#### PEDIATRIC ENDOCRINOLOGY FELLOWSHIP

#### <u>Overview</u>

The Division of Pediatric Endocrinology and Metabolism offers a Fellowship training program to residents successfully completing the two-year residency training in Pediatric Endocrinology. This additional training aims to provide structured individually tailored academic training; most trainees will use this time to complete a graduate degree in Epidemiology, Education, or Public Health or Ethics. Alternatively, this additional time is generally used to complete basic science or clinical research projects, under staff supervision. Generally, research activities will be linked to a formal academic program such as a PhD or Masters.

Trainees will spend more than 90% of their time involved in these activities; one clinic per week may be arranged to provide clinical contact. This limited contact will not dilute the clinical exposure of any of the more junior house staff. The fellows will not be involved in any on-call activities. All clinical activities will be arranged according to the trainee's interest, as these are not considered a mandatory component of the Fellowship.

Dependent on fellow interest, opportunity exists to participate in a number of didactic educational activities including tutoring first year medical students in endocrine physiology tutorials or teaching of junior house staff. The trainee is invited to participate in all Department of Pediatrics academic activities including those within the Division. See below for a schedule of the usual activities. Prior to the onset of the fellowship, the fellow and program director will together predetermine an individualized set of training goals. Goals of the fellowship and trainee performance will be reviewed quarterly. The trainee will have reciprocal opportunities to assess their supervisors and the training program.

#### General information

The duration of this training will be a minimum of 12 months.

Trainees will only be eligible for this training if they are deemed eligible if they have or will soon receive Royal College or American Board certification in Endocrinology; this assures that they would be eligible to receive a training card from the *College des Medecins du Quebec*.

The Pediatric Endocrinology Program Director and the Training Committee will supervise the Fellowship program. They will be responsible for implementation, recruitment and supervision of

the Fellowship, and will ensure that the Endocrine or Pediatric residents or medical students will continue to experience adequate clinical exposure, supervision and educational content.

#### Graduate school programs

The Fellow will need to apply well in advance to the start of the Fellowship to ensure that they will be accepted. These details can be discussed in depth with the Program Director. The most frequent request by the potential Fellows is to apply and complete a Masters in Epidemiology at McGill. This can usually be completed in about 24-30 months; in the first year, all of the course material can be completed. The next year allows the completion of a thesis project, with an expectation to present and publish the findings. If the Fellow was an endocrine resident at McGill, the course work is often completed in the second year and the thesis is undertaken in the Fellowship.

Trainees may also apply to other graduate degrees at the university including Education. Alternatively, they may consider completing degrees by distance education in three main disciplines; Epidemiology, Medical Education or Public Health offered by such institutions as the London School of Hygiene and Tropical Medicine, Johns Hopkins or Aberdeen.

### Optional clinical activities

Generally the trainees are interested in attending a general endocrinology clinic on Monday or Tuesday afternoons (1300-1700). The staff consists of 2 physicians on Mondays (1 on Tuesday) and usually one endocrine resident, with perhaps a medical student and 1 or 2 residents. There are over 25 patients seen by the house staff on Mondays, less on Tuesdays. If the Fellow wishes to attend this clinic, then patients, who need to be seen more urgently and have been triaged to attend an 'office' visit by only the staff, could be seen by the Fellow. The staff, who would have evaluated the patient by themselves, can attend the clinic to review the case. If this staff is already booked in the clinic, then they will arrange their time to attend the clinic earlier than usual to review the Fellow's case/s. We have experience with this and have found that the house staff attending the usually scheduled clinic is given the usual amount of attention, while allowing the Fellow to see patients.

If the program director deems that the clinic has been assigned very few house staff, the Fellow can attend and work in parallel with the usual house staff.

## Weekly schedule

Monday afternoon- General endocrine clinic 1300- 1700 (if interested)\*

Tuesday morning Diabetes clinic 0800- 1200 (if interested)\*

Wednesday afternoon 1330-1630 Diabetes/Endocrinology rounds, journal club or research

presentation in the academic year

Thursday morning (twice per month) Lipid clinic 0900-1200\*

Thursday afternoon 1330-1530 Endocrine resident teaching (if interested)

Friday afternoon- house staff teaching (Fellow may be the facilitator, if interested)

\* the Fellow will select one of these clinics per week

## Division of Endocrinology and Metabolism Statistics:

## STATISTICS IN PEDIATRIC ENDOCRINOLOGY

	2001- 2001	2001- 2002	2002- 2003	2003- 2004	2004- 2005	2005- 2006	2006-2007
ENDOCRINOLOGY			·			·	
NEW PATIENTS/CONSULTS FOLLOW-UP ADMISSIONS	542 1775		756 2884	727 2870	550 1413	237 1632	468 1340
ENDO OFFICE (2005-2006-) NEW FOLLOW-UP						137 92	84 79
EMERGENCY: NEW WARDS: NEW					10 186	13 122	10 124
FOLLOW-UPS					1312	799	1013
LIPID CLINICS NEW PATIENTS/CONSULTS FOLLOW-UPS					64 133	109 27	131 28
BONE CLINICS NEW PATIENTS/CONSULTS FOLLOW-UPS					5 18	14 23	14 34
BONE OFFICE OFFICE CONSULTS FOLLOW-UPS						1 3	5 9

