# **CURRICULUM VITAE Richard Earl Miller, M.D.**

#### OFFICE ADDRESS & TELEPHONE NUMBERS:

Research Service (151)

Department of Veterans Affairs Medical Center

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**EDUCATION** 

1964 - B.S. University of Michigan, Ann Arbor - with High Distinction

1966 - M.D. University of Michigan, Ann Arbor - Cum Laude

**TRAINING** 

1972-1974 NIH Special Fellow, Clinical Instructor, Research Biochemist,

Division of Metabolic Disease, Department of Medicine,

University of California, San Diego, La Jolla, California 92093

(Chief, Daniel Steinberg)

1971-1972 Senior Staff Fellow, Laboratory of Biochemistry, National Heart

and Lung Institute, National Institutes of Health, Bethesda,

Maryland 20892 (Chief, Earl R. Stadtman)

1968-1971 Clinical Associate, United States Public Health Service,

Laboratory of Biochemistry, National Heart and Lung Institute, National Institutes of Health, Bethesda, Maryland 20892 (Chief,

Earl R. Stadtman)

1966-1968 Intern and Resident, Internal Medicine, Bronx Municipal Hospital

Center, Albert Einstein College of Medicine, Bronx, New York

10461

#### **FACULTY APPOINTMENTS**

1992-present Professor of Internal Medicine and Molecular Medicine &

Genetics, School of Medicine, Wayne State University, Detroit,

Michigan 48201.

1992-present Adjunct member of the Graduate Faculty in the Department of

Biochemistry, School of Medicine, Wayne State University,

Detroit, Michigan 48201.

1991-1992 Professor of Medicine and Professor of Biochemistry in Medicine,

School of Medicine, Case Western Reserve University, Cleveland,

Ohio 44106

1982-1991	Associate Professor of Medicine <i>and</i> Associate Professor of Biochemistry in Medicine, School of Medicine, Case Western Reserve, Cleveland, Ohio 44106
1975-1982	Assistant Professor of Medicine, School of Medicine, Case Western Reserve University, Cleveland, Ohio 44106
1974-1975	Acting Assistant Professor, Division of Metabolic Disease, Department of Medicine, University of California, San Diego, La Jolla, California 92093

#### **HOSPITAL APPOINTMENTS**

1992-present	Associate Chief of Staff for Research and Development, VA Medical Center, Detroit, Michigan 48201; and
1997-present	Network 11 Academic Affiliation Officer
1975-1992	Chief, Metabolism Section (1975-1992), <i>and</i> Chief, Endocrinology & Metabolism Section (1991-1992), Medical Service, Cleveland VA Medical Center, Cleveland, Ohio 44106
1982-1992	Associate Physician, Attending Physician, Division of Endocrinology and Metabolism, Department of Medicine, University Hospitals of Cleveland, Ohio 44106
1975-1982	Assistant Physician, Attending Physician, Division of Endocrinology and Metabolism, Department of Medicine, University Hospitals of Cleveland, Cleveland, Ohio 44106

#### MILITARY SERVICE

1968-1971 Senior Assistant Surgeon (R) and Surgeon Full Grade (R)(T),
United States Public Health Service (PHS # 28060); Clinical
Associate, Laboratory of Biochemistry, National Heart and Lung
Institute, National Institutes of Health, Bethesda, Maryland 20892

# MEMBERSHIP IN PROFESSIONAL SOCIETIES AND ASSOCIATIONS

American Society for Biochemistry and Molecular Biology, 1979-present. Membership Committee, 1983-1986.

American Diabetes Association (National), 1974-present.

Research Grant Review Panel, 1991-1994.

Central Society for Clinical Research, 1979-present.

Endocrine Society, 1976-present.

Diabetes Association of Greater Cleveland, 1975-1992.

Board of Trustees, 1977-1980; 1987-1990.

Research Committee, 1984-1988.

Chairman, Research Committee, 1987-1988.

American Heart Association, Northeast Ohio Affiliate.

Research Fellowship Committee, 1983-1985.

Research Study Section, 1985-1987.

#### MEDICAL LICENSES, DEA NUMBER & BOARD CERTIFICATIONS

Michigan #4301-027692 1967-present

California #C33087 1971-1993 (I did not renew in 1993.) Ohio #038771 1975-1992 (I did not renew in 1993.)

Drug Enforcement Agency (DEA) Registration Number: AM 6861163

<u>SPECIALTIES</u>: Diplomate of the American Board of Internal Medicine (ABIM) certified to practice the following

- Specialty of Internal Medicine. Certificate number 45603, June 19, 1974
- <u>Subspecialty of Endocrinology and Metabolism.</u> Certificate number 45603, October 21, 1975 (Certificate number [45603] is the same as above.)

#### ACADEMIC HONORS AND SOCIETIES

#### <u>University of Michigan, College of Literature Science and the Arts</u>

University of Michigan Regents-Alumni Scholarship, 1959-1962

William J. Branstrom Freshman Prize, 1960 (Award for academic performance.)

Phi Beta Kappa, 1965

Phi Kappa Phi, 1965

# University of Michigan Medical School

Roche Award, 1964 (Awarded to the medical school student ranked first in his class after two years of medical school.)

Alpha Omega Alpha, 1965, President, University of Michigan Chapter of Alpha Omega Alpha, 1965-1966

Valedictorian, Medical School Class of 1966 (Awarded to the medical student ranked first among the 191 graduating seniors in the class of 1966.)

Valedictory address: "The physicians role in the community".

Borden Undergraduate Research Award in Medicine, 1966 (Awarded for meritorious research completed during medical school.)

University of Michigan Medical School, Dean's Award, 1966 (Awarded to the five top ranking seniors.)

Lange Medical Publications Award, 1966 (Awarded for outstanding achievement as a medical student.)

#### **AWARDS**

Research and Development Award of the American Diabetes Association, 1974-1975

Travel Awards from the American Society for Biochemistry and Molecular Biology (formerly the American Society of Biological Chemistry) to attend the:

- 13th International Congress of Biochemistry, Amsterdam, The Netherlands, August 25 through August 30, 1985.
- 14th International Congress of Biochemistry, Prague, Czechoslovakia, July 10 through July 15, 1988.

