

Constantin Polychronakos, M.D., FRCPC

DATE OF BIRTH: 18 April, 1948
PLACE OF BIRTH: Edessa, Greece
CITIZENSHIP: Canadian

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EDUCATION

M.D. degree: Aristotelian University,
1972 Thessalonica, Greece

POSTGRADUATE TRAINING

1972-73 Rotating Internship, University of Manitoba
1973-74 Pediatric Residency, University of Manitoba
1974-75 Laboratory Medicine Residency, University of Ottawa
1975-77 Pediatric Residency, Dalhousie University
1977-79 Fellow in Pediatric Endocrinology, University of Montreal
(Hôpital Ste Justine)
1980-83 Research fellow, McGill University
(Polypeptide Hormone Laboratory and Montreal Children's Hospital)

ACADEMIC APPOINTMENTS

1979-80 Research Associate, Research Center for Human Growth,
University of Montreal
1983-89 Assistant Professor, Department of Pediatrics, McGill University
1989-2000 Associate Professor, Departments of Pediatrics, McGill
2000- Professor, Department of Pediatrics
1991- Associate Member, Experimental Medicine, McGill
1997- Associate Member, Department of Human Genetics, McGill

ACADEMIC APPOINTMENTS

1979-80 Research Associate, Research Center for Human Growth,
Université de Montréal

Montreal Children's Hospital

1995 - Fellowship Committee of Research Institute
1998 - Chair – Fellowship committee of RI-MUHC

McGill University Health Center Research Inst.:

2001 – 2006 Vice-chair, MUHC-RI Research Council
1998 - Co-leader – MUHC-RI Endocrine Axis
2001 - Member of the Management committee
2002 - Phenotyping Committee, International T1D Genetics Consortium (NIH/JDRF)

2002 - **International Type 1 Diabetes Genetics Consortium** Phenotyping Committee.

Royal College of Physicians of Canada

1996 - 2000 Member of the Endocrinology Nucleus Committee .

Committee for the accreditation and infrastructure financing of graduate studies program

1997 – 2002 Ministry of Education, Hellenic Republic (Greece)

HOSPITAL APPOINTMENTS

1983- Physician, Endocrinology, Montreal Children's Hospital
1998- Director, Endocrinology, Montreal Children's Hospital
1997- Director, Endocrine Genetics Laboratory, Montreal Children's Hospital
Research Institute

COLLABORATIONS

- Rob Sladek, McGill and Philippe Froguel, Imperial College London, Genetics of type 2 diabetes.
- Hakon Hakonarson, Children's Hospital of Philadelphia, Genetics of type 1 diabetes
- Gerald Nepom and Ivana Durinovic-Bello, U Washington, Seattle, a humanized mouse model for immune tolerance to insulin.

SPECIALIST CERTIFICATIONS

1977 Fellow of The Royal College of Physicians of Canada (Pediatrics)
1978 Pediatrics (Québec)
1979 Endocrinology (Québec)

SPECIAL HONORS, AWARDS, RECOGNITION

1966-1972

Award: IKY scholarship – National Scholarships

Amount: 12,000 drachmas per year awarded to the 10 top students in each class

Institution: National Scholarships Foundation (Greece)

1981 – 1983

Award: Research fellowship

Institution: Medical Research Council of Canada

1983 – 1985

Award: Junior Research Scientist

Institution: Montreal Children’s Hospital Research Institute

2005

Award: Award of Excellence in Research from Aldo Group

Institution: Montreal Children’s Hospital

2008-2013

Sessenwein Award: Academic Excellence

Institution: Montreal Children’s Hospital Foundation

Amount: \$39,000. Yearly

PATENTS

1. DNA Assay for the Prediction of Autoimmune Diabetes, U.S. Patent No. 6,534,272 B2, July 23, 2001; Co-inventors: Dr. Constantin Polychronakos, Dr. Petros Vafiadis, Rosemarie Grabs, and Dr. Houria Ounissi-Benkhalha
2. Direct Determination of DNA Sequence Melting Temperatures by Automated, Temperature Dependent, Electrochemical Impedance Measurements, 2000
Co-Inventors: Drs. M.F. Lawrence, Isabelle Lawrence, C. Marquette
3. Genetic Predictors of Risk for Type 2 Diabetes Mellitus. Patent Application being filed.
Lead Inventor: C. Polychronakos. Co-inventors: Robert Sladek and Philippe Froguel.
4. Two novel loci for the prediction of type 1 diabetes. Lead Inventor: Constantin Polychronakos. Co-inventor: Huiqi Qu.

E. TEACHING

PAST RESEARCH TRAINEES

GRADUATE STUDENTS

	<u>Period</u>	<u>Source of funding</u>
Yongqin Xu Ph.D. Program, Experimental Medicine PhD obtained March 1998 Parental imprinting of the <i>IGF2R</i> gene	1991-98	Montreal Children's Hospital- Research Institute & MRC grant
Nick Giannoukakis Ph.D. Program, Anatomy PhD obtained May 1997 Genetic and epigenetic control of <i>IGF2</i> transcription	1992-97	FCAR
Petros Vafiadis Ph.D. Program Experimental Medicine PhD 1998 (Dean's list), Oelbaum award from JDRF) Functional evaluation of the <i>IDDM2</i> locus	1995-98	MRC doctoral scholarship
Jean-Pierre Cloarec Ph.D. Program, École Centrale de Lyon Mésures d'impédance électrique pour la détection des séquences spécifiques d'ADN. Joint supervision during 18 months work in my laboratory PhD obtained December 1997	1997	French Government Bursary
Jennifer McCann Ph.D. Program Experimental Medicine Genetic control of transcription of the human <i>IGF2R</i> gene	1998-2003	Liver Foundation Scholarship
Suzana Anjos Ph.D. program Department of Human Genetics The human cytotoxic T-lymphocyte antigen-4: functional significance of a signal peptide polymorphism associated with autoimmune endocrinopathies	2000-02	CIHR / Thyroid Foundation