	STATIST	ICS IN PEL		NDOCKINC	JLOGY		
	2001-	2001-	2002-	2003-	2004-	2005-	0000 0007
	2001	2002	2003	2004	2005	2006	2006-2007
WEIGHT MANAGEMENT NEW PATIENTS/CONSULTS	43	44	55	46	60	51	42
FOLLOW-UPS	28	58	114	149	137	107	80
WEIGHT MANAGEMENT OFFICE CONSULTS						35	22
FOLLOW-UPS						35 80	23 48
CIU: NEW PATIENTS/CONSULTS FOLLOW-UPS	157 431		183 494	125 485	50 393	45 426	34 381
TOTALS	2976	102	4486	4402	4331	3953	3947
METABOLISM NEW PATIENTS/CONSULTS	64	69	69	119	98	96	65
FOLLOW-UPS	1691	1724	1833	1684	1810	1807	1978
ADMISSIONS	66	80	77	56	87	73	71
SUBTOTALS	1821	1873	1979	1859	1995	1976	2114
GRAND TOTALS	4797		6465	6261	6326	5929	6,061

STATISTICS IN PEDIATRIC ENDOCRINOLOGY

### Additional pedagogic activities

All trainees are encouraged to attend at least one conference per year; this is often the Endocrine Society, American Diabetes Association or the Canadian Diabetes meeting/ Endocrinology meeting. Our division has adequate funding to assist with registration costs and some travel costs for endocrine residents and Fellows.

The Fellows are also able to be granted additional funds from the MCH research institute, if their abstracts have been accepted for presentation.

#### Research Activities:

#### Cynthia Gates Goodyer Ph.D.

For over twenty-five years, my laboratory has been studying various aspects of early growth and development in the human. Our target community has been those fetuses and infants who do not grow well despite the absence of chronic disease. Most recently, we have focused on molecular aspects of the hGH receptor and their clinical implications. We are:

1) mapping the 5' flanking region of the hGHR gene and analysing the promoter regulatory mechanisms;

2) searching human adipocyte and chondrocyte cDNA libraries for novel tissue-specific hGHR mRNA variants;

3) characterising the hGHR subtypes present in fetal vs postnatal liver as well as the ontogeny of hGHR-activated signal transduction pathways in human hepatocytes;

4) examining the promoter regions of the hGHR gene for polymorphisms/mutations in individuals from both Canada and Japan exhibiting idiopathic short stature, in collaboration with Dr. Tsutomu Ogata, Center for Child Health and Development, Tokyo, Japan; Dr. Ogata is responsible for the sequencing/SNP analyses and my laboratory will examine the functional significance of the SNPs more frequently expressed in the low growth cohorts compared to adult controls;

5) studying the mechanisms regulating hGHR expression in human adipocytes and chondrocytes and the role of the hGH/hGHR axis in these cells during development and with patho-physiological states (obesity, short stature).

#### Aimee K. Ryan, Ph.D.

My lab is interested in understanding how organs are formed and patterned during embryonic development. The pituitary gland originates from an invagination of oral ectoderm (Rathke's pouch) and the evagination of the infundibulum from the ventral diencephalon (site of the future hypothalamus) within the first 5 weeks of embryogenesis. Subsequently differentiated cell types appear in response to signalling molecules released from the surrounding tissues and intracellular

interactions. In addition, we are studying the function of the homeodomain transcription factor, Pitx2. Mutations in the Pitx2 homeodomain and transactivation domain lead to Rieger's syndrome, an autosomal dominant disorder which often has associated growth defects.

## C. Rodd M.D.

1. STOPP Steroid-induced Osteoporosis in the Pediatric Populations – Canadian Incidence Study (STOPP-CIS). I am a Co-PI in a multicentre CIHR funded, longitudinal study looking at the impact of glucocorticoids on bone health in children with leukemia, rheumatologic disorders and nephrotic syndrome. Outcomes of interest are bone density, fractures and restitution of bone mass. Dr. Leanne Ward, CHEO is the PI for this project.

2. Prevalence of vertebral fractures in children with systemic disease. Little is know about the natural history and cause of vertebral fractures in children. This prompted Dr. Scuccimarri, Rheumatology and myself to carry out a prevalence study in a high risk population, children with chronic inflammatory disorders, receiving high dose glucocoriticoids and /or methotrexate. This project is funded by the MCH-RI.

3. A randomized controlled double-blind trial in children with Crohn's disease and osteopenia of Zometa (zoledronate) as a 'rescue' agent. The Crohn's and Colitis Foundation of Canada has funded this project, which is under the direction of Dr. Forget and myself. We are evaluating the safety and efficacy of this bisphosphonate in children with severe osteopenia and Crohn's disease.

4. Dose finding study of vitamin D3 in breastfed infants in Montreal. Dr Hope Weiler and myself have submitted proposals for a large trial of different doses of vitamin D supplements for breastfed Montreal infants. A pilot project carried out in conjunction with a Masters student in Clinical Nutrition is underway to allow us to optimally proceed with the larger trail. Our concern is that infants are not routinely receiving adequate vitamin D and our proposal plans to evaluate 4 different doses of vitamin D3 supplementation and evaluate markers of bone health.

### R. Barnes, M.D.

Pediatric type 1 diabetes believed to be increasing in incidence. The province of Quebec does not

have a surveillance mechanism to monitor incidence and prevalence of any type of pediatric

diabetes. Our multicentre group is performing a feasibility study on the establishment of a Quebec-

wide registry of pediatric diabetes. Supported by a grant from Diabète Québec.

