molecular signature of cancer cachexia: regulation of the ATP-ubiquitin-proteasome dependent proteolytic system in skeletal muscle. November 13, 2003

Sixth International Workshop on Proteasomes, Clermont-Ferrand, France. Role of the ubiquitin system in spermatogenesis. April 26, 2005.

National Research Council Canada Biotechnology Research Institute, Montreal, Canada. Functions of ubiquitin dependent proteolysis during spermatid development. June 28, 2005

Shanghai Jiaotong University, Dept. of Endocrinology and Metabolism, Shanghai, China. Role of the USP19 deubiquitinating enzyme in cell proliferation and muscle wasting. June 18, 2007

Cold Spring Harbor Laboratory Banbury Center Meeting on Molecular Mechanisms Modulating Skeletal Muscle Mass and Function, Lloyd Harbor, New York. Role of the

USP19 deubiquitinating enzyme in muscle cell proliferation and differentiation. April 6-9, 2008.

4. Clinical Teaching

Students:
One hour teaching session on endocrine emergencies to clinical clerks (1-2 times per year until 1998).
Tutorial on Care and Feeding of Diabetic Patients. March 29, 2001
Tutorial on Thyroid Enlargement, MedII Introduction to Clinical Medicine April 10, 2006

Residents, Fellows:
Teaching session at weekly Diabetes Clinic (1996-2001)
Supervision of residents on the endocrine consultation service 5 weeks per year
Supervision of journal club 2 - 3 times per year.
Lecture on Insulin Regimens to medical residents, March 29, 1999, October 23, 2000, October 15, 2001, October 24, 2003, November 22, 2005, September 6, 2006
Lecture on Perioperative Management of Diabetes to medical residents, February 16, 2007
Teaching session to Endocrine Residents on Do's and Don'ts of Presentations at Rounds, Sept. 25, 2000, November 20, 2006, February 11, 2008
Teaching session on Thyroid to medical residents, March 19, 2001
Introduction to Basic Science Series for Endocrine Residents, July, 2002, Sept. 8, 2003, August 21, 2006
Teaching session to Endocrine Residents on Multiple Endocrine Neoplasias June 14, 2004, September 19, 2005, January 22, 2007
Teaching session to Endocrine Residents on Diabetic Ketoacidosis and Hyperosmolar Nonketotic States, July 26, 2004

F. OTHER CONTRIBUTIONS

1. Journals

Ad hoc reviewer for (Number of manuscripts reviewed from 2001-present):
American Journal of Physiology Regulatory, Integrative and Comparative Physiology -1 article
American Journal of Physiology Cell Physiology - 1 article
American Journal of Pathology – 1 article
Biology of Reproduction – 2 articles
British Journal of Cancer - 2 articles
Cancer Letters – 1 article
Diabetes - 1 article

Endocrinology -1 article
Intensive Care Medicine -1 article
International Journal of Biochemistry and Cell Biology – 5 articles
Journal of Biological Chemistry - 4 articles
Journal of Nutritional Biochemistry - 1 article
Metabolism –1 article
Molecular and Cellular Biology – 2 articles
Molecular and Cellular Biochemistry - 1 article
Protein Science -1 article
Trends in Genetics – 1 article

2. Grant Reviews

Panel member for Royal Victoria Hospital Research Institute in Spring, 1993, Fall 1994, Spring 1997 to 1999 (2 days per year)

Panel member, Studentships Committee, MUHC Research Institute 2002 to present (2 half days/year)

Review committee for Royal Victoria Hospital Dept. of Medicine Research and Education Fund, Fall 1995 to Spring 1997 (two half days per year).

Invited member, Metabolism and Nutrition Committee, Medical Research Council of Canada, Fall, 1999 (3 days)

Member, Metabolism and Nutrition Committee, Canadian Institutes of Health Research, 2000-2003 (6 days/year)

Member, Clinical Investigator Committee, Alberta Heritage Research Foundation 2001-2004 (1 day/year + 1 conference call/year)

Invited member, Biochemistry and Molecular Biology B Committee, Canadian Institutes of Health Research, Fall, 2004 (2 days)

In addition to above, ad hoc reviews from 2001 to present for:
Health Services Utilization and Research Commission of Saskatchewan
Hospital for Sick Children Foundation
Wellcome Trust (UK)
Canadian Diabetes Association
Medical Research Council (UK)
Cancer Research (UK)