- 15th International Congress of Biochemistry, Jerusalem, Israel, August 4 through August 8, 1991.
- Student Committee on Medical Education (SCME) Faculty Teaching Award, 1987-88 and 1988-89; given by the SCME of Case Western Reserve University School of Medicine in recognition of outstanding teaching.

Kaiser Permanente Award for Excellence in Teaching Preclinical Science, 1990.

#### **SERVICE**

#### PATIENT CARE AND CLINICAL SERVICE ACTIVITIES

Chief Metabolism Section, Cleveland VA Medical Center, 1975-1992.

**Direct Patient Care:** 

Cleveland VA Endocrinology and Metabolism Clinic, 1975-1992.

Detroit VA Endocrinology/Primary Care Clinic: 1994-present

Inpatient rounds conducted:

# General Internal Medicine:

Cleveland VAMC: 75 hrs/year (1 month), 1975-1984; 150 hrs/year (2 months), 1985-1992,

Detroit VAMC: 100 hrs/ year (1 month), 1992-present.

#### Endocrinology and Metabolism:

Cleve. VAMC: 40 to 120 hrs/year (1 to 3 months), 1975-1992.

#### JOURNAL AND GRANT REVIEWS

#### **Editorial Boards:**

Endocrine Research, 1976 - present.

BioFactors, 1990 - 1992.

Journal of Laboratory and Clinical Medicine, 1991 - 1996.

Ad Hoc Journal Reviews: American Journal of Physiology, Archives of Biochemistry and Biophysics; Endocrinology; FASEB Journal; Journal of Biological Chemistry; Journal of Cell Biology; Journal of Laboratory and Clinical Medicine; Proceedings of the National Academy of Sciences, USA.

Research Study Sections: (See Associations, above) American Heart Association, Northeast Ohio Affiliate, 1983-1987; Diabetes Association of Greater Cleveland. 1984-1988. National American Diabetes Association Research Grant Review Panel, 1991-1994. VA Career Development Review Committee – 1995.

#### Ad Hoc Grant Reviews:

National Institutes of Health, Biochemistry Study Section (Subcommittee 2), Alexander S. Liacouras, Ph.D., Executive Secretary. Outside reviewer, 1985-1988. Special Reviewer (Ad Hoc member), October 13 and 14, 1988.

National Science Foundation.

# VA AND MEDICAL SCHOOL COMMITTEES at Wayne State University

<u>John D. Dingell (Detroit) Veterans Affairs Medical Center Committees:</u>
ACOS-Surgery (Chief of Surgery) Search Committee, Chair, 1999present

Research and Development Committee (Research Svc.), 1992-present Clinical Investigation Committee, 1992-present.

Dean's Committee (Academic Partnership Committee), 1992-present

Executive Health Care Leadership Board (EHLB), 1997-present

Clinical Executive Board, 1992-1997 (replaced by the EHLB)

Professional Standards Board, 1992-present

Radiation Safety Committee, 1992-present

Board of Directors, Secretary-Treasurer, Metropolitan Detroit Research & Education Foundation 1992 - present

Medical Center Strategic Planning Committee, 1996-present.

VA-University affiliation committee 1997

Medical Center reorganization committee, 1996-1997

Education Committee, 1992-1996

#### VA Integrated Service Network 11 (VISN 11) Committees

Strategic Planning Committee, 1996-present

Clinical Leadership Board (Chiefs of Staff), 1997-present

Academic Affiliation Committee, Chairman, 1997-present

Education Board, 1997-present

Research Strategic Planning Committee, 1997-present

# **VA National Committees**

National Research Equipment Committee, Chairman, 1996-present Animal Facility Equipment Committee, 1996-present

Ad Hoc Deputy Director of Medical Research Svc selection cttee, 2000 Ad Hoc Information Systems Administrator selection committee, 1998

Merit Review Council -- 1993 through 1995.

Site Visit Team: VAMC, Columbia, Missouri-- 1996.

#### Wayne State University School of Medicine Committees

#### **Department of Medicine**

Research Committee, 1992-present

Research Reserve Fund Committee, 1995-present

AIDS Research Advisory Committee, 1993-1995

VA/Dept. Medicine task force, 1994 (Chairman)

#### **Center for Molecular Medicine and Genetics**

Faculty Recruitment Committee, 1995-1996 and 1998-present

Promotion and Tenure Committee, 1996

Professor P&T Committee, 1999

Department of Medicine Liaison Committee, 1995-1996

Biochemistry Teaching Committee, 1993-1994

Dean's Strategic Planning Committee, 1994

Work group on research, 1994

Neurosciences task force, 1994

Detroit Medical Center, System-Wide Graduate Medical Education Review Committee (Fernando G. Diaz, chairman; John M. Malone, Jr., M.D., Associate Dean, Executive Secretary) 1998-1999

#### VA AND MEDICAL SCHOOL COMMITTEES at Case Western Reserve University

#### Department of Veterans Affairs Medical Center:

Faculty Development Advisory Committee (Medical Svc.), 1990-1992.

Research Advisory Committee (Medical Service), 1990-1992.

Research and Development Committee (Research Service),

January 1979 to January 1983 and January 1988 to January 1991. Chairman, January 1980 to January 1983.

Radiation Safety Committee, 1985-1990.

Library Committee, 1977-1982.

Nutrition Committee, 1978-1980.

#### Case Western Reserve University School of Medicine

Committee on Medical Education (CME) 7/1/89 through 6/30/92; CME subcommittee on student laboratories - 1990.

Core Academic Program - Curriculum Revitalization Committee, 1984; Section Leader for "Cellular and Developmental Biology" 1984-1992.

Metabolism Training Program (Principal investigator, Richard W. Hanson, Ph.D., NIH grant number 5T32 DK07319), 1980-1992; Steering Committee, 1981-1992.

Curricular Electives Committee, 1977-1984.