PAST RESEARCH TRAINEES**GRADUATE STUDENTS**

	<u>Period</u>	<u>Source of funding</u>
Michael Palumbo Ph.D. Program Department of Experimental Medicine Insulin expressing cells in the thymus	2000-02	Canadian Diabetes Association
Mary Demian M.Sc. Program Department of Human Genetics Parent-of-Origin bias in IGF2R-LOH in breast cancer	2001-02	Canadian Breast Cancer Research Initiative

CURRENT RESEARCH TRAINEES**STUDENTS**

	<u>Period</u>	<u>Source of funding</u>
Dina Levi M.Sc., Department of Human Genetics Proinsulin-producing medullary thymic epithelial clones.	2004-	
Yang Lu M.Sc. Human Genetics Effects of common sequence variants on translational efficiency of polymorphic mRNA transcripts	2005-	
Hana Zouk Graduate Student Ph D – Human Genetics Project title: Mechanisms of novel susceptibility loci for type 1 diabetes	2006	JDRF
Xiaoyu Du Ph.D. Experimental Medicine The role of the <i>Plagl1</i> gene in β-cell development and function	2002-	

POST-DOCTORAL FELLOWS

Name	Period	Project	Source of funding
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Colm Costigan	1983-84	IGF-II receptors in growth hormone deficiency	The MCH Research Institute
Asterios Kukuvtis	1993-95	Molecular genetics of diabetes and hypoglycemia	Alan Ross Academic Fellowship (McGill U)
Robert Barnes	1996-98	Physical mapping of the <i>IDDM12</i> locus	Canadian Diabetes Association
Suzanne Demczuk	1997-99	Transcript mapping and epigenetic modifications in the DiGeorge syndrome critical region	National Research Council (recipient of the prestigious H.L. Holmes award)
Aziz Alami Chentoufi	1999-2002	Thymic insulin expression in diabetes autoimmunity	Canadian Diabetes Association
Hui Qi Qu MD. Ph.D.	2003-	Genomics of type 1 diabetes	Juvenile Diabetes Research Foundation
Mimi Kim, M.D.	2004-2005	Regulatory T-cells in type 1 diabetes	JDRF grant
Miranda Nakhla	2004-2006	Immunogenetics of Type 1 Genetics	Eli Lilly Canada Inc. – Canadian Pediatric Endocrinology Fellowship
Ghislain Rocheleau	2005-	Analysis of genotyping and expression microarray data for Type 2 diabetes.	
Brandy Wicklow	2006-2008	Functional Evaluation of diabetes-associated Nonsynonymous polymorphism of the <i>ALCAM</i> gene	Eli Lilly Canada Inc. – Canadian Pediatric Endocrinology Fellowship
Julien Saint-Jean Ph.D.	2007-	Effects of common polymorphisms on translational efficiency.	Genome Canada (GRiD project)
Nadine Taleb, M.D.	2007-	1) Genetic factors of an insulin resistance syndrome in a Lebanese Family 2) Novel gene necessary for the development of the endocrine pancreas	JDRF grant
Hugues Beauchemin	2007-	A mouse model for human diabetes-associated polymorphisms	JDRF grant

F. OTHER CONTRIBUTIONS

1) JOURNALS

EDITORIAL

Associate Editor: *Journal of Medical Genetics* (IF=5.1).

Editorial board: *Hormones, Archives de Pédiatrie, Clinical and Investigative Medicine*

Regular external reviews for *Nature Genetics, Diabetes, Diabetes Care, J Clin Endocrinol Metab* and many others.

One review for *Science* in 2006 and two for *Nature* in 2007.

F. OTHER CONTRIBUTIONS

2) GRANT REVIEWS

Sept 96 – March 1997	Medical Research Council of Canada. Endocrinology panel.
2000 – 2003	CIHR: Committee member, Endocrinology panel.
1996 – 2001	Canadian Diabetes Association. Personnel Awards Committee.
2003 -2006	Canadian Diabetes Association. Operating Grants committee A.
2003 -	NIH-NIDDK study session on RFA: Bed-to-bedside research in type 1 diabetes.
1992 - 1998	FRSQ-FCAR studentships. Subcommittee chair.
1993	FRSQ chercheurs-cliniciens.
1989 – 1993	FRSQ Centers and Institutes Committee
	FRSQ Site visits committee. Several hospitals.
1991, 1996-7	FRSQ-Ministry of Industry special funds site-visit committee for CHUL. 1991 and follow-up visits in 1996 and 1997.

Ad-hoc reviews for the Wellcome Trust and many other funding agencies.

3) **COMMITTEES**

PEER REVIEW COMMITTEES 2002-2007

2003 – 2006	Canadian Diabetes Association: Operating Grants A
2003 -	NIH: Bench-to-Bedside RFA for type 1 diabetes
1997 – 2002	YPETH-EPEAEK, Hellenic Republic (Greek equivalent of CFI-CIHR) Canadian Multiple Sclerosis Foundation. Committee for Foundation Grants.
1996 – 1998	MRC-CIHR Endocrinology Committee
2000 - 2003	MRC-CIHR Endocrinology Committee
2001	Canadian Diabetes Association: Personnel Awards
2003 -	Canadian Diabetes Association. Operating Grants A . Canadian Multiple Sclerosis Foundation. Member, grant panel.

4) **PROFESSIONAL AND /OR LEARNED SOCIETIES**

1994 – 1997	Member of the panel for the approval of free growth hormone for the province of Québec. (abolished with new drug insurance scheme).
1996	External reviewer for the graduate program in Endocrinology-Physiology, Laval University.