The reliability of the records of self-monitoring of blood glucose for people with diabetes has been questioned. In the setting of a diabetic children's camp, older campers were provided the responsibility of recording their blood sugars in their individual logsheets. Each camper's glucometer memory was downloaded at the end of the camping session, providing an opportunity to perform a safety audit of the camp's policy of relaxing supervision of individual blood sugar records. This audit will assess the frequency of discrepancies between the recorded and actual blood sugar result, and may provide guidance on adjusting the policy in the camp setting. This is a

supervised project to fulfill the requirements for a M.Sc. degree in Epidemiology & Biostatistics (student: Dr. Preetha Krishnamoorthy).

## P. Krishnamoorthy, M.D.

- In cystic fibrosis, defective water and chloride transport leads to viscous secretions causing scarring and destruction of multiple organs. This may result in exocrine and endocrine pancreatic insufficiency as well as in cystic fibrosis-related diabetes (CFRD). In conjunction with members of the Endocrinology and Respirology Divisions at both the MCH and Hopital Sainte-Justine, we have been studying glucose metabolism in pediatric cystic fibrosis patients from both centers. We have also been interested in determining whether markers of oxidative stress, such as glutathione, HNE-P adducts and DHN-MA, are correlated to and may be predictive of glucose metabolism in CF patients.
- 2. Another project that Dr. Legault and I are working on with the Respirology Division of the MCH is the use of Repaglinide in pediatric CFRD.
- 3. Obesity has been associated with an increased risk of asthma, atopy, and obstructive sleep apnea. Asthma and, more recently, obstructive sleep apnea (OSA), are recognized as chronic inflammatory disorders. A subset of obese subjects has the metabolic syndrome, a chronic inflammatory condition. In collaboration with members of our Respirology Division, we are in the process of investigating the risk of developing asthma in obese children with and without the metabolic syndrome. We will also compare the prevalence of atopy and OSA between these two groups using screening questionnaires.

## (ii) Endocrine Genetics Laboratory

### C. Polychronakos M.D.

In the past 5 years my efforts have centered on elucidating the molecular genetics of diabetes.

<u>A large-scale search for type 1 diabetes (T1D) susceptibility loci.</u> 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. We identified two novel loci in Stage 1 (*Nature* 2007 Aug 2; 448(7153):591-4) In *Nature*'s top ten list for downloads in August 2007.

A genome-wide association study for type 2 diabetes: Facing the alarming increase of type 2 diabetes among children, I joined 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, funded by Genome Canada and Génome Québec. Four loci were discovered in Stage 1 (*Nature* 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.

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).

### (iii) Diabetes Research

### L. Legault, M.D.

 We can now be able to screen high risk families for the development of type 1 diabetes. This multicenter international study looks at the effect of nicotinamide as a potential treatment for delaying or perhaps preventing the occurrence of type 1 diabetes in high risk individuals.
 The genetic susceptibility to type 1 diabetes is explored using linkage studies in 1st degree relatives of known type 1 diabetic patients to look at markers of high risk for type I susceptibility in this multicenter pan-Canadian study.

Registre québécois du diabète-PI R.Barnes, feasability study on the possibility of establishing a registry for diabetes in the province of Quebec for type 1 diabetes - Co-PI

Impact of resistance training on insulin resistance and metabolic markers in 8-12 year old obese children, in collaboration with Concordia University's Kinesiology department (Dr Joanna Komorowski)

Mentors in Mention-Teenage obesity intervention study) (CIHR)

Metabolic profiles of mothers and daughters 15 years after a gestational pregnancy, co-PI, CIHR-funds managed at RVH-co-PIs; Sara Meltzer and Grace Egeland (2004-2006)

Repaglanide use in CFRD-Novo Nordisk-sponsor- (2005-)

Principal Investigator, Characterization of early signs of atherogenesis in a teenage obese population. (sponsored by Pfizer, Canada). (2004-)

### H. Bui, M.D.

Diabetic ketoacidosis (DKA) at presentation of type 1 diabetes is a preventable complication that affects 15 to 67% of children. I am interested in studying the factors that predispose to DKA at diagnosis, the prevalence of medical encounters prior to diagnosis, and the possible means to prevent this potentially fatal complication.

Poor metabolic control in type 1 diabetes, as evidenced by a high hemoglobin A1c (HbA1c), increases the risk of long-term microvascular complications. I am interested in studying potential adjuvant therapies with an aim to decrease HbA1c in poorly controlled adolescents, including insulin sensitizers and novel reminder techniques.

#### Research

The Fellow will select at least one project and usually work with one of these supervisors. We are lucky enough to have 2 other endocrine basic scientists (Drs Goodyer and Ryan), at the MCH-RI, who have also supervised Fellows. The Fellow might additionally contemplate a joint research project between the pediatric and adult endocrine sites at McGill.

At the end of the fellowship, the trainee will present to the Program Director with an updated copy of their CV, which will highlight their achievements over this time period.

### Administrative responsibilities

Fellows will be responsible for the coordination of their clinical activities. They may decide to attend the regularly scheduled clinics or wish to arrange to see more urgent referrals that would be seen exclusively by a staff member earlier than 6m waiting period it would otherwise take Additionally, they will be involved in the teaching schedule for house staff and may help to select topics and then supervise the Friday afternoon sessions.