#### TEACHING ACTIVITIES at Wayne State University, 1993-present

#### I MEDICAL SCHOOL

A. Diabetes clinical conference (whole class), 4 hours, 1994 -- present. Biochemistry, year one, discussion groups and case studies, 1993

B. Endocrine pathophysiology, year two

Problem solving sessions, 6-9 hours per year 1993 – present. Lectures (2 hours) 1) *Lipids* and 2) *Integration of Intermediary Metabolism*. 2000-present

C. <u>USMLE Review Coursefor year-two students</u>: 1997-present 2hours each year. (Course organizer: Ian Zitron)

#### II. GRADUATE MEDICAL EDUCATION

- A. <u>General internal medicine</u> *attending rounds*: 90 hrs/yr (1 month), 1993-present.
- B. Endocrinology/Primary Care clinic: 4 hours per week. 1994-present.
- C. <u>Endocrinology lectures</u> for residents and fellows. 1994- (intermittent).

#### III. GRADUATE SCHOOL

- A. <u>Molecular biology of cellular signaling</u>. Mol. Biol. & Genetics #740; 1993, 1995 two one hour lectures: 1) Insulin signal transduction, and 2) Nuclear transcription factors in signal transduction. (This course was given every other year.)
- B. Dissertation committees at WSU.

Sitting Chen: Defense: 1/5/96. Advisor: David Evans, Department of Biochemistry. PhD awarded February 1996.

# Anne Bouvier. 1998-present. Advisor: David Evans, Department of Biochemistry.

# C. <u>Dissertation advisor</u>:

Chongsuk Ryou. Center for Molecular Medicine and Genetics. 1995-1998. Ph.D. awarded 12/17/98. Postdoctoral fellow in my lab supported by a Morris J. Hood, Jr. Comprehensive Diabetes Center fellowship award March 1, 1999 through August 27, 1999. (Left to start fellowship with Stan Prusiner at UCSF)

# TEACHING ACTIVITIES at Case Western Reserve University, 1975-1992

# I. MEDICAL SCHOOL, YEAR ONE

- A. Subject Committee Teaching:
  - 1. <u>Cellular and Developmental Biology Committee</u>, 1982-1992. Section Leader, 1984-1992.
  - 2. <u>Metabolism Committee</u>, 1980-1984. Co-chairman, 1984.
  - 3. Gastroenterology, Endocrinology and Metabolism (GEM) 1986-1992.
- B. Electives Program/Flexible Program (Years 1 and 2), 1979-1984
- C. Program Administration:
  - 1. Curricular Electives Committee, 1977-1984.
  - 2. Core Academic Program Committee, 1984-1992.
- D. Academic counselor/student advisor, 1978-1985.

#### II. MEDICAL SCHOOL, YEAR TWO

- A. Subject Committee Teaching:
  - 1. <u>Endocrinology and Metabolism Committee</u>, 1976-1986; Co-chairman, 1984; (incorporated into GEM [I.A.3., above], 1986-1992).
  - 2. Case Oriented Problem Solving, 1987-1992.
- B. Electives Program/Flexible Program (See Year 1).
- C. Clinical Science Program, Physical diagnosis Preceptor: , 1980-1984, 48 to 112 hrs/yr. 1990-1992, 48 hrs/yr.
- D. Program Administration: (See Year 1).

#### III. MEDICAL SCHOOL, YEARS THREE AND FOUR

- A. <u>Core Clerkship</u>: Rounds conducted: General internal medicine; 40 hrs/yr, 1975-1984; 80 hrs/yr, 1985-1992.
- B. <u>Optional Clerkship</u>, Endocrinology and Metabolism Subspecialty rounds: 30 to 60 hrs/yr, 1975-1992; Clinic: 160 hrs/yr, 1975-1992.
- C. <u>Objective structured clinical examination</u> (OSCE) coordinator for the Division of Endocrinology/Metabolism and Hypertension: 1989-1992.

# IV. GRADUATE MEDICAL EDUCATION

A. Rounds conducted:

<u>General internal medicine</u>: 75 hrs/yr (1 month), 1975-1984; 150 hrs/yr (2 months/yr), 1985-1992.

Endocrinology and Metabolism: 40 to 120 hrs/yr, 1975-1992.

- B. Medical Grand Rounds
- C. Endocrinology and Metabolism Grand Rounds

# RESEARCH GRANT SUPPORT

# I. FUNDED RESEARCH SUPPORT: PAST AND PRESENT (direct costs)

Awarded to Richard E. Miller, M.D., Principal Investigator

# Veterans Administration Research Advisory Group (RAG)

Glutamine synthetase in rat adipose tissue and skeletal muscle. (1)

1975-1976 (1 year)

\$ 25,592

# Diabetes Association of Greater Cleveland (DAGC)

(1) Glutamine synthetase in cultured 3T3-L1 adipocytes.

1977-1978 (1 year)

\$ 11,000

(2) Sulfonylurea action in cultured 3T3 adipocytes.

1987-1988 (1 year)

\$ 20,139

(3) Glutamine synthetase in cultured 3T3 adipocytes: Differentiation-associated and hormone-mediated regulation of gene expression.

1989-1990 (1 year)

\$ 30,000

\$ 39,526 \$ 42,164 \$ 45,028

#### National Institutes of Health (NIH)

(1) Glutamine synthetase in cultured 3T3-L1 adipocytes. 1978-1981 (3 years) (#R01 AM 21145)

1978-1979	01	
1979-1980	02	
1980-1981	03	

Total: \$126,718

(2) Glutamine synthetase in cultured 3T3-L1 adipocytes. 1981-1984 (3 years) (#R01 AM 21145)

1981-1982	04		\$ 48,193
1982-1983	05		\$ 49,547
1983-1984	06		\$ 51,999
		Total:	\$149,739

Glutamine synthetase in cultured 3T3-L1 adipocytes. 1984-1988 (4 years) (3) (#R01 AM 21145) (Number changed to DK 21145 as of 1987)

1984-1985	07		\$ 53,377
1985-1986	08		\$ 56,868
1986-1987	09		\$ 56,203
1987-1988	10		\$ 62,643
		Total:	\$229,091

(4) Glutamine synthetase in cultured 3T3-L1 adipocytes. (Biomedical Research Support Grant administered by Case Western Reserve University.) BRSG #S07 RR-05410-27, 6/88 through 3/89. Amount: \$ 10,000

# Diabetes Research & Education Foundation:

(1) Transacting factors that regulate expression of the insulin gene: Expression of the insulin gene in non-islet cells. 1991-1992 (one year). \$20,000.