F. OTHER CONTRIBUTIONS

4)**PROFESSIONAL AND /OR LEARNED SOCIETIES**

1997 – 2002 Committee for the accreditation and infrastructure financing of graduate studies programs in Health Sciences, Ministry of Education, Hellenic Republic (Greece)

Member of ad-hoc committee to establish a Quebec network of Child-Mother Research Network.

The Lawson Wilkins Pediatric Endocrine Society.

1994 – 1997 Member of the Drugs and Therapeutics Committee

2001 Local Organizing Committee for the joint meeting of Pediatric Endocrine societies (2,500 participants).

CONSULTING ACTIVITIES

2004 - 2005 Québec Ministry of Health and Social Services. Consultative committee on newborn screening

1999 – 2002 Customs and Revenue Canada: Expert consultant for the evaluation of applications for tax credits for scientific research and development 1999-2002.

1998 Coroner's expert: Coroner's inquest into the death of a diabetic child at home 1998.

2002 - Pharmaceutical industry: Consultant on new diabetes-prevention project development, H3-Pharma

Expert Witness: Canadian Medical Protective Association. Three cases of professional liability.

G. RESEARCH

1. MOST SIGNIFICANT CONTRIBUTIONS

In the past 5 years my efforts have centered on elucidating the molecular genetics of diabetes. I have contributed to both the discovery of new loci and the elucidation of the mechanism of known ones.

A large-scale search for type 1 diabetes (T1D) susceptibility loci. Several years of attempts using the candidate-gene approach with relatively modest results (*Diabetologia* 49:958-961, 2006, *J Med Genet* 2006 43:129-32, *J Med Genet.* 2005 42:266-70, *Nature Genetics* 37:111-2, 2005, *Diabetes* 2007 56:270-5, *Diabetes* 2007 56:1174-6) came to an end with the availability of high-density genotyping arrays that permitted a genome-wide association (GWA) study on my collection of 1,300 families with type 1 diabetes, funded by the Juvenile Diabetes Foundation and the Children's Hospital of Philadelphia. We identified two novel loci in Stage 1 (*Nature* 2007 Aug 2; 448(7153):591-4) **In Nature's top ten list for August 2007 downloads.**

- **A genome-wide association study for type 2 diabetes:** I have contributed my expertise in genome-wide studies to the Diabetes Gene Discovery Group, a collaboration between McGill, Université de Montréal and Centre National de Recherche Scientifique in Lille, France aimed at elucidating the genetics of type 2 diabetes by a GWA study in a French cohort of 3,500 cases and 3,500 controls, funded by Genome Canada and Génome Québec. Four loci were discovered in Stage 1 (*Nature* 2007 Feb 445(7130):881-5), one of the first major proofs-of-principle for the GWA approach. I am corresponding author in this paper which had an accompanying *News and Views* write-up and was widely covered in the world media (e.g. *New York Times*, *Boston Globe*, *Daily Telegraph*, *Newsweek* website, CBC and CTV national evening news, front page in most major newspapers in Canada).
- **The insulin gene in type 1 diabetes (T1D).** Following up on a previous observation that a polymorphism upstream of the insulin gene confers diabetes risk by modulating expression levels in the thymus which, we hypothesized, modulates insulin-specific T-cell tolerance (*Nature Genetics* 15: 289-292, 1997, front page of the *Montreal Gazette*) I proceeded to test predictions of this model with functional studies in humans (*Diabetes*, 2005, S18-24, *Proc Natl Acad Sci*, 2006, 103:11683-8 and *Diabetes* 2007 56:709-13) and a mouse KO with thymus-specific deficiency (*Diabetes* 51:1383-1390, 2002). We also pinpointed the rare cells in the thymus that make insulin (*Diabetes*, 53:354-9, 2004) and show that insulin transcription in these cells depends on immune rather than metabolic stimuli (*Diabetes* 55:2595-601, 2006).
- **T1D association with CTLA4.** My laboratory contributed to the dissection of the molecular and biochemical basis on which a haplotype at the *CTLA-4* locus predisposes to T1D and other autoimmune endocrinopathies (*J Biol Chem* 277:46478-86, 2002, *J Clin Endocrinol Metab* 89:6257-65, 2004, *Genes and Immunity* 6:305-11, 2005, *J Autoimmun* 27:105-9, 2006).
- **Genomic imprinting:** My laboratory published the first report of imprinting in a human gene (*Nature Genetics* 1993, with accompanying editorial in *Nature*, 363:94). Although I am no longer active in the field, I was invited to write the Imprinting in Human Disease article in the *Encyclopedia of Genetics, Genomics, Proteomics and Bioinformatics* (Wiley, 2006).

PAST FUNDING

<i>Medical Research Council of Canada</i>	The physiology of the receptors for insulin and insulin-like growth factors	\$36,000/ year	1984-1986
		\$35,000/ year	1986-1988
		\$21,372 for 9 months	1988-1989
<i>Montreal Children's Hospital Research Institute</i>	Interactions between mannose 6-phosphate and insulin-like growth factor II on their common receptor	\$38,000	1989-1990
<i>Cancer Research Society Inc</i>	Insulin-like growth factor receptors in human malignancy (in collaboration with M.N. Pollack, Lady Davis Institute)	\$35,000 /year	01/07/88 – 30/6/90
		\$35,000 /year	1990-1991
<i>Medical Research Council of Canada</i>	Interactions between mannose-6-phosphate and insulin-like factor II on their common receptor	\$45,000 /year	1990-1992
<i>Canadian Diabetes Association</i>	Insulin-like growth factor II in diabetes susceptibility	\$53,000	01/01/93 – 31/12/93
** <i>The Cancer Research Society Inc.</i>	Molecular genetics of Wilms' tumor	\$25,000 /year	01/07/93 – 30/06/95
** <i>The Hospital for Sick Children Foundation</i>	Candidate genes for Wilms' tumor	\$18,370 /year	01/10/93 – 30/09/95

** The above two grants constitute complementary funding for the same project.

<i>Canadian Diabetes Association</i>	IGF2 as a susceptibility gene for insulin-dependent diabetes mellitus	\$51,120	01/01/94 – 31/12/94
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Past Funding (continued)

<i>The National Research Council of Canada</i>	Transcript mapping and epigenetic changes in the DiGeorge syndrome critical region on chr. 22q11	\$100,000/year	01/09/97 – 31/08/99
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(The HL Holmes award to my post-doctoral fellow Suzanne Demczuk, covering her salary and expenses.)

