

**BIOGRAPHICAL SKETCH**

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NAME: Dorothy J. Becker, M.B.B.Ch.

eRA COMMONS USER NAME (credential, e.g., agency login): DJBecker

POSITION TITLE: Professor of Pediatrics

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Witwaterstrand, Johannesburg, SA	M.B.B.Ch.	1964	
Baragwanath Hospital, Johannesburg, SA	Intern	1966	Medicine
Johannesburg General Hospital	Intern	1966-67	Surgery, Medicine
Red Cross Hospital, Cape Town, SA	Sr. Intern	1967	Pediatrics
Red Cross Hospital, Cape Town, SA	Resident	1970-72	Pediatrics

**A. Personal Statement**

I was appointed to the faculty of Pediatric Endocrinology at the Childrens Hospital and University as Assistant Professor in 1976 have been and rose through the ranks to Professor and ultimately the Chief of the Division of Pediatric Endocrinology and Diabetes in the Department of Pediatrics from 1998 to 2014 and PI of the Pediatric Endocrinology and Diabetes Training grant from 2005 to 2014. Our program has been exceptional over the years in training superb academic pediatric endocrinologists now in academic position around the country including a number of division chiefs. We admit about 250 new onset diabetes patients per year <19 years of age and have a very large endocrine population

Having stepped down from the above positions in 2014, I continued my role as a full time Professor of Pediatrics allowing more time as a principal investigator and co-investigator of my NIH grants, and with continuous NIH funding since 1977. My current focus is both completion of research projects and mentoring of junior colleagues and fellows in their clinical training, research projects and career development. I became a part time Professor in July 2019, and am now Professor emerita with continued grant funding as Co Investigator in TrialNet and clinical sessions teaching in our diabetes clinic. I am very conscious of the need to assist my trainees to be lead authors and junior colleagues to be senior authors of publications and to promote their careers to become the top 1 diabetes researchers of the future.

As much of my research has been aimed to prevent type 1 diabetes (T1D) and its complications, I am acutely aware of the need for scientific research to understand the pathogenesis and heterogeneity of T1D in order to develop appropriate prevention as well as treatment strategies to retain insulin secretory capacity in both new onset T1D patients and those at risk for T1D. Specifically I plan to continue my activities in these areas of research, while continuing to support and help mold young investigators. I have been PI of a RO1 T1D epidemiology study spanning over 3 decades and am involved in a number of NIH funded

epidemiology and prevention trials in T1D including TrialNet and TRIGR having been the USA PI since its initiation. I am committed to the continued investigations and collaboration with the other researchers of these projects. I have been able to sustain these efforts despite the considerable effort required for preparation and maintenance of these grants in the current daunting fiscal environment. In addition to being the first president of the ADA Youth Council and past president of the pediatric Endocrine society, I have been an Associate Editor of Diabetes Care, on the editorial boards of Diabetes Care (twice) and Pediatric Diabetes and a frequent NIH grant reviewer and was a member of the NDDG, DSMB's including DirecNet .

## **B. APPOINTMENTS AND POSITIONS**

- 1967-1968 Dept. of Med., Iron and Red Cell Metabolic Unit, University of Witwatersrand, Research Fellow
- 1968-1970 Dept. of Child Health, University of Cape Town, Research Fellow
- 1970-1972 Red Cross Hospital, Cape Town, Pediatric Resident
- 1/73-7/74 Dept. of Medicine, Groote Schuur Hospital, Cape Town, Endocrinology Resident
- 9/74-6/76 Dept. of Pediatrics, Children's Hospital of Pittsburgh, Endocrinology Fellow
- 1976-1982 University of Pittsburgh, School of Medicine, Assistant Professor of Pediatrics
- 4/77-3/80 Children's Hospital of Pgh., Clinical Assoc. Physician, NIH Clinical Research Center
- 1982-1990 Univ. of Pittsburgh, School of Medicine, Associate Professor of Pediatrics
- 1981-1994 Children's Hospital of Pittsburgh, Associate Director, NIH, CRC
- 1990-Present Univ. of Pittsburgh, School of Medicine, Professor of Pediatrics
- 9/96 -12/97 Children's Hospital of Pittsburgh, Interim Director, Division of Endocrinology
- 1/98 -1/2014 Children's Hospital of Pittsburgh, Director, Division of Endocrinology and Diabetes