### **Evaluation**

The Program Director will meet with the Fellow at least quarterly; the progress with the course work, research project and possible clinical exposure will be explored. Evaluation forms will be reviewed at this time. If issues arise prior to these meetings, the Fellow may approach the Program Directors, the Training Committee members or any member of the staff to discuss issues. At the end of the Fellowship, a final written evaluation will be completed and placed in the Fellow's file. The Fellow

The Fellow will have the opportunity to provide feedback to the Training Committee and Fellowship Program Director anonymously. The Training Committee will assess the quality of the curriculum of the Fellowship, at least on an annual basis.

The Fellow will received a signed certificate outlining the duration of their training at McGill University.

If the trainee is involved in clinical outpatient care, the specific objectives and evaluation form for this type of exposure will also be completed on a quarterly basis

## **General competencies**

### **Medical Expert-**

1. To apply relevant clinical or basic science information to research development

2. To demonstrate medical expertise in situations other than direct patient care

3. To provide advice and education to other health care providers with respect to patient care, and legal opinions.

## Communicator

1. To document research ideas as a protocol, manuscript or lecture

2. To develop good communication skills with research subjects, supervisor, trainees and/or team members.

## Collaborator

1. To contribute effectively to other interdisciplinary team activities, particularly those most often associated with endocrinology

2. To acquire the skill of identifying potential collaborators locally, nationally or internationally and the skill of proposing a mutually beneficial academic collaboration

## Manager

1. To appropriately allocate time to research education, and other professional commitments

2. To utilize resources effectively when designing and implementing a research project

3> To manage a research operating budget

## Health advocate

- 1. To identify determinants of health that affect a patient
- 2. To use research as a tool to advocate for health changes and to disseminate health information

## Scholar

- 1. To formulate a clinical/research question and research protocol.
- 2. To complete a project based on this question
- 3. To contribute to the development of new knowledge
- 4. To critically appraise medical literature

5. To undertake and complete advanced course work (in epidemiology, public or community health, or educational programs).

## Professional

1. To exhibit appropriate personal and interpersonal professional behaviour

2. To demonstrate responsibility and self-discipline

3. To recognize one's own limitations

4.To demonstrate a willingness to accept peer and supervisor reviews of professional competence.

5. To demonstrate an understanding of the principles of medical ethics as they relate to clinical research

including autonomy, beneficence/ nonmalificennce, justice and confidentiality

If the trainee is involved in clinical outpatient care, the specific objectives and evaluation form for this type of exposure will also be completed on a quarterly basis



#### 罗 McGill

#### POSTGRADUATE MEDICAL TRAINING PROGRAMS ROTATION IN-TRAINING ASSESSMENT

Program:	Period of T FROM:	raining	TO:		
Resident: I II II III IV V VI VI VII VIII	Research		Site:		
	RINOLOGY - RE				
	Could Not	Unsatis-	Borderline	Satisfactory	Sup
MEDICAL EXPERT To apply clinical or basic science information to research development	Judge	factory			C
To demonstrate medical expertise in situations other than direct patient care To respond and advise requests from other hfealth care providers					0
with respect to patient care, education of provider and legal opinions COMMUNICATOR	_	_	_	_	
To document research ideas as a protocol, manuscript or lecture To develop good comunication skills with research subjects, supervisor, trainees or team members					C
COLLABORATOR To contribute effectively to other interdisciplinary team activities, particularly those most often associated with endocrinology					[
To acquire the skill of identifying potential collaborators locally, nationally or internationally and the skill of proposing a mutually beneficial academic collaboration					0
MANAGER To allocate time appropriately to address research priorities with educational priorities and other professional commitments					[
To utilize resources effectively when designing and implementing research project					[
To manage a research operating budget HEALTH ADVOCATE To identify determinants of health that affect a patient					[
To use research as a tool to advocate for health changes/ dissemination of health information SCHOLAR					[
To formulate a clinical/research question and research protocol To complete a project based on this question To contribute to the development of new knowledge					[
To critically appraise medical literature To undertake and comoplete advanced course work (in epidemiology, public or community health, or educational programs).					
PROFESSIONAL To exihit appropriate personal and interpersonal professional behaviours					[
To demonstrate responsibility and self-discipline To recognize one's own limitations To demnstrate a willingness to accept peer and supervisor reviews of professional competence. (is this more an understanding and					
acceptance of constructive criticism?) To demontrate an understanding of the principles of medical ethics as they relate to clinical research including autonomy, beneficence/normalificence, confidentiality					[
GLOBAL EVALUATION OF COMPETENCE AND PROGRESS:	Incomplete				
COMMENTS (Including Strengths, Weaknesses and Need for Special A					
Signature of Supervisor Date	Signature of Trainee		DISAGREE		Date

## APPLICATION FORM FOR FELLOWSHIPS

#### Name of institution: McGill University

#### Location: Montreal

# Type of Fellowship: Clinical research or basic research- in conjunction with graduate school degree

- □ Program Information:
- Number of fellowship positions requested 2
- Academic affiliation- McGill University
- □ Name of hospitals involved in training- Montreal Children's Hospital
  - o % time spent by the fellow in each institution 100%

#### □ Background:

The Division of Pediatric Endocrinology and Metabolism offers a Fellowship training program to residents successfully completing the two-year residency training in Pediatric Endocrinology. This additional training aims to provide structured individually tailored academic training; most trainees will use this time to complete a graduate degree in Epidemiology, Education, or Public Health or Ethics. Alternatively, this additional time is generally used to complete basic science or clinical research projects, under staff supervision. Generally, research activities will be linked to a formal academic program such as a PhD or Masters.