<i>The Cancer Research</i>	The IGF2R gene in Wilms tumor	\$45,000 /year	01/07/1995 –
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<i>Society Inc</i>			30/06/1999
<i>The Cancer Research Society Inc.</i>	Allelic control of p73 transcription	\$49,000 /year	01/07/1999 – 30/06/2001
<i>Medical Research Council of Canada</i>	Parental imprinting of the genes for insulin-like growth factor II and its receptor	\$56,800 /year	01/04/1995 - 31/03/1998
		\$76,800 /year	01/04/1998 - 31/03/2002
<i>Juvenile Diabetes Foundation International</i>	Functional evaluation of the <i>IDDM2</i> locus	\$135,000 U.S. per year	01/09/1996 – 31/08/2003
<i>CIHR</i>	Direct detection of specific DNA sequences by electrochemical impedance measurements". Co-investigator with M. Lawrence (50% of budget to be spent in my lab).	\$45,300 /year	01/09/1997 – 30/09/2003
<i>Canadian Breast Cancer Research Institute</i>	Insulin-like growth factors and breast cancer: A Canadian research network" Co-investigator Dr. C.L. Deal	\$80,631 /year	07/2000-06/2003
<i>Past Funding (continued)</i>			
<i>Réseau de recherche sur le développement, la santé et le bien-être de l'enfant</i>	Établissement d'une banque de donnée dynamique pour l'institution d'un réseau de traitement et de recherche en diabétologie pédiatrique" Co-investigators: Dr. L. Legault - McGill University, Dr. K. Khoury - Université de Sherbrooke, Dr. M. Lelièvre - Université Laval, and Dr. M. Buithieu - Université de Montréal	\$19,973 /year	01/04/2001 - 31/03/2002
		\$16,100 /year	01/04/2002 - 31/03/2003
<i>Canadian Diabetes Association</i>	Insulin expressing cells in the thymus	\$57,878 /year	01/07/2000 - 30/06/2002
		\$67,030 /year	01/07/2002 -

30/06/2004

<i>Juvenile Diabetes Research Foundation International</i>	A function-driven, large scale approach to the search for type 1 diabetes susceptibility genes	\$405,753 US / year	01/11/2001 - 31/10/2006
<i>Genome Canada II</i>	Functional genomics of type 1 diabetes. (PI Jayne Danska)	\$5,700,000/ 3 years Amount corresponding to my laboratory: \$975,000/ 3 years	01/09/2003 - 31/08/2006
<i>Juvenile Diabetes Research Foundation International</i>	Functional evaluation of IDDM loci	\$135,852.46 U.S./ year	01/08/2003 - 31/07/2006
<i>Genome Canada (Genomics and Proteomics in Human Health RFA)</i>	Genetics of type 2 diabetes (PI Barry I. Posner)	\$16M 174,000/y to my lab +I am one of three individuals to manage the \$3M genotyping budget.	Fall 2004- 2007

CURRENT FUNDING

<i>Juvenile Diabetes Research Foundation</i>	Functional Evaluation of IDDM Loci	\$159,912.70 yearly	11/2006 to 10/2009
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Time Commitment: 10%

<i>Juvenile Diabetes Research Foundation</i>	A novel gene necessary for the development of the Endocrine Pancreas	\$271,368. X 2 years	09/2007 to 08/2009
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Time Commitment: 5%

<i>National Institute of Health (NIH) (USA) via George Washington University</i>	TrialNet Major Affiliate	\$151,508.yearly	07-2007 to 06/2008
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Time Commitment: 10%
JDRF

Novel Genetic Susceptibility Loci for Type 1 Diabetes	494,835	June 1/2008 to May 31/2011
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Time commitment 15%
CIHR

Team in Immune Regulation and Biomarker Development for Pediatric and Adult Autoimmune Diseases	\$2,018,445.00 (\$50,000 in my lab)	July 1/2007 to June 30, 2012
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Time Commitment: 2%

<i>Genome Canada / Genome Quebec</i>	Gene Regulators in Disease (GRID) (PI T.J. Hudson)	10.79M 432,100 / 4 yrs in my lab	01/2006 – 06/2009
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Time Commitment: 10%

Ministère du Développement économique, de l'innovation et l'Exportation (MDEIE). Québec-China	Discovery of Novel Therapeutics for the Prevention of Type 1 Diabetes.	\$150,000 CDN over 3 years	02/2008 to 01/2011
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High-throughput drug screening for insulin expression in thymus cells.

Time Commitment : 5%
JDRF

Mechanisms involved in novel genetic associations with Type 1 diabetes	158,434 yearly	April 1, 2007 to March 31, 2010
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Time Commitment: 10%
CIHR

Novel Genetic Susceptibility Loci For Type 1 diabetes	\$187,062 US yearly	Sept 1, 2008 to Aug 31, 2011 Under Review
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Juvenile Diabetes Research Foundation – Biomarkers Autoimmunity

Integrating genetics with markers of immune response	\$250,000 US yearly	Under Review
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ORIGINAL ARTICLES

Asterisk indicates trainee/employee under my supervision.