## **HONORS, AWARDS, AND SERVICE**

- 1982-84 President: Council for Diabetes in Youth - ADA
- 1983-86 President American Diabetes Association, National Research Committee
- 1985-86 Midwest Society for Pediatric Research 1987-90
- 1987-90 Lawson Wilkins Pediatric Endocrine Society, Board of Directors
- 1989 Award for Outstanding Contributions to Diabetes in Youth; ADA
- 1992-1997 Metabolism Study Section - NIH (Chairman 1995-97)
- 2002-2014 DirectNet DSMB; DSMB Chair 2002 – 2008
- 2008 ISPAD Scientific Achievement Award
- 2008-2009 Lawson Wilkins Pediatric Endocrine Society - President Elect
- 2009-2010 Lawson Wilkins Pediatric Endocrine Society – President
- 2010-2011 Pediatric Endocrine society—Past President

## **C. Contribution to Science**

My CV currently has 340 peer reviewed papers

1) My research career started in South Africa where I described the perturbations of the endocrine system caused by protein-calorie malnutrition (PCM) with an emphasis on the abnormalities of insulin secretion and carbohydrate metabolism (16 publications).

- a) **Becker DJ**, Pimstone BL, Hansen JDL, and Hendricks S: , 1971 Insulin Secretion in Protein-Calorie Malnutrition: I. Quantitative Abnormalities and the Response to Treatment. Diabetes 20: 542-551.
- b). **Becker DJ**, Pimstone BL, Hansen JDL, MacHutchon B, and Drysdale. 1972 A: Patterns of Insulin Response to Glucose in Protein-Calorie Malnutrition. American Journal of Clinical Nutrition 25: 499.

- c). **Becker DJ**, Murray P, Hansen JDL, and Pimstone BL: 1973 Circulating "Big" Insulin in P.C.M. British Journal of Nutrition 30: 345-350,.
- d) **Becker DJ**, Mann M, Weinkove E, and Pimstone B: 1975 Early insulin release, and its response to potassium supplementation in protein-calorie malnutrition. Diabetologia 11: 237-239,

2) This interest led naturally to a career directed to investigations of diabetes which led me to Pittsburgh. My career has been directed to investigations of the prediction and prevention of T1D and its complications. I established and maintained multidisciplinary collaborations as it was clear to me 3 decades ago that this approach would move us forward most effectively. These collaborations included the DCCT ( the model of a multicenter intervention trial) and with our Department of Epidemiology with Drs Ron Laporte (Epidemiology of T1D ) and Trevor Orchard ( Epidemiology of Diabetes Complications (EDC) which we initiated together until I decided to concentrate on T1D pathogenesis and prevention. Some examples are :

- a) Orchard TJ, Olson JC, Erbey JR, Williams K, Forrest KY, Smithline Kinder L, Ellis D, **Becker DJ**: 2003 Insulin resistance related factors, but not glycemia, predict coronary artery disease in type 1 diabetes: Ten-year follow-up data from the Pittsburgh Epidemiology of Diabetes Complications Study. Diabetes Care May 26(5):1374-1379. PMID 12716791
- b)) Pambianco G, Costacou T, Ellis D, **Becker DJ**, Orchard TJ: 2006 The 30-year natural history of type 1 diabetes complications. The Pittsburgh Epidemiology of Diabetes Complications (EDC) Study. Diabetes 55:1463-1469, PMID 16644706.
- c) Miller RG, Secrest AM, Ellis D, **Becker DJ**, Orchard TJ. 2013 Changing impact of modifiable risk factors on the incidence of major outcomes of type 1 diabetes: the Pittsburgh Epidemiology of Diabetes Complications Study. Diabetes Care. Dec;36(12):3999-4006. Epub 2013 Oct 29. PMID: 24170748 PMCID PMC3836155
- d) Williams KV, Cristaldi CL, Miller RG, Arena VC, Libman I, Huang Y, **Becker DJ**, Orchard TJ. Celiac Autoimmunity Is Associated With Lower Blood Pressure and Renal Risk in Type 1 Diabetes. J Clin Endocrinol Metab. 2018 Oct 1;103(10):3828-3836. doi: 10.1210/jc.2018-00908. PMID:30099548. PMCID: PMC6179181

3) This led to further collaborations with immunologists Drs Massimo Trucco , Massimo Pietropaolo and Michael Dosch and then as PI of a TrialNet study center and PI of TRIGR USA -- both being international consortiums working toward prevention of T1D .