3. Administrative Responsibilities

Organized the collection of information for preparation of a web site for the MUHC

Endocrine Division (now on the Internet) (1998)

Director, Endocrinology and Metabolism Residency Training Program, McGill University, July, 2000 to March, 2002

Director of the McGill Clinical Investigator Training Program – January, 2003 to December, 2003

Director, Division of Endocrinology and Metabolism, McGill University - November, 2003 - present

Organized and shepherded through MUHC committees new order forms for IV insulin therapy and subcutaneous insulin therapy (2002-2003)

4. Committtees (Other than grant review committees)

Outside McGill:

Member, Examination Board for Endocrinology & Metabolism, Royal College of Physicians and Surgeons of Canada (2002-present)

Member, Clinical Investigator Advisory Committee, Royal College of Physicians and Surgeons of Canada (2003)

Member, Program Committee for Annual Meeting of the Canadian Society for Endocrinology and Metabolism (2006-present)

External reviewer for promotion of candidate to full professor, Dept. of Medicine, University of Toronto, March 2007.

McGill:
Faculty of Medicine Animal Care Committee, Representative for Donner/Strathcona Facility, Feb. 1997 to 2002. 30 hrs/year of meetings; 20 hrs/year reviewing animal protocols in preparation for the meetings.

Division of Experimental Medicine Executive Committee. 2003 to present (4 hours/year)

Chair, Subcommittee on Faculty for the Faculty of Medicine Self-Study Task Force charged with preparation for the accreditation of the Medical School by the Association of Faculties of Medicine of Canada and the Association of American Medical Colleges 2007 (6 hours)

Thesis Committees and Oral Defenses (McGill unless otherwise indicated)
Weihua LI, MSc, Dept. of Microbiology and Immunology. Thesis examiner. April,

1995

Sandrine TEMPARIS, PhD, Dept. of Physiology, Université Blaise Pascal, Aubiere France. External examiner at oral defense. October, 1995

Qingwei CHU, MSc, Dept. of Physiology. Thesis examiner. May, 1997

Sic Lung CHAN, PhD, Dept. of Microbiology and Immunology. Thesis Committee and External examiner at oral defense. December, 1997

Chantelle GWOZD, PhD, Dept. of Biochemistry, University of Alberta, Edmonton. External examiner at oral defense. July, 1997

Daniel AUCLAIR, PhD, Dept. of Nutrition, Université de Montréal. External examiner at oral defense. August, 1998

Paola BLANCHETTE, PhD, Dept. of Biochemistry, University of Ottawa. External examiner at oral defense. March 26, 2002.

Kamal SHARMA, PhD, Dept. of Experimental Medicine. Thesis Committee. 1996 to 1998

Audrey NGUYEN, PhD, Dept. of Experimental Medicine. Thesis Committee. 1997 to 2001

Julie CARETTE, PhD, Dept. of Experimental Medicine. Thesis Committee. 1998

Tanya FOURNIER, PhD, Dept. of Biochemistry. Examiner at oral defense. Mar. 30, 2001.

Sangwon KIM, PhD, Dept. of Experimental Medicine. Examiner at oral defense. Oct. 3, 2001.

Sem KEBACHE, PhD, Dept. of Experimental Medicine. Thesis Committee. 1998 to 2002

Stephane LEFRANÇOIS, PhD, Dept. of Anatomy and Cell Biology. Thesis Committee. 1999 to 2002.

Genevieve HUPPE, MSc, Dept. of Surgery. Thesis Committee 2002

Weirong XING, PhD, Dept. of Experimental Medicine. Examiner at oral defense. Apr. 24, 2002.

Edor KABASHI, MSc, Dept. of Neurology. Thesis Committee 2002 to 2007

Lisa MANDRUSIAK, MSc, Dept. of Human Genetics. Thesis Committee 2002 to 2003

Angela KUMAR, MSc, Dept. of Biology. External examiner. October, 2002

Emily CROWE, PhD, Dept. of Biochemistry and Molecular Biology, University of British Columbia. External Examiner January, 2003