# Department of Veterans Affairs (VA) Merit Review Awards:

(1)	Hormonal regulation of mammalian nitrogen metal	bolism. 1976-	1979
	1976-1977 (FY 77)		\$ 20,059
	1977-1978 (FY 78)		\$ 23,621
	1978-1979 (FY 79)		\$ 32,500
	,	Total:	\$ 76,180
(2)	Amino acid metabolism in cultured 3T3-L1 adipoc	ytes. 1979-19	982
	1979-1980 (FY 80)		\$ 44,416
	1980-1981 (FY 81)		\$ 30,784
	1981-1982 (FY 82)		\$ 30,616
		Total:	\$105,816
(3)	Glycerol-3-P dehydrogenase in cultured 3T3-L1 ad	lipocytes.	1982-1986
	1982-1983 (FY 83)		\$ 34,381
	1983-1984 (FY 84)		\$ 39,393
	1984-1985 (FY 85)		\$ 34,226
	1985-1986 (FY 86)		\$ 20,745
		Total:	\$128,745
(4)	Glycerol-3-P dehydrogenase in cultured 3T3 adipo	cytes. 1987-1	989
	1987-1988 (FY 88)		\$ 30,400
	1988-1989 (FY 89)		<u>\$ 30,400</u>
		Total:	\$ 60,800
(5) 1992	Glutamine synthetase gene expression during adipo	ocyte different	iation. 1989-
1772	1989-1990 (FY 90)		\$ 70,255
	1990-1991 (FY 91)		\$ 70,255
	1991-1992 (FY 92)		\$ 70,255
	1771-1772 (1 1 72)	Total:	\$210,765
			Ψ210,703
(6)	Gene expression during adipocyte differentiation.	1992-1995	
	1992-1993 (FY93)		\$ 48,980
	1993-1994 (FY94)		\$ 56,900
	1994-1995 (FY95)		\$ 56,900
		Total:	\$160,780
Wayne State	•		
	Gene expression during adipocyte differentiation.	1992-1997.	
	1992-1995		\$ 50,000
	1995-1996		\$ 25,000
	1996-1997	_	\$ 25,000
		Total:	\$100,000
Metropolitan	Detroit Research and Education Foundation. (MDR	EF)	
_	Gene expression during adipocyte differentiation.	1996-1997.	\$25,000

#### Department of Veterans Affairs (VA) Merit Review Awards (continued):

(7) Gene expression during adipocyte differentiation. 1998-2002.

1998-1999 (FY98/99)	\$119,700
1999-2000 (FY99/00)	\$99,700
2000-2001 (FY00/01)	\$99,700
2001-2002 (FY01/02)	\$99,700
, ,	\$418,800

(8) Regulation of gene expression by glucose and insulin. (a) Source: VA Research Enhancement Award Program (REAP); Identifying number: none, Principal investigators: Richard E. Miller, M.D.; (b) Effort: 15%; (c) Funding period: 5 years beginning 4/1/2000); (d) Direct costs \$350,000 for the first year and \$250,000 for subsequent years. \$1,350,000 for the entire period. (e) Comments: This award serves as a training grant and as a mechanism for enhancement of VA-funded projects. There were 4qualifying investigators at the time of the submission, the PIs plus James D Marsh, M.D. and Anjan Kowluru, Ph.D.. (The co-PIs are consider to be equivalent by the VA.). Dr. Sowers left Wayne State University in December 1999. With the approval of VA Headquarters Dr. Miller has become the sole PI and Dr. Alan Hudson replaced Dr. Sowers as the 4<sup>th</sup> qualifying investigator.

#### II. PENDING RESEARCH SUPPORT

Richard E. Miller, M.D., Principal Investigator

none

# III. GRANT APPLICATIONS APPROVED BUT NOT FUNDED;

Richard E. Miller, M.D., Principal Investigator \*\*

(Required for standard Wayne State University format.)

\* Alternative to a funded application (See above). \*\* Richard E. Miller is the PI on all except No. 25.

#, Subsequently funded by the same or another agency (See above).

#### Submitted from Case Western Reserve University School of Medicine, 1976-1992.

- 1.# DAGC, 1976: *Title*: Glutamine synthetase in cultured 3T3 adipocytes. (a) *Source*: Diabetes Association of Greater Cleveland (DAGC); *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 30%; (c) *Funding period requested*: 1 year beginning 1/1/77; (d) *Direct costs requested*: \$25,771 for the first year. (e) *Submitted*: 10/1/76; (f) *Comments*: Resubmitted 4/1/77 and funded as of 7/1/77.
- 2.# NIH, 1977: *Title*: Glutamine synthetase in cultured 3T3 adipocytes. (a) *Source*: NIH; *Identifying number*: 1 R01 AM21145; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 30%; (c) *Funding period requested*: 3 years beginning 9/1/77; (d) *Direct costs requested*: \$86,287 for the first year and \$278,768 for the entire period. (e) *Submitted*: 3/1/77; (f) *Comments*: Resubmitted 11/1/77 and funded by NIH as of 7/1/78.