- a) Libman IM, Pietropaolo M, Arslanian S, Laporte RE, **Becker DJ**: 2003 Evidence for heterogeneous pathogenesis of insulin-treated diabetes in black and white children. Diabetes Care Oct 26(10):2876-2882, PMID 14514595.
- b) Cedillo M, Libman IM, Arena VC, Zhou L, Trucco M, Ize-Ludlow D, Pietropaolo M, **Becker D**. 2015 Obesity, islet cell autoimmunity and cardiovascular risk factors in youth at onset of type 1 autoimmune diabetes. J Clin Endocrinol Metab. 100(1):E82-6. [2014 Sep Epub ahead of print] PMID: 25250632 PMCID4283021
- c) Buryk MA, Dosch HM, Libman I, Arena VC, Huang Y, Cheung RK, Trucco M, Pietropaolo M, **Becker DJ**. Neuronal T-cell autoreactivity is amplified in overweight children with new-onset insulin-requiring diabetes. Diabetes Care. 2015 Jan; 38(1):43-50. PMID: 25414154 PMCID:PMC4274776
- d) Knip M, Akerblom HK, **Becker D**, Dosch HM, Dupre J, Fraser W, Howard N, Ilonen J, Krischer JP, Kordonouri O, Lawson ML, Palmer JP, Savilahti E, Vaarala O, Virtanen SM; for the TRIGR Study Group. 2014 Hydrolyzed Infant Formula and Early  $\beta$ -Cell Autoimmunity: A Randomized Clinical Trial. JAMA; 311(22): 2279-2287. PMID:24915259, PMCID: PMC4225544.
- e) Long AE, Wilson IV, **Becker DJ**, Libman IM, Arena VC, Wong FS, Steck AK, Rewers MJ, Yu L, AchenbachP, Casas R, Ludvigsson J, Williams AJK, Gillespie KM. Characteristics of slow progression to in multiple islet

autoantibody-positive individuals from five longitudinal cohorts: the SNAIL Study. Diabetologia. 2018 Jun;61(6):1484-1490. . Epub 2018 Mar 12. PMID:29532109

4) I have also collaborated with psychologists and with a neuropsychologist Dr Christopher Ryan to explore mechanisms and effects of insulin/glucose clamp induced hypoglycemia on counterregulatory hormones and cognitive function ( the first in children)

a) Gschwend S, Ryan C, Atchison J, Arslanian S, **Becker DJ**. 1995. Effects of acute hyperglycemia on mental efficiency and counterregulatory hormones in adolescents with insulin dependent diabetes mellitus. J Pediatr 126:178-184,

b) Jarjour IT, Ryan CM, **Becker DJ**. 1995 Regional cerebral blood flow during hypoglycemia in children with insulin-dependent diabetes mellitus. Diabetologia 38:1090-95,.

c) Ryan CM, Dulay D, Suprasongsin C, **Becker DJ**: 2002 Detection of symptoms by adolescents and young adults with type 1 diabetes during experimental induction of mild hypoglycemia: Role of hormonal and psychosocial variables. Diabetes Care May 25(5):852-858 PMID11978680.

d) Helgeson VS, Vaughn AK, Seltman H, Orchard T, **Becker D**, Libman I. Relation of parent knowledge to glycemic control among emerging adults with type 1 diabetes: a mediational model. J Behav Med. 2018Apr;41(2):186-194. PMID:28918521

## D. Research Support

### Current

U01 DK 061058-11 (PI: Becker) 09/29/01-12/30/19

NIH/NIDDK

TrialNet (Prediction and Prevention of Type 1 Diabetes)

TrialNet is a collaborative study of 14 centers in the U.S. and 5 in Europe to plan and implement intervention strategies to maintain beta cell function in new onset patients with type 1 diabetes and prevent diabetes in first- degree relatives at high risk.