Wendy L. PARKER, PhD, Dept. of Experimental Surgery. Internal examiner. May 2003

Jasmine ABELLA, MSc, Dept. of Biochemistry. Thesis Committee 2003 to present

Pascal PESCHARD, PhD, Dept. of Biochemistry. Thesis Committee 2002 to 2006

Gabriel CHAN, MSc, Dept. of Experimental Surgery. Thesis Committee 2003 to 2005

Assim AL-FADDA, MSc, Dept. of Physiology. Thesis Committee 2002 to 2003

Xin Xin QUAN, PhD, Dept. of Physiology. Thesis Committee 2003 to present

Renu HEIR, MSc, Dept. of Anatomy and Cell Biology. Thesis Committee 2006

Marcos DI FALCO, PhD, Dept. of Biochemistry, Examiner at thesis defense. Jan. 17, 2003

Michel MASSAD, PhD, Dept. of Biochemistry. Examiner at thesis defense. Nov. 28, 2003

Gity MOUSAVI, MSc, Dept. of Human Genetics. External examiner. October, 2004

Deborah STEWART, PhD, Institute of Parasitology. External examiner. December 22, 2004

Grigorios N. PALIOURAS, PhD, Experimental Medicine. Thesis Committee. Dec., 2004

Mathieu LUPIEN, PhD, Experimental Medicine. Internal examiner at thesis defense. September 29, 2005-

Sheun-Yuan Chen, PhD, Dept. of Biochemistry. Thesis Committee. Dec., 2005-

Chi Ying Cheng, PhD, Dept. of Biochemistry. Thesis Committee. Dec., 2005

Pascal PESCHARD, PhD, Dept. of Biochemistry, Examiner at thesis defense, Dec. 15, 2005.

Philippe COULOMBE, PhD, Molecular biology, Université de Montréal, External

examiner at thesis defense, Aug. 28, 2006

Catherine BELANGER, MSc., Neurosciences, McGill University, External examiner, Nov., 2006

Sophie VENTADOUR, PhD, Medicine, Université d'Auvergne, Clermont Ferrand, France. External examiner at thesis defense, Dec. 15, 2006

Edor KABASHI, PhD, Neurosciences, McGill University, Examiner at thesis defense. Jan. 12, 2007

Ching Yin LEE, PhD, Experimental Medicine, McGill University, Internal examiner at thesis defense, June 5, 2007.

Maria FLORIAN, PhD, Dept. of Physiology, McGill University, Examiner at thesis defense, July 25, 2007.

Xiao ZHU, MSc, Dept. of Biochemistry, Université de Montréal, External examiner of thesis. January, 2008.

Ye WANG, MSc, Experimental Medicine, McGill University, External examiner of thesis, April 2008.

Hospital:
Royal Victoria Hospital Research and Education Committee, member, Fall 1995 – Spring 1997 6 hrs/year of meetings, 12 hrs/year reviewing applications in preparation for the meetings

Royal Victoria Hospital Division of Endocrinology, Chair of Adhoc Committee on Recruitment of Graduate Students 1993-94 (12 hrs total)

Royal Victoria Hospital Research Institute Research Committee, Representative from Dept. of Medicine, Spring 1997 to Spring, 2000. 24 hrs/year of meetings, 36 hrs/year reviewing applications in preparation for the meetings.

McGill University Health Centre Division of Endocrinology Executive Committee Nov. 1996 to 2001.

McGill University Health Centre Search Committee for Director of Division of Hematology. 2005 to 2007

5. Professional and/or Learned Societies

Memberships in
Canadian Society for Clinical Investigation
Canadian Society of Endocrinology and Metabolism

Clinical and Scientific Section of the Canadian Diabetes Association
American Diabetes Association
Endocrine Society (USA)
American Society for Clinical Investigation
Quebec/Canadian Medical Association
Christian Medical and Dental Society
Association des Medecins Endocrinologues du Quebec
Royal College of Physicians and Surgeons of Canada

