

PROMOTION RECOMMENDATION
 UNIVERSITY OF MICHIGAN MEDICAL SCHOOL
 DEPARTMENT OF INTERNAL MEDICINE
 DEPARTMENT OF PEDIATRICS AND COMMUNICABLE DISEASES

Massimo T. Pietropaolo, M.D. Associate Professor of Internal Medicine, with tenure, Department of Internal Medicine, and Associate Professor of Pediatrics and Communicable Diseases, without tenure, Department of Pediatrics and Communicable Diseases, Medical School, is recommended for promotion to Professor of Internal Medicine, with tenure, Department of Internal Medicine, and Professor of Pediatrics and Communicable Diseases, without tenure, Department of Pediatrics and Communicable Diseases, Medical School.

Academic Degrees:

M.D.	1983	University of Perugia, Perugia, Italy
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Professional Record:

2006–Present	Associate Professor of Internal Medicine and Associate Professor of Pediatrics and Communicable Diseases, University of Michigan
2003–2006	Associate Professor of Pediatrics, Medicine and Immunology, University of Pittsburgh
2001–2003	Research Associate Professor of Immunology, University of Pittsburgh
2001–2006	Associate Professor of Epidemiology, University of Pittsburgh
2001–2003	Research Associate Professor of Medicine, University of Pittsburgh
1995–2001	Research Assistant Professor of Pediatrics, University of Pittsburgh

Summary of Evaluation:

Teaching: Dr. Pietropaolo is a sound teacher and an active mentor. He is a member of the University of Michigan Graduate Program in Immunology and teaches at multiple levels. He has been a facilitator for the MD/PhD enrichment program (Research Basis of Medical Knowledge) and has been involved in the E&M Pathobiology courses. He has participated in the first- and second-year medical student teaching sessions and has served as a facilitator in Group Problem-based Learning Sessions in the Endocrine Disorders Course and in the Clinical Pharmacology Course for fourth-year medical students. Dr. Pietropaolo was a co-director of a course on Contemporary Topics in Immunology entitled: “Autoimmunity” for both MD/PhD students and PhD students. He was the advisor for a MD/PhD student in the Department of Human Genetics and Graduate School of Public Health. During this period of training, the student published several articles and was completing an original manuscript. He defended his PhD thesis on this topic and this piece of work was later published in the *Journal of Biological Chemistry*. He completed his residency program in Internal Medicine at Massachusetts General Hospital and has been accepted in the Rheumatology fellowship program there. Dr. Pietropaolo has effectively mentored a number of graduate students and fellows who have come to his laboratory

from different parts of the world to learn about genes associated with Type 1 diabetes. Three post-doctoral fellows trained by Dr. Pietropaolo have secured junior faculty positions in academic institutions worldwide. He is also involved in the academic teaching activities that are geared towards MD and PhD students and research fellow training. These sessions include laboratory meetings, journal clubs, and basic and clinical science conferences.

Research: Dr. Pietropaolo is an accomplished researcher. While at Joslin Diabetes Center, he was the first scientist to discover the islet cell autoantigen ICA69; this work was published in the *Journal of Clinical Investigation*. The JCI dedicated the cover to this novel diabetes-related autoantigen.

Dr. Pietropaolo's research focuses on the immunology and genetics of Type 1 diabetes. In particular, his laboratory is investigating the role of relevant islet autoantibodies, HLA genotypes and novel potential susceptibility genetic loci in Type 1 diabetes. The study of islet cell autoimmunity in Type 1 diabetes is being exploited using proteomic-based technology to identify novel pancreatic islet proteins reactive with autoantibodies in the sera of Type 1 diabetic patients. They are also investigating the genetic, immunologic and metabolic abnormalities of the diabetes disease process in those antibody positive Type 2 diabetic patients to determine whether this is autoimmune form of diabetes at an older age or a different disease process.

A major goal of Dr. Pietropaolo's is to identify novel immunogenetic markers for predicting Type 1 diabetes and to characterize genetic elements controlling the islet cell autoantigen 69 kDa (ICA69) expression from the gene *ICA1*. Studies by Dr. Pietropaolo's group have suggested that the gene *ICA1* may have a biological role in the genetic regulation of ICA69 expression in the thymus. He has recently reported in the *Journal of Biological Chemistry* the genomic structure and functional promoters within the 5' regulatory region of *ICA1*. A number of single nucleotide polymorphisms have already been identified within the *ICA1* locus. These studies may reveal a new role of this gene in T1DM susceptibility.

Another highlighted research area is clinical research of islet cell autoimmunity in Type 2 diabetes. A second NIH R01 grant proposal, entitled "Epidemiology of Heterogeneity in NIDDM" in which he is the principal investigator, has been funded by the National Institutes of Health. This work has received national and international attention with multiple invitations in a number of conferences and with publications of several original articles and editorials in this field.

In 2005, the American Medical Association hosted the "Diabetes: Understanding & Advancements" media briefing. Dr. Pietropaolo was invited to give a Breaking News Lecture on a combination of biomarkers that help physicians to more accurately predict who will develop Type 1 diabetes. The topics presented in this media briefing received national and international attention and appeared in publications, totaling approximately 125 million media impressions. Stories appeared on online news sites including forbes.com and healthday.com, there was also radio and television coverage of this event.