2-5-A6403 (PI: Davidson)

10/01/17 – 09/30/2019

0.12 Calendar Months

JDRF/University of Colorado, Denver

\$11,849

*Biobanking samples from high risk subjects*

The overall goal of this study is to fulfill the need for additional longitudinal samples from high risk, multiple autoantibody positive subjects. The proposal is to bank at least 204 longitudinal samples drawn at 3012 month intervals from a cohort of 30-50 high risk subjects.

### Recent Completed

R01 DK 24021-31 (PI: Becker) 03/01/96-05/31/15

NIH/NIDK

Juvenile Diabetes Mellitus: Epidemiology and Etiology

This 35 -year study in no cost extension , which evaluates the immunologic, genetic and environmental determinants of the risk of insulin dependent diabetes mellitus in children and families of children with probands with type 1 diabetes .This application is for the competing renewal of this award.

T32 DK 007729-18(PI: Becker until 7/1/14)

07/01/95-6/30/15

NIH/NIDDK

Research Training in Pediatric Endocrinology

The goal of this training grant is to provide state-of-the-art training in the molecular, cellular, physiologic, and genetic and biochemical aspects of pediatric endocrinology to ensure that the physician-

scientists who graduate from this program are well prepared for productive academic careers in translational research related to pediatric endocrinology.

U01 HD42444-12 (PI: Becker)

09/27/01-06/30/16

NIH/NICHHD

TRIGR: Trial to Prevent Insulin-Dependent Diabetes in the Genetically at Risk: Nutritional Primary Prevention of Type 1 Diabetes

This an International double blind, randomized controlled trial in subjects with an affected first degree relative and risk-associated HLA genotypes which enrolled 2060 eligible infants followed in 73 centers in 15 countries. The 6-8 month intervention is designed to compare the post weaning effects of either hydrolysed casein or standard cow milk based formula over 10 years of follow-up with measurements of serological markers of intact cow milk exposure, diabetes predictive autoantibodies and the clinical and/or metabolic indices of diabetes (the end point at age 10 years). Pittsburgh is a major center and the coordinating center for the United States

R01 DK60586-11 (PI: Helgeson)

07/01/12-06/30/17

NIH/Carnegie-Mellon University

From Adolescence to Adulthood: Persons With and Without Diabetes

Assessment of hypoglycemia from patients' glucose meters and evaluation of metabolic control and diabetes- related complications.

UO1 DK063790( PI -Krischer)

01/01/07-02/28/17

NIH/NIDDK/University of Southern Florida

TEDDY; The Environmental Determinants of Diabetes in the Young

Multicenter epidemiologic study of the environmental pathogenesis of autoimmunity in first degree relatives of subjects with type1 1 diabetes.

JDRF 6-2012-483 (PI Becker)

04/01/15-12/31/16

0.12 Calendar

JDRF/ University of Bristol

\$12,545

*What protects islet autoantibody positive T1D relatives who do not progress*

This project attempts to identify individuals at very high risk of developing type 1 diabetes (i.e. they have 2 or more markers of ongoing beta cell destruction) and have been followed longitudinally for many years but have not developed type 1 diabetes.

GT11302/2.0/25 (PI Becker)

07/11/14-07/10/17

0.12 Calendar

Grifols Therapeutics Inc.

\$12,545

*A Randomized, Partial-Blinded, Multi-Center, Placebo-Controlled Study to Evaluate the Efficacy and Safety of a Human Plasma-Derived, Alpha-Proteinase Inhibitor in Children and Adults with Recent-Onset Type 1 Diabetes Mellitus*

The primary objectives of this study are to examine changes in stimulated C-peptide AUC in subjects with T1DM receiving Alpha1-PI as compared to placebo, and to evaluate the safety and tolerability of two separate IV doses (90 mg/kg/wk and 180 mg/kg/wk) of Alpha1-PI over 13 and 26 weeks of treatment.

## **OVERLAP**

There is no scientific or budgetary overlap amongst these studies