1. **Polychronakos C**, Letarte J, Collu R, Ducharme JR. Carbohydrate intolerance in children and adolescents with Turner's syndrome. *J Pediatr* 96:1009-1014, 1980.

2. Savoie S, **Polychronakos C**, Forest MG, Haour F, Collu R, Ducharme JR. Perinatal activity of the hypothalamic-pituitary-gonadal axis in the lamb. III. LH, testosterone and prolactin secretory pattern in newborn lambs. *Hormone Research* 1981, 15:167.
3. Hamel R, Forest MG, Haour F, **Polychronakos C**, Charpenet G, Gibb W, Collu R, Ducharme JR. Perinatal activity of the hypothalamic-pituitary-gonadal axis in the lamb. IV Testicular responsiveness to hCG from 1 through 28 days of life. *Hormone Research* 1981, 15:179.
4. **Polychronakos C**, Tsoukas G, Ducharme JR, Letarte J, Collu R. Gigantism and hyperprolactinemia in polyostotic fibrous dysplasia. *J Endocrinol Invest* 1982, 5:323.
5. **Polychronakos C**, Ruggere MD, Benjamin A, Posner BI, and Guyda H. The role of cell age in the difference in insulin binding between adult and cord erythrocytes. *J Clin Endocrinol Metab* 1982, 55:290.
6. **Polychronakos C**, Guyda HJ, Posner BI. Receptors for the insulin-like growth factors on human erythrocytes. *J Clin Endocrinol Metab* 1983, 57: 436.
7. Burnstein R, **Polychronakos C**, Toews CJ, McDougall JD, Guyda HJ, Posner BI. Acute reversal of the enhanced insulin action in trained athletes: Association with insulin receptor changes. *Diabetes* 1985, 34:756-760.
8. **Polychronakos C**, Guyda HJ, and Posner BI. Increase in type 2 insulin-like growth factor receptors in the rat kidney during compensatory growth. *Biochemical & Biophysical Research Communications* 1985, 132:418.
9. **Polychronakos C**, Guyda HJ, Patel B, and Posner BI. Increase in the number of insulin-like growth factor receptors during propyl-thiuracil-induced hyperplasia in the rat thyroid. *Endocrinology* 1986, 119:1204-1209.
10. Schiffrin A, **Polychronakos C**, *Abu-Srair H. Glycogen storage disease Type I. [Letter reporting original observations] *N. Engl. J. Med.* 1986, 315(8): 520-521.
11. Desjardins JG, Khan AH, Montupet P, Collin PP, Leboeuf G, **Polychronakos C**, Simard P, Boisvert J, and Dube LJ. Management of thyroid nodules in children: a 20-year experience. *J of Pediatric Surgery.* 1987, 22(8): 736-739.
12. Barenton B, Guyda HJ, Goodyer C, **Polychronakos C**, Posner BI. Specificity of insulin-like growth factor binding to type II IGF receptors in rabbit mammary gland and hypophysectomized rat liver. *Biochemical and Biophysical Research Communications.* 1987, 149(2): 555-561.
13. *Costigan CD, **Polychronakos C**, Guyda HJ, and Posner BI. Increase in specific

- binding of insulin-like growth factor (IGF) II to type I (IGF) receptors on erythrocytes of hypopituitary children receiving GH therapy. *Clin. Invest. Med.* 1988, 11(1): 47-51.
14. Pollak M, **Polychronakos C**, Youssefi S, Richard M. Characterizations of IGF-I receptors in the MCF-7 breast cancer cell line. *Biochem. Biophys. Res. Commun.* 1988, 154:326-331.
 15. Belmonte MM, Schiffrin A, Dufresne J, Suissa S, Goldman H, **Polychronakos C**. Impact of home blood glucose monitoring on control of diabetes as measured by HbA1c. A 3 year survey of a juvenile IDDM clinic. *Diabetes Care* 1988, 11: 484-488.
 16. **Polychronakos C**, Piscina R. Endocytosis of receptor-bound IGF-II is enhanced by mannose-6-phosphate in IM9 cells. *Endocrinology* 1988, 123:2146.
 17. **Polychronakos C**, Guyda H, *Abu-Srair H. Transient growth deceleration in normal short children: a potential source of bias in growth studies. *European Journal of Pediatrics* 1988, 147:582-3.
 18. **Polychronakos C**, Guyda HJ, Posner BI. Mannose-6-phosphate increases the affinity of its cation- independent receptor for insulin-like growth factor II by displacing inhibitory endogenous ligands. *Biochem. Biophys. Res. Commun.* 1988, 157:632.
 19. **Polychronakos C**, Piscina R, Fantus IG. Enhancement of cytosolic tyrosine kinase activity by Propylthiouracil-induced hyperplasia in the rat thyroid. *Endocrinology* 1989, 124:505.
 20. Pollak M, **Polychronakos C**, Guyda H. Somatostatin analogue SMS 201-995 reduces serum IGF-I levels in patients with neoplasms potentially dependent on IGF-I. *Anticancer Research* 1989, 9:889-892.
 21. Pollak MN, **Polychronakos C**, Richard M. Insulin-like growth factor - I: a potent mitogen for human osteogenic sarcoma. *Journal of the National Cancer Institute* 1990, 82(4):301-305.
 22. **Polychronakos C**, Guyda HJ, Janthly U, Posner BI. Effects of mannose 6-phosphate on receptor-mediated endocytosis of IGF-II. *Endocrinology* 127:(4) 1990, 1861-1866.
 23. Pollak M, **Polychronakos C**, *Blauer S, Guyda H, Margolese R. Effect of tamoxifen on serum insulin-like growth factor-I levels of Stage I breast cancer patients. *J. Natl. Cancer Inst.* 1990, 82:(21) 1693-1697.
 24. **Polychronakos C**, Janthly U, Lehoux JC, Koutsilieris M. Mitogenic effects of insulin and insulin-like growth factors on PA-III rat prostate adenocarcinoma cells: characterization of the receptors involved. *The Prostate* 1991, 19:313-321.