- NSF, 1977: *Title*: Glutamine synthetase in cultured 3T3 adipocytes. (a) *Source*: National Science Foundation (NSF); *Identifying number*: none assigned; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 30%; (c) *Funding period requested*: 3 years beginning 7/1/78; (d) *Direct costs requested*: \$58,043 for the first year and \$177,553 for the entire period. (e) *Submitted*: 11/22/77; (f) *Comments*: Approved for funding with a high priority. This application was alternative to NIH 1977; therefore, this NSF application was withdrawn when NIH application AM21145 was funded.
- 4.\* DAGC, 1978: *Title*: Glutamine synthetase in cultured 3T3 adipocytes. (a) *Source*: Diabetes Association of Greater Cleveland (DAGC); *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 30%; (c) *Funding period requested*: 1 year beginning 7/1/78; (d) *Direct costs requested*: \$13,764 for the year. (e) *Submitted*: 4/1/78; (f) *Comments*: This competing renewal of my funded DAGC grant was alternative to my NIH application (AM21145). This DAGC application was approved for funding but it was withdrawn when the NIH application was funded.
- 5.# NIH, 1981: *Title*: Glycerol-3-phosphate dehydrogenase in cultured 3T3-L1 adipocytes. (a) *Source*: NIH; *Identifying number*: 1 RO1 AM30569; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 10%; (c) *Funding period requested*: 3 years beginning 12/1/81; (d) *Direct costs requested*: \$26,010 for the first year and \$84,762 for the entire period. (e) *Submitted*: 3/81; (f) *Comments*: This application was approved but not funded. A revised and updated application was submitted to the VA in 1982. It was approved and funded.
- 6.\* DAGC, 1981: *Title*: Glutamine synthetase in cultured 3T3-L1 adipocytes. (a) *Source*: Diabetes Association of Greater Cleveland (DAGC); *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 30%; (c) *Funding period requested*: 1 year beginning 7/1/81; (d) *Direct costs requested*: \$16,132 for the year. (e) *Submitted*: 4/1/81 (f) *Comments*: This application was alternative to my NIH competing renewal application (R01 AM21145-04). This application was approved for funding but it was withdrawn when the NIH application was funded.
- 7. VA, 1985-1: *Title*: Glutamine synthetase in cultured Fao hepatoma cells. (a) *Source*: VA; *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 5 years beginning 10/1/85; (d) *Direct costs requested*: \$46,539 for the first year and \$211,683 for the entire period. (e) *Submitted*: 6/25/85.
- VA, 1985-2: *Title*: Glutamine synthetase in cultured hepatoma cells. (a) *Source*: VA; *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 3 years beginning 4/1/86; (d) *Direct costs requested*: \$33,728 for the first year and \$101,100 for the entire period. (e) *Submitted*: 12/26/85.

- 9. ACS, 1986: *Title*: Glutamine synthetase in cultured hepatoma cells. (a) *Source*: American Cancer Society (ACS); *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 2 years beginning 7/1/86; (d) *Direct costs requested*: \$42,438 for the first year and \$88,048 for the entire period. (e) *Submitted*: 3/20/86.
- 10.# VA, 1986: *Title*: Sulfonylurea action in cultured 3T3 Adipocytes. (a) *Source*: VA; *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 3 years beginning 10/1/86; (d) *Direct costs requested*: \$32,600 for the first year and \$97,800 for the entire period. (e) *Submitted*: 7/1/86; (f) *Comments*: Subsequently submitted to DAGC in 1986 and funded.
- 11.# NIH, 1987: *Title*: Glutamine synthetase in cultured 3T3 adipocytes. (a) *Source*: NIH; *Identifying number*: 2R01 DK21145-11; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 5 years beginning 7/1/88; (d) *Direct costs requested*: \$103,120 for the first year and \$687,854 for the entire period. (e) *Submitted*: 10/14/87; (f) *Comments*: This was a competing renewal application. This project was subsequently funded by the VA.
- 12. ACS, 1988; *Title*: Cachectin (tumor necrosis factor) action in cultured 3T3 adipocytes.

  (a) *Source*: American Cancer Society (ACS); *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 15%; (c) *Funding period requested*: 2 years beginning 1/1/89; (d) *Direct costs requested*: \$69,000 for the first year and \$140,750 for the entire period. (e) *Submitted*: 3/18/88.
- 13.# DREF, 1988: *Title*: Regulation of gene transcription by insulin. (a) *Source*: Diabetes Research and Education Foundation (DREF); *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 15%; (c) *Funding period requested*: 1 year beginning 7/1/88; (d) *Direct costs requested*: \$20,500 for the year. (e) *Submitted*: 4/1/88; (f) *Comments*: This project is a portion of one that was subsequently funded by the VA (1989-present).
- 14.# NIH, 1988: *Title*: Glutamine synthetase in cultured 3T3 adipocytes. (a) *Source*: NIH; *Identifying number*: 2R01 DK21145-11A1; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 3 years beginning 4/1/89; (d) *Direct costs requested*: \$75,000 for the first year and \$287,220 for the entire period. (e) *Submitted*: 6/9/88; (f) *Comments*: This project was subsequently funded by the VA beginning in 1989.
- 15.\* NSF, 1988: *Title*: Glutamine synthetase in cultured 3T3 adipocytes. (a) *Source*: National Science Foundation (NSF); *Identifying number*: none assigned; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 3 years beginning 1/1/89; (d) *Direct costs requested*: \$84,563 for the first year and \$263,410 for the entire period. (e) *Submitted*: 6/13/88; (f) *Comments*: This application was alternative to NIH 1988 (above).