Recent and Significant Publications:

Morran MP, McInerney MF, Pietropaolo M. Innate and Adaptive Autoimmunity in Type 1 Diabetes Pediatric Diabetes (in press).

Pietropaolo M, Barinas-Mitchell E, Kuller LH. Perspective in Diabetes: The Heterogeneity of Diabetes Mellitus. Unraveling a Dispute: Is Systemic Inflammation Related To Islet Autoimmunity? *Diabetes* 56:1189-1197, 2007.

Barinas-Mitchell E, Kuller LH, Pietropaolo S, Zhang YJ, Henderson T, Pietropaolo M. The Prevalence of GAD65 Autoantibodies by Glucose Tolerance Status in Elderly Patients from the Cardiovascular Health Study. *J Clin Endocrinol Metab* 91(8):2871-2877, 2006.

Barinas-Mitchell E, Pietropaolo S, Zhang YJ, Henderson T, Trucco M, Kuller LH, Pietropaolo M. Islet cell autoimmunity in a Trehnic Adult Population of the national Health and Nutrition Examination Survey (NHANES) III. *Diabetes* 53(5):1293-1302, 2004.

Friday RP, Pietropaolo SL, Profozich J, Trucco M, Pietropaolo M: Alternative core promoters regulate tissue-specific transcription from the autoimmune diabetes-related ICA1 (ICA69) gene locus. *J Biol Chem* 278(2):853-63, 2003.

Service: Dr. Pietropaolo is a member of the Endocrine Society and the American Diabetes Association. He served as the Chair of the Immunology Section at the national conference of the American Diabetes Association in 1999, 2001, 2005 and 2006. He is a member of the national Type 1 diabetes TrialNet Clinical Research Steering Committee and is the principal investigator for the University of Michigan Affiliate TrialNet site. He chaired a number of study sections as detailed in his curriculum vitae and is a member of the NIH study section: Diabetes, Endocrinology and Metabolic Diseases B Subcommittee. He also served as a reviewer for the Endocrinology Research Center (DERC) program, University of California San Francisco, the University of Colorado Health Sciences Center and Endocrinology Research Center (DERC), Aurora, CO, the University of Massachusetts Endocrinology Research Center (DERC), Worcester, MA and for the Endocrine Fellows Foundation, Los Angeles, CA among others. At the University of Pittsburgh, he served on a number of committees including the Committee for junior faculty evaluation in the Department of Pediatrics and the Institutional Biosafety Committee at Children's Hospital of Pittsburgh. As a faculty member of the University of Michigan Graduate Program in Immunology, Dr. Pietropaolo actively participates in the recruitment of undergraduate and graduate students in this program. He also serves as an Executive Committee Member of the Michigan Diabetes Research and Training Center

External Review:

Reviewer A: "His scholarly niche where he is well recognized by his peers is islet autoimmunity studies both in the clinical and experimentally...The work on type 1 diabetes prediction and delineation of clinical phenotypes in diabetes and diabetes risk has professionally brought him to the very top to become a sought after expert."

Reviewer B: "Dr. Pietropaolo also has an outstanding teaching record, as he has been involved in teaching/mentoring undergraduate and graduate medical students since 1983 and continues to do so...At my institution, he would definitely be awarded the rank of Professor with tenure at this time in his career."

Reviewer C: "...Max has provided a variety of contributions to the type 1 diabetes field, the most noteworthy being his descriptions of the biochemical nature of the autoantigens recognized by type 1 diabetes associated autoantibodies....I believe he has developed a 'niche' and amongst his peerage, he would be considered an expert in this field....I believe Max is amongst the most 'well pedigreed' investigators in the U.S. type 1 diabetes research community."

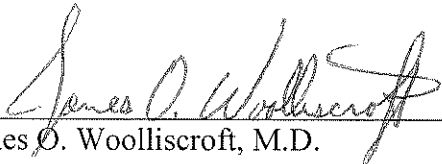
Reviewer D: "He has been a keynote speaker at a number of international conferences that I have attended and gives a stimulating account of his work and its implications for future research. His competence, drive and ambition are unquestionable and his achievements thus far have been substantial."

Reviewer E: "Massimo is among the world's leaders in the field of humoral autoimmunity in T1D, as documented by the many articles and reviews that he has published on this topic."

Reviewer F: "Dr. Pietropaolo is both nationally and internationally known for his research in immunology of Type 1 Diabetes... His publications are of a very high standard and have earned him international reputation....One of the better signs of an accomplished scientist is the ability to receive NIH funding and Max has certainly accomplished this over the past decade with many NIH grants in the field of immunity and type 1 diabetes."

Summary of Recommendation:

Dr. Pietropaolo is a renowned expert in Type I diabetes and I enthusiastically support his promotion to Professor of Internal Medicine, with tenure, and Professor of Pediatrics and Communicable Diseases, without tenure.



James O. Woolliscroft, M.D.
Dean

Lyle C. Roll Professor of Medicine

May 2008