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- Research activity- see above
- Publications from all physicians:-

CONSTANTIN POLYCHRONAKOS, M.D.

- 1. Ducharme FM, Chabot G, **Polychronakos C**, Glorieux F and B Mazer. Safety profile of frequent short courses of oral glucocorticoids in acute pediatric asthma: impact on bone metabolism, bone density, and adrenal function. *Pediatrics* 2003, Feb;11(2):376-83.
- 2. \*Punthakee Z, Legault L and **C Polychronakos.** Prednisolone in the treatment of adrenal insufficiency: A reevaluation of relative potency. *J Pediatr.* 2003, Sep;143(3):402-5.
- 3. Macanovic A, Marquette C, Polychronakos C and MF Lawrence. Impedance-based detection of

DNA sequences using a silicon transducer with PNA as the probelayer. Nucleic Acids Research

2004, Jan 22;32(2):E20.

- 4. \*Chentoufi A, \*Palumbo M and **C Polychronakos**. Proinsulin expression by Hassall's corpuscles in the mouse thymus. Diabetes 2004, 53(2):354-9.
- \*Kukuvitis A, Georgiou I, Syrrou M, Andronikou S, Dickerman A, \*Islam A, \*McCann J and C Polychronakos. Lack of association of birth size with polymorphisms of two imprinted genes, IGF2R and GRB10. J Ped Endocrinol Metab 2004, 17:1215-1220.
- \*McCann JA, \*Xu YQ, \*Frechette R, Guazzarotti R and Polychronakos C. The insulin-like growth factor-II receptor gene is associated with type 1 diabetes: evidence of a maternal effect. J Clin Endocrinol Metab. 2004, 89(11):5700-6.
- \*Anjos S, \*Tessier MC and C Polychronakos. Association of the CTLA4 gene with type 1 diabetes: independent effects of two SNPs on the same haplotype block. J Clin Endocrinol Metab 2004, 89:5700-6.
- \*Mitchell J, \*Punthakee Z, Lo B, Bernard B, Chong K, Newman C, Cartier L, Desilets V, Cutz E, Hansen IL, Riley P and **C Polychronakos**. Neonatal diabetes, with hypoplastic pancreas, intestinal atresia and gallbladder hypoplasia: A search for the etiology of a new autosomal recessive syndrome. Diabetologia 2004, Dec;47(12):2160-7
- 9. \*Qu H, \*Tessier M-C, Hudson TJ and **Polychronakos C**. Confirmation of the association of the R620W polymorphism in the protein tyrosine phosphatase PTPN22 with type 1 Diabetes in a family-based study. Journal of Medical Genetics. 2005, 42(3) 266-270.

- 10.\*Qu H, Bharaj B, Liu XQ, Curtis JA, Newhook LA, Paterson AD, Hudson TJ and **C Polychronakos.** Assessing the validity of the association between the SUMO4 M55V variant and risk of type 1 diabetes. Nature Genetics. 2005, 37:111-112.
- 11.\*Anjos S, \*Shao W, \*Marchand L and **C Polychronakos**. Allelic effects on gene regulation at the autoimmunity-predisposing CTLA4 locus: a re-evaluation of the 3' +6230G>A polymorphism. Genes and Immunity 2005, 6(4):305-11.
- 12. Tessier MC, Qu HQ, Frechette R, Bacot F, Grabs R, Taback SP, Lawson ML, Kirsch SE, Hudson TJ and **Polychronakos C**. Type 1 diabetes and the OAS gene cluster: association with splicing polymorphism or haplotype? J Med Genet. 43:129-32 2006
- 13. Durinovic-Belló I, \*Jelinek E, Schlosser M, Eiermann T, Boehm BO, Karges W, \*Marchand L and **Polychronakos C**. Class III alleles at the insulin VNTR polymorphism are associated with regulatory T-lymphocyte responses to proinsulin epitopes in HLA-DR4, DQ8 individuals. Diabetes 2005 54:S18-S24.
- 14. Qu H, Tessier M C Tessier, Frechette R, Bacot F, **Polychronakos C**. Lack of association of type 1 diabetes with the IL4R gene. Diabetologia 49:958-961, 2006.
- 15. Legault L, **Polychronakos C**. Annual incidence of type 1 diabetes in Quebec between 1989-2000 in children. Clin Invest Med. 29:10-3, 2006
- 16.\*Qu H, \*Guo F, Majewski J and **Polychronakos C**. Strand bias of complementary singlenucleotide polymorphisms in transcribed human sequences: evidence for functional effects of synonymous substitutions. BMC Genomics. 2006 Aug 17;7:213.
- 17.\*Palumbo M, \*Levi D, \*Chentoufi AA and **C Polychronakos.** Isolation and Characterization of Proinsulin-producing medullary thymic epithelial cell clones. Diabetes 2006, 55(9):2595-601
- 18. Durinovic-Belló, Rosinger S, Olson JA, Congia M, Ahmad RC, Rickert M, Hamp J, Kalbacher H, Drijfhout JW, Mellins ED, Al Dahouk S, Roep BO, Nepom GT, Kamradt T, Maeurer MJ, KargesW, Boehm BO, Nhan C\*, **Polychronakos C**, McDevitt HO and Sønderstrup G. DRB1\*0401-restricted human T-cell clone, specific for the major proinsulin 73-90 epitope expresses a regulatory T helper 2 phenotype. Proc Natl Acad Sci USA. Aug 2006 103(31):11683-8,.
- 19. Marchand L, **Polychronakos C**. Evaluation of Polymorphic Splicing in the Mechanism of the Association of the Insulin Gene with Type 1 Diabetes. Diabetes 2007 Mar;56(3):709-13.
- 20. Qu H., Yang L., Montpetit A., **Polychronakos C**. Genetic control of alternative splicing in the TAP2 gene: Possible implication in the genetics of type 1 diabetes. Diabetes 2007 56:270-275,2007.
- 21. Qu HQ, Marchand L, Frechette R, Bacot F, Lu Y, **Polychronakos C.** No association of type 1 diabetes with a functional polymorphism of the LRAP gene. Molecular Immunology. 44:2145-8, 2007.