G. RESEARCH

1. Summary of Research Activities

The level of expression of a particular protein in the cell depends not only on its rate of synthesis, but also on its rate of degradation. Many recent studies now indicate that the ubiquitin (Ub) dependent proteolytic system plays an important role in such regulation of gene expression by selective proteolysis. In this proteolytic pathway, Ub, an 8 kDa peptide, becomes covalently linked to protein substrates and this post-translational modification marks the protein for recognition and degradation by a large protease complex, the 26S proteasome. My research is focussed on characterizing the regulation and function of this proteolytic system in mammalian tissues. My initial work focused on the role of this pathway in mediating muscle protein catabolism and was driven by the clinical importance of muscle wasting as a complication of many diseases such as strokes, hyperthyroidism, cancer or cardiac cachexia. Subsequently, due to the accidental discovery of some genes in the ubiquitin system that were highly regulated in the testis, I have also branched out into studying the role of this pathway in mediating the developmental maturation of spermatids. My overall approach has been to initially identify highly regulated enzymes in this pathway that modulate the state of ubiquitination of proteins. Once these enzymes are identified, we characterize them biochemically and elucidate their physiological function. Biochemical analyses have included the use of mutagenesis to gain insights into structure function relationships and now focus primarily on the identification of potential substrates/interacting proteins by using mass spectrometry to identify proteins that co-immunoprecipitate with the enzymes. We evaluate physiological functions by determining the effects of inactivation of the genes in transgenic mice and by using siRNA approaches to deplete the enzyme in cultured cells.

To date, we have cloned and characterized two ubiquitin conjugating enzymes, $E2_{14k}$ and UBC4-testis. The former is induced in atrophying skeletal muscles and the latter is induced in round and elongating spermatids. Surprisingly, study of mice lacking the $E2_{14k}$ gene showed no abnormality in the catabolic response to fasting in muscle and mice lacking the UBC4-testis gene maintained normal spermatogenesis and sperm function. Presently, we are characterizing in similar fashion two ubiquitin protein ligases and two deubiquitinating enzymes. We have and continue to collaborate with other investigators in determining the role of ubiquitination in degradation of specific proteins and also as a signal for internalization of membrane proteins.

2. Personal Support Awards

Medical Research Council of Canada Clinician Scientist Award Phase II - April 1993 - March 1999.

Fonds de la Recherche en Santé du Québec Senior Chercheur Boursier Award, July 1999 – June, 2003

Fonds de la Recherche en Santé du Québec Chercheur Nationaux Award, July 2003-June 2008

3. Research Grants

Current:

Canadian Institutes of Health Research – Function of ubiquitin dependent proteolysis during spermatogenesis. Oct/05-Sept./08 $111,975/year. Principal Investigator: S. Wing

Canadian Institutes of Health Research – Function of USP19 deubiquitinating enzyme in muscle wasting. Apr/07-Mar/10 $101,341/year. Principal Investigator: S. Wing

National Cancer Institute of Canada - Role of the USP 19 deubiquitinating enzyme in cell proliferation. July/07-June/10 $122,003/year. Principal Investigator: S. Wing

Past:

Royal Victoria Hospital Research Institute operating grant; Function of ubiquitin dependant proteolysis in skeletal muscle; $35,000/year July, 1992 - June, 1993. Principal Investigator: S. Wing

Medical Research Council of Canada operating grant; Function of ubiquitin dependant proteolysis in skeletal muscle; $54,000/year, July, 1993 - June, 1996. Principal Investigator: S. Wing

Medical Research Council of Canada Clinician Scientist Award research allowance; Function of ubiquitin dependant proteolysis in skeletal muscle; $40,000/year, April, 1993 - March, 1996.

Canadian Diabetes Association operating grant; Regulation of ubiquitin dependant proteolysis by insulin and other glucoregulatory hormones; $53,000/year, January, 1993 - June, 1995. Principal Investigator: S. Wing

Juvenile Diabetes Foundation International operating grant, Regulation by insulin and IGF-1 of conjugation of ubiquitin to skeletal muscle proteins; Year 1 US$ 43,712; Year 2 US$ 41,057, Sept, 1995 - Aug, 1997. Principal Investigator: S. Wing

Canadian Diabetes Association - Identification and regulation by insulin of ubiquitin protein ligases in skeletal muscle. Jul/97-Jun/99. $52,000/year. Principal Investigator: S. Wing

Medical Research Council of Canada - Function of ubiquitin dependent proteolysis in skeletal muscle and during spermatogenesis. Oct/96-Sept/99. Year 1 and Year 3 - $80,000/year; Year 2 $57,600/year. Principal Investigator: S. Wing

Medical Research Council of Canada - Function of a deubiquitinating enzyme during spermatogenesis. Apr/98-Mar/01. $56,054/year. Principal Investigator: S. Wing

Medical Research Council of Canada – Function and regulation of conjugation of ubiquitin to proteins during spermatogenesis. Oct/99-Sept/02. $79,800/year. Principal Investigator: S. Wing