25. Koutsilieris M, **Polychronakos C**. Proteinolytic activity against IGF-binding proteins involved in the paracrine interactions between prostate adenocarcinoma cells and osteoblasts. *Anticancer Research* 1992, 12:905-910.
26. *Giannoukakis N, Deal C, Paquette J, Goodyer CG, **Polychronakos C**. Parental genomic imprinting of the human *IGF2* gene. *Nature Genetics* 1993, 4:98-101.
27. Koutsilieris M, Frenette G, Lazure C, Lehoux JC, Govindan MV, **Polychronakos C**. Urokinase-type plasminogen activator: a paracrine factor regulating the bioavailability of IGFs in PA-III cell-induced osteoblastic metastases. *Anticancer Research* 1993, 13:481-486.
28. *Xu Y, Goodyer CG, Deal C, **Polychronakos C**. Functional polymorphism in the parental imprinting of the human *IGF2R* gene. *Biochemical and Biophysical Research Communications* 1993, 197:747-754.
29. **Polychronakos C**, Ligier S. Resuspension of intermediate-acting insulin as a source of error in insulin dosing. *Diabetes Care* 1994, 17:1234-1235.
30. **Polychronakos C**, Giannoukakis N, Kukuvtis A and E Colle. Parental imprinting effect at the *INS-IGF2* diabetes susceptibility locus. *Diabetologia*, 1995, 38(6):715-719.
31. *Kukuvtis K, Matte C and **C Polychronakos**. Central precocious puberty following cure of a feminizing granulosa ovarian tumor. *Hormone Research*, 1995, 44:268-270.
32. **Polychronakos C**, Giannoukakis N and C Deal. Imprinting of *IGF2*, insulin-dependent diabetes, immune function and apoptosis: A Hypothesis. *Developmental Genetics* 1995, 17:253-62.
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ARTISTIC WORK: Computer-generated image for the cover of *Nature Genetics*, September 2005 issue. <http://www.nature.com/ng/journal/v37/n9/covers/index.html>

BOOK CHAPTERS, REVIEWS, COMMENTARY, COMMITTEE REPORTS, etc.

1. **C. Polychronakos**. The mannose-6-phosphate/IGF-II receptor. In: *Molecular and Cellular Biology of Insulin-like Growth Factors and Their Receptors*. D. LeRoith, M. Raizada, (eds), Plenum Press, New York, pp. 369-380, 1989.
2. **C. Polychronakos**. Parental imprinting of the genes for IGF-II and its receptor. In: *Advances in Experimental Medicine and Biology*. 189-203, 1994.
3. Furlanetto RW et al.. Guidelines for the use of growth hormone in children with short stature; A report by the Drug and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society. *J Pediatrics* 127:897--67, 1995.
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7. **Polychronakos C**. Programmed cell death in the pathogenesis of autoimmune diabetes. *Programmed Cell Death, Volume II, Role in Disease, Pathogenesis and Prevention* Ed. by M.P. Mattson, S. Estus and V.M. Rangnekar. 55-79, 2001 Elsevier Science.
8. **Polychronakos C**. The Human Genome Project: What is in it for the Endocrinologist? International symposium on a Current Review of Pediatric Endocrinology, jointly sponsored by Serono Symposia USA and The Lawson Wilkins Pediatric Endocrine Society, July 10-13, 2001, Montreal, Canada, Proceedings: pp. 165-173, 2001.

9. **Polychronakos C**, *Palumbo M. Stem cells in the treatment of diabetes. [In Greek] *PENDI*, 18:9-12, 2002
10. **Polychronakos C**. New insights into the genetics of neonatal diabetes. Invited review, *Reviews in Endocrine and Metabolic Disorders*, 4:19-22, 2003.
11. **Polychronakos C**. Impact of the human genome project on Pediatric Endocrinology. Invited review in Hormone Research. *Hormone Research*, 59(2):55-56, 2003.
12. *Kukuvitis A and **C Polychronakos**. Parental Genomic imprinting in endocrinopathies. Invited review, *European Journal of Endocrinology*.
13. **Polychronakos C**. *Punthakee Z. Molecular concepts and techniques in Endocrinology. Invited book chapter in *Pediatric Endocrinology Mechanisms, Manifestations, and Management*, O. Peskovitz, ed. Lippincott, Williams and Wilkins first edition 2004.
14. *Anjos S, **Polychronakos C**. Mechanisms of genetic susceptibility to type 1 diabetes: beyond HLA. Invited review in *Molecular Genetics and Metabolism Mar*; 81(3):187-95, 2004.
15. **Polychronakos C**. Animal models of spontaneous autoimmune diabetes: notes on their relevance to the human disease. Invited editorial in *Current Diabetes Reports*, 4(2):151-4, 2004.
16. **Polychronakos C**. Early-onset diabetes: tip or iceberg? Invited editorial in *Pediatric Diabetes*. 5: 171-173, 2004
17. Kim MS, **Polychronakos C**. Immunogenetics of Type 1 Diabetes. *Hormone Research*. 2005 Oct 24;64(4):180-188.
18. Nakhla M, **Polychronakos C**. Monogenic and other unusual causes of diabetes mellitus. *Pediatric Clinics of North America*. 2005 Dec;52(6):1637-50.
19. Punthakee Z, **Polychronakos C**. Diabetes Mellitus. In *Essential Pediatric Endocrinology and Inborn Errors of Metabolism*. K. Sarafoglou, editor, McGraw-Hill. In press.
20. **Polychronakos C**. Genetic testing in clinical endocrinology. *Hormones (Athens)*. 2003 2:201-10.
21. **Polychronakos C**. Genetic variation and health; towards individualized medicine. *Pediatr Endocrinol Rev*. 2004 Aug;1 Suppl 3:540-4.
22. **Polychronakos, C**. New applications of microarray data analysis: integrating genetics with 'Omics'. *Pharmacogenomics*. 2008 Jan;9(1):15-7.