- 22. Qu HQ and **Polychronakos C**. Toward further mapping of the association between the IL2RA locus and type 1 diabetes. Diabetes 2007 Apr;56(4):1174-6.
- 23. Robert Sladek, Ghislain Rocheleau, Johan Rung, Christian Dina, Lishuang Shen, David Serre, Philippe Boutin, Daniel Vincent, Alexandre Belisle, Samy Hadjadj, Beverley Balkau, Barbara Heude, Guillaume Charpentier, Thomas J. Hudson, Alexandre Montpetit, Mark Prentki, Barry I. Posner, David J. Balding, DavidMeyre, Constantin Polychronakos, Philippe Froguel. A genome-wide association study identifies novel susceptibility loci for type 2 diabetes mellitus. Nature 2007 Feb 22;445(7130):881-5. I am the corresponding author in this paper.
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#### Mission-

To train pediatric endocrinology residents to become academicians, which usually entails combined research training and graduate degrees in either Epidemiology, Public Health or Education.

#### Outline how intended fellowship will enhance residency training

The Fellows will act as role models and provide some mentorship for the residents. They will likely be able to provide some insight into the rationale for extra training, the process of application for an academic position. On a daily basis, they may provide some academic and clinical insights.

#### Names of the Teaching Faculty: this includes the entire faculty

#### □ Roles

Our division has a large number of staff involved in many academic endeavours including patient care, research and education. We see a wide range of pathologies and run several specialized clinics. The staff have a broad base of knowledge, as well, most have focused areas of clinical and basic research and patient care.

- Summary of clinical practice-please see above for clinic details
- Major strengths

Our division has been recognized for a long time as being one that provides outstanding clinical teaching, mentoring skills as well as fulfills the academic mandate of being involved in both basic and clinical research.

## Academic facilities

There is a well-equipped PICU, which admits our diabetic patients with DKA for intensive intravenous insulin management using our protocol. Neonatal ICU patients are seen at the MCH (9C) or in the two other MUHC Level II nurseries (RVH and JGH). Patients are usually seen first in the ER by our trainees, where investigation and treatment are initiated under staff supervision. Similarly, ICU's and/or patients with other acute metabolic disorders (e.g. hypoglycaemia, adrenal crises, D.I., etc.) are seen first by the residents and then managed under our staff supervision. We prefer to admit non-diabetic patients to the ward teams so that the paediatric residents can participate in the care of these cases, and our residents can learn to function as consultants.

## Interdisciplinary Communication

- 1. **Neuroendocrinology**: There is an active Dept. of Neurosurgery with 3 GFT staff. They see 359 new and 866 follow-up patients annually. We look after all pre-operative orders, include fluid balance, for patients undergoing hypothalamic-pituitary procedures. We also evaluate and follow-up those receiving cranial irradiation via Radiation Oncology.
- Imaging Dept.: This is a large facility, including a new MRI. They perform over 73,200
  procedures annually, including 3400 CT's and 1600 MRI's. We have monthly Neuroradiology Endocrinology Rounds to review CT and MR studies. Examples of cases reviewed are
  congenital hypopituitarism and CNS tumours.
- 3. **Oncology**: Given the improving long term prognosis for children post therapies and the potential for endocrine disorders arising from chemo and/or radiotherapies, we follow a substantial proportion of these children.
- 4. **Nephrology**: We interact on numerous cases related to hypertension, Nephrogenic D.I., hypophosphatemic rickets, etc. We have part of our J. Club/Research Seminar series conjointly with them due to several collaborative research studies. Dr. Goodyer's RASS study.
- 5. **Biochemical Genetics**: We interact on complex metabolic disorders, including proteinopathies and organic acidurias, including Glycogen Storage Disease patients, which we manage. Drs. Barnes and Mitchell are appointed to both Services and facilitate these interactions.
- 6. **Réseau Génetique**: We are responsible for the McGill component of the neonatal screening program for congenital hypothyroidism. Trainees are able to experience first-hand the operation and cost-benefit of this program.
- 7. Intersex Management Team: This team was structured in November 1991 to deal with the acute and chronic management of sexual differentiation disorders and neonatal sex assignment. Members consist of an endocrinologist
- 8. **latrogenic Cushings**: Many services (e.g. GI, Asthma Clinic, Neurosurgery, Dermatology) use pharmacologic glucocorticoids. This provides the opportunity for our trainees to see the adverse effects of steroids on linear growth and adrenal suppression. They are able to implement our protocol of tapering and discontinuation, with assessment of restoration of adrenal function.