Canadian Institutes of Health Research Multi-user Equipment and Maintenance Grant – Multi-user major equipment grant. Jan/01-March/01. $140.806 Co-applicant. Principal Investigator: B. Posner Co-investigators: M. Greenwood, L. Larose, S. Wing

Canadian Institutes of Health Research Multi-user Equipment and Maintenance Grant – Mult-user equipment for image detection and analysis. Jan/02-March/02. $171,966. Principal Investigator: S. Wing Co applicants: J.J.M. Bergeron, M. Greenwood, N. Lamarche-Vane, L. Larose, B. Posner

Canadian Institutes of Health Research - Function of a deubiquitinating enzyme during spermatogenesis. Apr/01-Mar/05. $89,148/year. Principal Investigator: S. Wing

Canadian Institutes of Health Research – Pilot project grant in Palliative and End of Life Care - Role of lysosomal proteolysis in mediating the muscle wasting of cachexia. Jan/04 – Dec/04. $89,410. Principal Investigator: S. Wing

Canadian Institutes of Health Research – Function and regulation of conjugation of ubiquitin to proteins during spermatogenesis. Oct/02-Sept/05. $109,000/year. Principal Investigator: S. Wing

Genome Canada/Genome Quebec – Genomic and proteomic approaches to Type 2 diabetes mellitus – Oct/04 – Mar/07 Principal investigators: B. Posner, M. Prentki Total $15 million over 3 years – Amount for S. Wing ~$170,000 per year.

Canadian Institutes of Health Research Multi-User Equipment Grant – Multi-user equipment for the molecular and cell biological analysis of cell signaling and membrane dynamics. Apr/05 to Mar/06 $225,056 Principal Investigator: B. Posner. Co-investigators: F. Bedford, M. Greenwood, M. Kaartinen, L. Larose, M. Latterich, C.

Mandato, S. Wing

4. Publications

4.1. Articles in peer-reviewed journals (*indicates that the first author was my trainee):

Michaliszyn GA, Wing SS, and Meighen EA. Purification and properties of a NAD(P)H:flavin oxidoreductase from the luminous bacterium, Beneckea harveyi. J. Biol. Chem. 1977; 252:7495-7499.

Moroz LA, Wing S, and Liote F. Miniplasminogen-like fragments of plasminogen in synovial fluid in acute inflammatory arthritis. Thrombosis Res. 1986; 43: 417-424

Ismall AA, Wing S; Ferguson J, Hutchison TA, Magder S and Flegel KM. Inter-observer agreement by auscultation about the presence of a third heart sound in patients with congestive heart failure. Chest 1987; 91:870-873

Wing SS and Fantus IG. Adverse immunologic effects of anti-thyroid drugs. Can. Med. Assoc. J. 1987; 136:121-127

Mitchell TH, Abraham G, Wing S, Magder SA, Cosio MG, Deschamps A and Marliss EB. Intravenous bicarbonate and sodium chloride both prolong endurance during intense cycle ergometer exercise. Amer. J. of the Med. Sci. 1990; 300:88-97

Wing SS, Chiang HL, Goldberg AL and Dice JF. Proteins containing peptide sequences related to Lys-Phe-Glu-Arg-Gln are selectively depleted in liver and heart but not skeletal muscle of fasted rats. Biochem. J. 1991; 275:165-169

Wing SS, Dumas F, and Banville D. A rabbit reticulocyte ubiquitin carrier protein that supports ubiquitin-dependent proteolysis ($E2_{14k}$) is homologous to the yeast DNA repair gene RAD6. J. Biol. Chem. 1992; 267:6495-6501

Wing SS and Goldberg AL. Glucocorticoids activate the ATP-ubiquitin dependent proteolytic system in skeletal muscle during fasting. Am. J. Physiol. 1993; 264:E668-E676

Wing SS, and Banville, D. The 14 kDa ubiquitin conjugating enzyme - Structure of the rat gene and regulation upon fasting and by insulin. Am. J. Physiol. 1994; 267 (Endocrinol. Metab. 30): E39-E48

Wing SS, and Jain, P. Molecular cloning, expression and characterization of a ubiquitin conjugating enzyme ($E2_{17kB}$) highly expressed in rat testis. Biochem. J. 1995; 305:125-132

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