23. **Polychronakos, C.** Common and Rare Alleles as Causes of Complex Phenotypes. *Current Atherosclerosis Reports*. May 2008. In press.
24. **C. Polychronakos.** What Is New in the Genetics of Type 2 Diabetes. *Med Sci (Paris)*. 2008 Mar;24(3):241-242.1
25. Ounissi-Benkalha H, **Polychronakos C.** The molecular genetics of type 1 diabetes. New genes and emerging mechanisms. *Trends in Molecular Medicine* 2008 (accepted for publication).
26. Chentoufi AA, Binder Nr, Berka N, Abunadi T, Polychronakos C. Advances in Type 1 Diabetes Associated Tolerance Mechanisms. *Scand J Immunol*. 2008 May 9 2008 may 9. Epub ahead of print.

PRESENTATIONS

Outside McGill

1	<i>Recepteurs de l'insuline et des IGF</i>	St Justine Hospital, weekly research seminars	1982
2	<i>Insulin receptor modulation</i>	Grand Rounds, CHEO, Ottawa	1983
3,4 ,5	<i>Les IGF</i>	Two one-hour lectures, part of the <i>Hormones peptidiques</i> course at Université de Montréal	1987, 1989, 1991
6	<i>Les IGF et leurs récepteurs</i>	Department of Pediatrics, Centre Hospitalier Université Laval, Québec	1987
7	<i>Les IGF dans le diabète et le cancer</i>	St. François-d'Assise Hospital Research Center	1989
9	<i>Les IGF dans le diabète et le cancer</i>	Hôpital Notre-Dame Research Center Seminar series	1990
10	<i>Disease self-management:</i>	European Society of Ambulatory Pediatrics. Annual	1990

- diabetes as a model* meeting, Athens, Greece
- 11 *Effector mechanisms of non-HLA genetic susceptibility to β -cell autoimmunity.* Gordon Research Conference, Ventura Ca, January 1997
- 12 *Off-label uses of growth hormone* Health Canada, Bureau of Drug Research Ottawa March 1997
- 13 *The genetics of type 1 diabetes: beyond HLA* Humatrope^R symposium, Banff Alberta. Sponsored by Eli Lilly February 1998
- 14 *The IDDM2 locus: functional evaluation and parent-of-origin effects* Research Seminar, Children's Hospital of Philadelphia, Dept. of Pediatrics, U of Pennsylvania January 1998
- 15 *Mitochondrial Diabetes* Symposium: *The Molecular Basis of Diabetes Mellitus*, University of Athens, Greece April 1998
Other invited speakers included S. Taylor, NIH, and T. Merriman, Oxford
- 16 *A cure for juvenile diabetes. How far are we?* The first Congress of the Hellenic Diabetic Federation. Athens, Greece April 1998
- 17 *Parental imprinting: relevance to human disease* Faculty of Medicine, University of Ioannina. Ioannina Greece. Sponsored by Bayer April 1998
- 18 *Functional Evaluation of the IDDM2 locus* Research Seminar, Department of Medicine, University of Ioannina, Greece. Sponsored by the Hellenic Diabetes Federation April 1998
- 19 *Genotype-dependent parent-of-origin effects* The Spring Meeting of the British Genetical Society, Warwick, England April 1998
- 20 *Genetic risk factors for insulin-dependent diabetes* NIH workshop on vaccines and autoimmune diabetes. US National Institutes of Health, Bethesda MD May 1998

21	<i>Genetic control of epigenetic modifications in imprinted genes</i>	NIEH-sponsored symposium on Imprinting and environmental disease susceptibility. <i>Duke University</i>	October 1998
22	<i>Functional evaluation of IDDM2 locus</i>	Schneider Children's Medical Center, Tel Aviv	March 1999
23	<i>Parental imprinting</i>	Schneider Children's Medical Center, Tel Aviv	March 1999
24	<i>Molecular endocrinology of cancer</i>	Annual Meeting of the Hellenic Endocrine Society	March 1999
25	<i>The IGF system in cancer</i>	Annual Meeting of the Hellenic Endocrine Society, Athens	March 1999
26	<i>The genetics of autoimmune diabetes: beyond HLA</i>	Dept. of Genetics, University of Manitoba	Feb. 2000
24	<i>The insulin VNTR in diabetes</i>	City-wide Endocrine Rounds, U of Toronto	Feb. 2000
27	<i>Viral infections in the etiology of autoimmune diabetes</i>	“Infection and chronic disease: strange bedfellows” Conference sponsored by the Canadian Public Health Alliance and Health Canada	May 2000
28	<i>Genetics of type 1 diabetes</i>	American University of Beirut, Dept. of Peds	Feb 2001
29	<i>Immunogenetics of diabetes</i>	University of Pittsburgh	March 2001
30	<i>The Human Genome Project: what is in it for the endocrinologist?</i>	Serono Symposium: Review of Pediatric Endocrinology	July 2001
31	<i>Immunogenetics of Diabetes</i>	Joint International Pediatric Endocrine Societies meeting, Montreal	July 2001
32	<i>Transient Neonatal Diabetes: a model of endocrine disease due to defects in parental imprinting</i>	The Annual Congress of the Italian Society for Pediatric Endocrinology, Trieste, Italy	October 2001