- 9. **Nutrition Services**: Trainees interact regularly with the dieticians in care of our diabetic patients, being involved in the teaching of patients and their families. They also assist in the care of our patients with GSD, hypoglycaemia, ketogenic diets, under-nutrition and some high-risk Obesity patients. We do limited intervention for the other children with obesity using Canada Food Guide recommendations. We must return the patients to their own physicians, local clinics (CLSC's, which may not offer paediatric support), and nutrition clinics or services such as Weight-Watchers.
- 10. **Psychosocial**: There is a full-time social worker assigned to our Service, R. D'Orazio, who particularly supports the diabetics. She attends the Diabetes Clinic, post-clinic psychosocial rounds and facilitates care for our Endocrine patients too. A psychiatrist, Dr. K. Minde, provides acute intervention when required. Dr. M. Sufrategui is available to provide psychological care of our diabetic patients. We meet with her monthly. Thus the trainees are regularly exposed to these significant aspects of chronic disease.
- 11. Quality Assurance: Dr. Barnes supervises this hospital-wide program. We regularly receive his input during Service rounds.

#### **Clinical Laboratory Facilities**

<u>Clinical Endocrinology Laboratory</u>: This laboratory is now under the auspices of Biochemistry. Dr. Celia Rodd has been the Medical Director for over 5 years. She serves on the MCH Laboratory Services Director's Committee and on the MUHC Laboratory Consolidation Committee. The interface between the Endocrine lab and Biochemistry is open and productive.

The above organization provides the trainees with opportunities for electives, but also provides ongoing input to important aspects of Laboratory Medicine, including cost-containment, and proper use of diagnostic laboratory facilities. Finally, this ensures that all important laboratory results are provided directly to the respective trainee and staff, for discussion at Service Rounds.

<u>Pathology</u>: Although we have a small and growing Pathology Division, we have been able to arrange several Endocrinology - Pathology Rounds every few years. The residents attend the weekly Tumor Board Rounds, if the cases are Endocrine in nature. The exposure is limited but steps have been taken to improve this, such as CD's and other teaching material in Pathology have been purchased to supplement the training.

<u>Nuclear Medicine</u>: Drs. Raymond Lambert and Turpin provide excellent service, even though they are based at Hôpital Ste-Justine. We have no difficulty with the scheduling and interpretation of neonatal thyroid scans, examinations for solitary thyroid nodules (isotope scans, ultrasound). The laboratory has recently been upgraded allowing us to perform 1131 scans. Additional Nuclear Medicine experience has been arranged with the JGH and was felt to be worthwhile.

<u>Research Institute</u>: There are two separate endocrine and metabolic research laboratories within the structure of the MCH Research Institute. These are:

a) Endocrine Research, Room R-415, MCH Research Institute, Place Toulon, C. Goodyer, Ph.D., Aimée Ryan, Ph.D.

b) Molecular Endocrinology, Room R-414, MCH Research Institute, Place Toulon, C. Polychronakos, MD

#### Summary of Adequacy of Resources

We are indeed fortunate to have the largest faculty for Paediatric Endocrinology & Metabolism in Canada. This luxury permits us to offer the expansive and controlled teaching program that we have in place. Each teaching staff/faculty member is expected to perform approximately 1/4 clinical service duties. This provides ample time for each of us to carry significant independent research careers, and to meet the teaching and patient care requirements of the Service. When providing service and teaching, the staff is expected to place his other activities into a secondary position for the relatively brief time required. The number of staff also guaranties that we can continue to function despite our overall commitments to CME activities, writing of grants and manuscripts, and other academic endeavours.

#### Laboratory:

My laboratory at the Research Institute of the McGill University Health Center (Montreal Children's Hospital site), occupies 2,000 square feet of space and has all the necessary equipment for molecular genetics, including equipment bought with a 2005 CFI grant to the Montreal Diabetes Research Center: A state of the art Janus robotic system, a fluorescence polarization detector for genotyping and a FACSaria cell sorter were awarded specifically to me within this \$14M grant. In addition, the Institute has all required shared facilities including tissue culture (three incubators and two hoods exclusive to my lab, including one of each dedicated to ES cell work).

Through the GriD and diabetes genetics projects, I am also in close contact with the McGill/Genome Quebec Innovation Center (MGQIC). Ghislain Rocheleau, one of my current postdocs, is physically located full-time at the MGQIC and three members of the technical personnel there are my former research assistants, trained by me.

#### Clinical:

I am the director of endocrinology at the Montreal Children's Hospital and have established a longstanding program for obtaining blood for research, both for DNA for functional studies on fresh blood cells. Total population almost 500 children (age over 18 years) with diabetes, almost all type 1. Research coordinator team has had a stellar record in past large-scale studies, such as the natural history nephropathy study, DPT1 and we are a major affiliate of Trial Net.

#### Computer:

Each senior member of my laboratory has access to a terminal connected to the hospital network. For large-scale data management, we have access to the Nankuq system at the McGill /Genome Quebec Innovation Centre (used routinely for our Genotyping) and for computationally demanding

applications we can access the CLUMEQ supercomputing facility (used in Sladek et al. Nature 2007)

Major Equipment:

The Solexa system is being set up at the Center for Applied Genomics, Children's Hospital of Philadelphia, which will do the resequencing on a collaborative basis, including all computational work.