- 16.# DAGC 1988: *Title*: Glutamine synthetase in cultured 3T3 adipocytes: Regulation of gene expression by insulin. (a) *Source*: Diabetes Association of Greater Cleveland (DAGC); *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 15%; (c) *Funding period requested*: 1 year beginning 7/1/88; (d) *Direct costs requested*: \$30,763 for the year. (e) *Submitted*: 4/1/88 (f) *Comments*: Revised application subsequently funded by DAGC in 1989.
- 17.\* AHA, 1988: *Title*: Glutamine synthetase in cultured 3T3 adipocytes. (a) *Source*: American Heart Association (AHA); *Identifying number*: 4639; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 1 year beginning 1/1/89; (d) *Direct costs requested*: \$23,000 for the year. (e) *Submitted*: 10/1/88 (f) *Comments*: This application was alternative to an application submitted to the Diabetes Association of Greater Cleveland (DAGC) entitled *Glutamine synthetase in cultured 3T3 adipocytes*: *Differentiation-associated and hormone-mediated regulation of gene expression*. The DAGC application was approved and funded, therefore, this AHA application was withdrawn.
- 18.\* NIH, 1989: *Title*: Gene expression during adipocyte differentiation. (a) *Source*: NIH; *Identifying number*: 1R01 DK42006-01; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 3 years beginning 12/1/89; (d) *Direct costs requested*: \$82,500 for the first year and \$256,924 for the entire period. (e) *Submitted*: 2/1/89; (f) *Comments*: This NIH application was alternative to a nearly identical VA application. This VA application entitled *Glutamine synthetase gene expression during adipocyte differentiation* was submitted 1/1/89; it was approved and funded beginning in 1989.
- 19.\* ACS, 1989: *Title*: Gene expression during adipocyte differentiation. (a) *Source*: American Cancer Society (ACS); *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 3 years beginning 1/1/90; (d) *Direct costs requested*: \$103,125 for the first year and \$321,738 for the entire period. (e) *Submitted*: 3/20/89; (f) *Comments*: This ACS application was alternative to a nearly identical application submitted to the VA. This VA application entitled *Glutamine synthetase gene expression during adipocyte differentiation* was approved and funded.
- 20.\* NSF, 1989: *Title*: Gene expression during adipocyte differentiation. (a) *Source*: National Science Foundation (NSF); *Identifying number*: none assigned; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 3 years beginning 1/1/90; (d) *Direct costs requested*: \$111,709 for the first year and \$348,111 for the entire period. (e) *Submitted*: 6/1/89; (f) *Comments*: This NSF application was alternative to a nearly identical application submitted to the VA. This VA application entitled *Glutamine synthetase gene expression during adipocyte differentiation* was approved and funded.

- 21. DAGC, 1991: *Title*: <u>Trans-acting factors that stimulate transcription of the human insulin gene.</u> (a) *Source*: Diabetes Association of Greater Cleveland (DAGC); *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 15%; (c) *Funding period requested*: 2 years beginning 1/1/92; (d) *Direct costs requested*: \$30,210 for the first year and \$60,210 for the entire period. (e) *Submitted*: 10/1/91; (f) *Comments*: Currently this project is supported, in part, by a National Research Service Award to Dennis J. DeLuca, Ph.D., a postdoctoral fellow in my laboratory.
- NIH, 1992: *Title*: Gene expression during adipocyte differentiation. (a) *Source*: NIH; *Identifying number*: 1R01 DK45986-01; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 4 years beginning 12/1/92; (d) *Direct costs requested*: \$138,125 for the first year and \$748,130 for the entire period. (e) *Submitted*: 2/1/92; (f) *Comments*: This NIH application was alternative to a nearly identical VA application. The VA application entitled *Gene expression during adipocyte differentiation* was submitted 12/21/91; it was approved and funded beginning 10/1/92.

# **Submitted from Wayne State University School of Medicine (1994-present)**

- 23.# VA, 1994: *Title*: Gene expression during adipocyte differentiation. (a) *Source*: VA; *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 3 years beginning 10/1/95; (d) *Direct costs requested*: \$76,100 for the first year and \$228,300 for the entire period. (e) *Submitted*: 12/21/94; (f) *Comments: Amended version submitted* 12/21/95.
- 24.# VA, 1995: Title: Gene expression during adipocyte differentiation. (a) Source: VA; Identifying number: none; Principal investigator: Richard E. Miller, M.D.; (b) Effort: 25%; (c) Funding period requested: 3 years beginning 10/1/96; (d) Direct costs requested: \$86,000 for the first year and \$258,300 for the entire period. (e) Submitted: 12/21/95. (f) Comments: This application was approved with priority score of 19.2 and a percentile score of 22. The payline was set at the 21st percentile. An amended version was submitted 12/21/96.
- 25.\*\* VA, 1996-1: VA-JDF Diabetes Research Center Application submitted in response to an RFA. Title: Mechanisms of hyperglycemia-mediated cellular dysfunction: Vascular, racial and therapeutic implications. (a) Source: VA and Juvenile Diabetes Foundation (JDF); Identifying number: none; Principal investigator: Lawrence M. Resnick, M.D. Directed costs requested: \$601,600 for the first year and \$2,599,600 for the entire period. Project 5: Principal investigator: Richard E. Miller, M.D.; (b) Effort: 25%; (c) Funding period requested: 5 years beginning second quarter, FY97; (d) Direct costs requested: \$55,000 for the first year and \$275,000 for the entire period. (e) Submitted: 8/15/96. (f) Comments: none.
- VA-1996-2: *Title*: Gene expression during adipocyte differentiation. (a) *Source*: VA; *Identifying number*: none; *Principal investigator*: Richard E. Miller, M.D.; (b) *Effort*: 25%; (c) *Funding period requested*: 3 years beginning 10/1/97; (d) *Direct costs requested*: \$98,700 for the first year and \$394,800 for the entire period. (e) *Submitted*: 12/21/96. (f) *Comments*: The priority score was 20.0. The payline was set at 19.0.

NIH-1997: *Title*: Gene expression during adipocyte differentiation. (a) *Source*: NIH; *Identifying number*: 1R01DK53202-01. *Principal investigator*: Richard E. Miller, M.D.; (b) *Total Effort*: 25%; (c) *Funding period requested*: 4 years beginning 12/1/97; (d) *Direct costs requested*: \$146,187 for the first year and \$620,776 for the entire period. (e) *Submitted*: 2/1/97. (f) *Comments*: This application overlaps with the VA grant described above (VA 1996-2). This application was not assigned a priority score.