33	<i>Diabète type 1 génétique et génomique</i>	Réunion Scientifique de l'Hôpital Ste-Justine, Montréal, Québec	January 2002
34	<i>Parental genomic imprinting: Implications for health, disease and organism cloning</i>	Université de Montréal.	April 2003
35	<i>Genetic testing in Endocrine Research and Practice</i>	12th Balkan Congress of Endocrinology, Thessaloniki Greece.	May 2003
36	<i>Newly discovered forms of Mendelian diabetes in the young: insights and puzzles</i>	The Lawson Wilkins Pediatric Endocrine Society annual meeting, Seattle.	May 2003
37	<i>Insulin: expression in the thymus and T-cell self-tolerance</i>	Symposium talk at annual meeting of American Diabetes Association, New Orleans.	June 2003
38	<i>Genome Science and the Individual: lessons from type 1 diabetes</i>	The Harry Medovy lectureship. Department of Pediatrics. University of Manitoba, Winnipeg	May 2004
39	<i>Genomics for the Endocrinologist</i>	2 nd International Conference on Adult consequences of Pediatric Disease. Ahtens, Greece.	May 2004
40	<i>Insulin: thymic hormone or thymic antigen?</i>	6th Symposium of the International Group on Insulin Secretion. St-Jean Cap Ferrat, France	March 2005
41	<i>Genetics of type 1 diabetes</i>	Biomedical Conference U of Ulm, Germany	Sept 2005
42	<i>Dissecting the genetic determinants of complex traits: lessons from diabetes</i>	Canadian Federation of Biological Societies U of Guelph,	June 2005
43	<i>Strand asymmetry in transcribed human sequences: evidence for functional effects</i>	<i>Human Genome Variation 2006</i> meeting, Hong Kong, China	Sept 2006
44	<i>La génétique du diabète type 1</i>	Université de Montréal (Centre de Recherche Guy Bernier) March 2006	March 2006
45	<i>Genetics of diabetes in the HapMap era</i>	Immunogenetics seminar, U Pittsburgh	Mar 2007
46	<i>Genetics of diabetes in the HapMap era</i>	Canadian Pediatric Endocrine Group Annual Meeting, London, Ontario	April 2007

47	<i>A genome-wide association study for type 1 diabetes</i>	Canadian Genetic Diseases Network Annual Meeting, St. Sauveur, Quebec	April 2007
48	<i>Genetics of diabetes in the HapMap era</i>	<i>Institute of Pharmacology, Chinese Academy of Medical Sciences, Beijing</i>	Apr 2007
49	<i>Insulin in the thymus: hormone or antigen?</i>	<i>Institute of Pharmacology, Chinese Academy of Medical Sciences, Beijing</i>	Apr 2007
50	<i>A Genome-wide View of Human Variation and Its use in Gaining Functional Insights: Diabetes as Paradigm</i>	Metabolomics Approach to Human Diseases. Genomics and Peptidomics. 13 th Samsung International Symposium on Molecular Medicine, Seoul, Korea,	Oct 2007
51	<i>Genes and Type 2 diabetes. How far is genetic prediction in children?</i>	33 rd Annual Meeting International Society for Pediatric and Adolescent Diabetes, annual meeting, Berlin, Germany.	Sept 2007
52	<i>The genetics of diabetes in the HapMap era</i>	Symposium talk at the Australian Diabetes Society (ADS) & the New Zealand Society for the Study of Diabetes Joint Scientific Meeting, Christchurch New Zealand.	Sept 2007
53	<i>Type 1 diabetes: from prediction to prevention</i>	Plenary talk at the Australian Diabetes Society (ADS) & the New Zealand Society for the Study of Diabetes Joint Scientific Meeting, Christchurch New Zealand.	Sept 2007
54	<i>What is new in the genetics of diabetes</i>	Westmead Children's Hospital, Sydney, Australia	Sept 2007
55	<i>Destiny, Diversity and DNA: The Diabetic Homunculus as a Post-Genome Paradigm.</i>	Pediatric Medical Grand Rounds, McGill University Health Centre.	Oct 2007
56	<i>Common and rare forms of diabetes: what can genetics teach us about the beta cell?</i>	Canadian Beta Cell Group annual meeting, Toronto	Nov 2007
57	<i>Recent progress in the genetics of diabetes</i>	City-wide Endocrine Rounds, Toronto	Nov 2007
58	<i>Recent breakthroughs in the genetics of diabetes</i>	Keynote address to the Annual Meeting, Diabetology Society of Northern Greece.	Nov 2007
59	<i>The genetics of type 1 diabetes: recent, past and the future</i>	Erasmus University, Rotterdam	Feb 11/2008
60	<i>The genetics of type 1 diabetes: recent past and the future</i>	University of Turku, Finland	Feb 2008
61	<i>Studies on the Genetics of T1D</i>	Longwood Medical Area Research Seminars in Diabetes and Metabolism, Joslin Diabetes Center, Boston	April 2008
62		Genotyping and Large-Scale Association Studies Conference – Cambridge Healthtech Institute, San Francisco, California	June 9-10/08
63	<i>Thymus and diabetes</i>	Eurothymaide International Symposium, Royal Academy of Medicine of Belgium in Brussels	March 19-21, 2009
64	?	36 th Pahlennic Congress of Endocrinology and Metabolism, Alexandroupoli (City of Thrace)	April 8-11/2009

Genetics and the development of Type 1 diabetes

Recent Advances in Beta-Cell Biology: Scientific and Clinical Implications

Oct 16-17/2009

Symposium of the International Diabetes Federation
20th World Diabetes Congress Toronto

ABSTRACTS

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Asterisk indicates trainee/employee under my supervision