Genotyping will be performed at MGQIC on the Sequenom iPlex system used in our previous publications.

Cell sorting for the expression studies will be performed on a FACSaria obtained by funds awarded to the PI by the CFE, specifically for use in diabetes research

### Library access, materials relevant to fellowship training

- McGill University: world-class with broad range of electronic journal subscription, Uptodate.com.
- MCH Paediatric Library: well stocked, with on-line searching capability
- Endocrine Sub-library: contains relevant textbooks and periodicals in two locations on E-315 (Clinical) and
- C-1228 (Research) and on-line searching capability
- Staff offices wide range of textbooks and articles.

### Multimedial learning materials available- quote hospital details please

There are three computers with hardwire connections to allow for on-line searches, for downloading of articles and Internet and email in the two trainee offices. As well, all ward computers and support staff computers can be used for these activities, if needed because the computers are networked and allow multiusers.

### □ Availability of a skills lab, if applicable- not applicable

### Fellow Duties and Responsibilities

- □ Call responsibilities to cover service- None
- □ Include whether the fellow is he senior supervisor of residents- No
- D Outline whether threw are fixed rotations at various institutions- No
- D Outpatient clinic responsibilities need to be outlined-

Generally the trainees are interested in attending either a general endocrinology clinic on Monday afternoons (1300-1700). 2 physicians and usually one endocrine resident staff this with perhaps a medical student and 1 or 2 residents. There are over 25 patients seen by the house staff. If the Fellow wishes to attend this clinic, then patients, who need to be seen more urgently and have been triaged to attend an 'office' visit by only the staff, could be seen by the Fellow. The staff, who would have evaluated the patient by themselves, can attend the clinic to review the case. If this

staff is already booked in the clinic, then they will arrange their time to attend the clinic earlier than usual to review the Fellow's case/s. We have experience with this and have found that the house staff attending the usually scheduled clinic is given the usual amount of attention, while allowing the Fellow to see patients.

If the clinic has very few house staff assigned to it, as deemed by the Program Director, then the Fellow can attend and work in parallel with the usual house staff.

### Weekly schedule

Monday afternoon- General endocrine clinic 1300- 1700 (if interested)\* Tuesday morning Diabetes clinic 0800- 1200 (if interested)\* Wednesday afternoon 1330- 1630 Diabetes/Endocrinology rounds, journal club or research presentation in the academic year Thursday morning (twice per month) Lipid clinic 0900-1200\* Thursday afternoon 1330-1530 Endocrine resident teaching (if interested) Friday afternoon- house staff teaching (Fellow may be the facilitator, if interested)

#### \* the Fellow will select one of these clinics per week

- Outline role of the fellow towards residents on service- None
- Teaching responsibilities towards residentssee above
- Outline participation in academician activities involving the residents: seminars, outcome assessment (morbidity and mortality rounds etc)

# Describe any support staff available to the fellow: program coordinator, nurse, clinician, secretarial

Our administrative secretary assists in coordinating all rotations, the application and acceptance process. If the Fellow participates in clinics, then he/she has access to our secretaries, who are in charge of the clinics.

#### Proposed meetings to be attended by the fellows <u>Additional pedagogic activities</u>

All trainees are encouraged to attend at least one conference per year; this is often the Endocrine

Society, American Diabetes Association or the Canadian Diabetes meeting/ Endocrinology

meeting. Our division has adequate funding to assist with registration costs and some travel costs

for endocrine residents and Fellows.

The Fellows are also able to be granted additional funds from the MCH research institute, if their abstracts have been accepted for presentation.

#### Research productivity and publications expected by the Fellow

Most Fellows would be expected to present, prepare and present a abstract/manuscript that reflects their academic activities during the Fellowship. Some trainees may be capable of additional manuscripts. If she/he are enrolled in a graduate program, then their thesis would be expected to be completed during the Fellowship or shortly thereafter, depending on the course or research load in that particular period.

#### Curriculum

- Intended case load- none
- □ Intended percentage of varieties of cases- n/a
- Regular reading materials provided-
- Conference weekly schedules-Conferences/ Service Rounds:
  - 1. Pediatric Research Seminars, Room C-417, Mondays at 12:00h
  - 2. Endocrine Clinic Intake Conference, Room B-230, Mondays at 16:30h
  - 3. Endocrine Clinic Intake Conference, Room B-230, Tuesdays at 16:30h
  - 4. Diabetic Clinic Conference, Room C-1235, Wednesdays at 13:30h
  - 5. Endocrine/Metabolism Service Rounds, Room C-1235, Wednesdays at 14:30h
  - 6. Journal Club/Research Seminar Series, Room C-1235, Wednesdays at 15:30h
  - 7. Diabetes Clinic Rounds, Room A-311, Tuesdays at 11:30 monthly
  - 8. Diabetes Teaching for new diabetics, as required
  - 9. Endocrine Fellow Teaching Rounds, Room C-1235, Thursday 13:30h
  - 10. Short Cycle Teaching Rounds, E-315, Friday afternoons
  - 11. Pediatric Grand Rounds, D-182, Wednesdays at 8:00h
  - 12. Attendance at conjoint rounds and conferences:
  - MUHC Endocrine Combined Rounds, Thursdays at 8:00h

#### □ Role of fellow in attending, presenting, supervising, organization

The Fellow is involved in presenting her/his research work, works to organize the year and weekly schedule and is involved in some supervisional activities but these are mostly related to her/his research.