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#### **PUBLICATIONS**

#### I. ORIGINAL ARTICLES (in refereed journals)

- 1. Vander AJ and **Miller RE.** (1964) Control of renin secretion in the anesthetized dog. Am. J. Physiol. 207, 537-546.
- 2. **Miller RE**, Vander AJ, Kowalczyk RS and Geelhoed G. (1968) Aldosterone secretion and plasma renin during renin infusion and acute salt depletion. <u>Am. J. Physiol.</u> 214, 228-231.
- 3. **Miller RE** and Stadtman ER. (1972) Glutamate synthase from *Escherichia coli* an iron sulfide flavoprotein. J. Biol. Chem. 247, 7407-7419.
- 4. Prusiner SB, **Miller RE** and Valentine RC. (1972) Cyclic AMP control of the enzymes of glutamine metabolism in *E. coli*. <u>Proc. Natl. Acad. Sci. USA 69</u>, 2922-2926.
- 5. **Miller RE**, Shelton E. and Stadtman ER. (1974) Zinc induced paracrystalline aggregation of glutamine synthetase. Arch. Biochem. Biophys. 163, 155-171.
- 6. **Miller RE.** (1974) Glutamate synthase from *Escherichia coli*-An iron-sulfur flavoprotein separation and analysis of non-identical subunits. <u>Biochim. Biophys. Acta</u> 364, 243-249.
- 7. Miller EA, Fredholm B, **Miller RE**, Steinberg D. and Mayer SE. (1975) Enzymes regulating glycogen metabolism in swine subcutaneous adipose tissue: I. Glycogen phosphorylase and phosphatase. <u>Biochemistry 14</u>, 2470-2480.
- 8. **Miller RE**, Miller EA, Fredholm B, Yellin JB, Eichner RD, Mayer SE and Steinberg D. (1975) Enzymes regulating glycogen metabolism in swine subcutaneous adipose tissue: II. Glycogen synthase. <u>Biochemistry</u> 14, 2481-2488.
- 9. **Miller RE.** (1976) Quantification of L-glutamine using E. coli glutamate synthase A sensitive fluorometric assay. <u>Anal. Biochem.</u> 75, 91-99.
- 10. **Miller RE**, Hackenberg RW and Gershman H. (1978) Regulation of glutamine synthetase in cultured 3T3-L1 cells by insulin, hydrocortisone, and dibutyryl cyclic AMP. Proc. Natl. Acad. Sci. USA 75, 1418-1422.
- 11. **Miller RE** and Carrino DA. (1980) Dibutyryl cyclic AMP decreases glutamine synthetase in cultured 3T3-L1 adipocytes. J. Biol. Chem. 255, 5490-5500.
- 12. **Miller RE** and Carrino DA. (1981) An association between glutamine synthetase activity and adipocyte differentiation in cultured 3T3-L1 cells. <u>Arch. Biochem. Biophys.</u> 209, 486-503.

- 13. **Miller RE**, Pope SR, DeWille JW and Burns DM. (1983) Insulin decreases and hydrocortisone increases the synthesis of glutamine synthetase in cultured 3T3-L1 adipocytes. J. Biol. Chem. 258, 5405-5413.
- 14. Birnbaum RS, Mahoney WC, Burns DM, O'Neil JA, **Miller RE** and Roos BA. (1984) Identification of procalcitonin in a rat medullary thyroid carcinoma cell line. <u>J. Biol. Chem.</u> 259, 2870-2874.
- 15. Bhandari B and **Miller RE.** (1985) Glycerol-3-phosphate dehydrogenase mRNA content in cultured 3T3-L1 adipocytes: Regulation by dibutyryl cAMP. <u>Biochem.</u> Biophys. Res. Commun. 131, 1193-1197.
- 16. Burns DM, Bhandari B, Short JM, Sanders PG, Wilson RH and **Miller RE.** (1986) Selection of a rat glutamine synthetase cDNA clone. <u>Biochem. Biophys. Res. Commun.</u> 134, 146-151.
- 17. **Miller RE** and Bhandari B. (1986) Hormonal regulation of amino acid uptake by cultured 3T3-L1 adipocytes. Biochemistry International 12, 775-783.
- 18. Bhandari B, Burns DM, Hoffman RC and **Miller RE.** (1986) Glutamine synthetase mRNA in cultured 3T3-L1 adipocytes: Complexity, content and hormonal regulation. Mol. Cell. Endocrinol. 47, 49-57.
- 19. **Miller RE** and Bhandari B. (1986) Glyburide action in cultured 3T3-L1 adipocytes. Biochemistry International 13, 313-319.
- 20. Bhandari B and **Miller RE.** (1987) Glutamine synthetase gene transcription in cultured 3T3-L1 adipocytes: Regulation by dexamethasone, insulin and dibutyryl cyclic AMP. Mol. Cell. Endocrinol. 51, 7-11.
- 21. Bhandari B, Wilson RH, and **Miller RE.** (1987) Insulin and dexamethasone stimulate transcription of an amplified glutamine synthetase gene in Chinese hamster ovary cells. <u>Mol. Endocrinol.</u> 1, 403-407.
- 22. Bennett AL, Paulson KE, **Miller RE**, and Darnell JE, Jr. (1987) Acquisition of antigens characteristic of adult pericentral hepatocytes by differentiating fetal hepatoblasts *in vitro*. <u>J. Cell Biol.</u> 105, 1073-1085.
- Bhandari B, Beckwith KD, and **Miller RE.** (1988) Cloning, nucleotide sequence and potential regulatory elements of the glutamine synthetase gene from 3T3-L1 adipocytes: [Poly(dT-dG):poly dC-dA) element, glucocorticoid response elements, cAMP response elements and fat-specific elements]. Proc. Natl. Acad. Sci. USA 85, 5789-5793.
- 24. Bhandari B, Saini KS, and **Miller RE.** (1991) Glycerol-3-phosphate dehydrogenase gene expression in 3T3-L1 adipocytes: regulation by insulin, dexamethasone, and dibutyryl cyclic AMP at the level of mRNA abundance, transcription, and mRNA stability. Mol. Cell. Endocrinol. 76, 71-77.

- 25. Bhandari B, Roesler W, DeLisio K, Klemm D, Ross NS, and **Miller RE.** (1991) A functional promoter flanks an intronless glutamine synthetase gene. <u>J. Biol. Chem.</u> 266, 7784-7792.
- 26. Bethel CR, Vitullo JC, **Miller RE**, and Aron DC. (1994) Molecular cloning of mouse insulin like growth factor binding protein 4 (IGFBP4) cDNA and expression of a fusion protein with IGF-binding activity. <u>Biochemistry & Molecular Biology International</u>. 34, 385-392.
- 27. Hadden TJ, Ryou C, and **Miller RE.** (1997) Elements in the distal 5'-flanking sequence and the first intron function cooperatively to regulate glutamine synthetase transcription during adipocyte differentiation. Nucleic Acids Research 25, 3930-3936.
- 28. Ren JR, Gintant GA, **Miller RE**, and Davidoff AJ. (1997) High extracellular glucose impairs cardiac E-C (excitation-contraction) coupling in a glycosylation-dependent manner. Am. J. Physiol. 273, H2876-H2883. (*These studies implicate the hexosamine biosynthetic pathway, and therefore glutamine synthetase, in the glucose-mediated impairment of E-C coupling that occurs in poorly controlled diabetes mellitus.).*
- 29. Ryou C, **Miller RE** and Hadden TJ. (1999) The glutamine synthetase intron-1 regulatory region includes a constitutive enhancer and two preadipocyte-specific silencers. Proc Natl Acad Sci USA, *to be submitted*.

#### II. REVIEW ARTICLES/BOOK CHAPTERS:

- 1. **Miller R.E.** (1973) Glutamate synthase from *Escherichia coli* An iron sulfide flavoprotein. In <u>The Enzymes of Glutamine Metabolism</u>, (Prusiner, S., Stadtman, E.R., editors), pp 183-205, Academic Press, New York.
- 2. **Miller R.E.** (1974) Glutamate synthase. In <u>Microbial Iron Metabolism</u>, (Neilands, J.B., editor), pp 283-302, Academic Press, New York.
- 3. Steinberg D, Mayer SE, Khoo JC, Miller EA, **Miller RE,** Fredholm B and Eichner RD. (1975) Hormonal regulation of lipase, phosphorylase and glycogen synthase in adipose tissue. In <u>Advances in Cyclic Nucleotide Research</u>, (Drummond, GI, Greengard R, Robinson GA, editors), Vol 5, pp 549-568, Raven Press, New York.
- 4. **Miller R.E.** and Burns DM. (1985) Regulation of glutamine synthetase in cultured 3T3-L1 adipocytes by insulin, hydrocortisone and cyclic AMP. <u>Curr. Top. Cell. Regul.</u> 26, 65-78.
- 5. **Miller RE,** Burns DM and Bhandari B. (1987) Hormonal regulation of glutamine synthetase in cultured 3T3-L1 adipocytes. In <u>Biology of the Adipocyte: Research Approaches</u>, (Hausman G. and Martin R, editors), pp 198-228, Van Norstrand Reinhold Company, Inc., New York.

6. Vitullo JC, Aron DC, **Miller RE.** (1994) Control of insulin gene expression: Implications for insulin gene therapy. <u>J. Lab. Clin. Med.</u> 124, 328-334.

# III. ABSTRACTS (1994-present)

- 32. Chatzipanteli K, Goldberg RB, **Miller RE**, Howard GA, and Roos BA. (1994) Epinephrine-like effects of the neuropeptide calctonin gene-related peptide in adipose tissue. Endocrine Society Program & Abstracts, 74th Annual Meeting, 1994; page 372. (Abstract #687).
- 33. Kolesar JF, Lambie MD, and **Miller RE.** (1994) Glutamine synthetase gene expression during adipocyte differentiation of 3T3-L1 cells. <u>American Society for Biochemistry & Molecular Biology</u> (ASBMB), 85th Annual Meeting; May 21-25, 1994 Washington, D.C. *Late-Breaking Results, Special Poster Session, May 25*, Program addendum, page 20. Abstract #LB75).
- 34. Hadden TJ, Lambie MD, and **Miller RE** (1995) *Cis*-acting elements in pBLCAT3 drive expression of glutamine synthetase fusion genes during adipocyte differentiation. <u>FASEB J. 9</u>, A1380. (Abstract #721) (ASBMB/DBC-ACS Joint Meeting, May 21-25, 1995, San Francisco, CA.)
- 35. Hadden T J, Lambie MD, Ryou C, and **Miller RE.** (1996) An element in the first intron drives expression of the glutamine synthetase gene during adipocyte differentiation. *The 10th International Congress of Endocrinology*, San Francisco, CA, June, 1996, Endocrine Society Program & Abstracts, Vol. I, page 433 (Abstract # P2-115).
- 36. Hadden TJ, Ryou C and **Miller RE.** (1997) Elements in the first intron and the far upstream region drive glutamine synthetase gene expression during adipocyte differentiation. *17th International Congress of Biochemistry and Molecular Biology*, sponsored by the <u>International Union of Biochemists and Molecular Biologists</u>. San Francisco, CA, August 24-29, 1997, <u>FASEB J 11</u> (9), A1200 (Abstract # 2003).
- 37. Ryou C, **Miller RE**, Hadden TJ (1998) Adipocyte-specific glutamine synthetase transcription is conferred by elements in the first intron. <u>American Society for Biochemistry & Molecular Biology</u> (ASBMB), 1998 Annual Meeting; Washington, D.C., May 16-20, 1998. <u>FASEB J 12</u> (8), A1392 (Abstract #477).
- 38. Ryou C, Miller RE, Hadden TJ (1999) The glutamine synthetase intron-1 regulatory region includes a constitutive enhancer and two preadipocyte-specific silencers <u>American Society for Biochemistry & Molecular Biology</u> (ASBMB), 1999 Annual Meeting; San Francisco, CA, May 16-20, 1999. <u>FASEB J</u> 13 (7) Abstract #255.
- 39. Kadura I, Hadden TJ, Miller RE. (2000) Glutamine synthetase gene transcription is controlled by CAAT/enhancer binding protein (C/EBP). *To be submitted* to the

18 <sup>th</sup>	International	Congress	of :	Biochemistry	and	Molecular	Biology,	Birmingham	ı,
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