BIOGRAPHICAL SKETCH

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NAME: **Paul Charles Grimm**

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

POSITION TITLE: **Professor of Pediatrics, Medical Center Line, Stanford University**

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 Saskatchewan, Sask. Canada	MD with Dist.	05/1981	Medicine
Dept. of Peds, Dalhousie U., Halifax, Canada	Resident I&II	06/1985	Pediatrics
U of Manitoba, Manitoba Canada	Resident III	06/1986	Pediatrics
Dept. of Peds, Dalhousie U., Halifax, Canada	Fellowship	06/1988	Pediatric Nephrology
UCLA, Los Angeles, Div. Of Ped. Nephrology	Fellowship	06/1991	Transplant Immunology

A. Personal Statement

I have been involved in basic and clinical research for >25 years. My research has been focused on care of children with renal disease. This has included basic and clinical research in transplant, dialysis, ambulatory hypertension and anemia related to renal disease. My early basic work has been focused on the pathogenesis of subclinical rejection, and chronic allograft damage (chronic rejection). I spend the majority of my clinical practice caring for children who need or have received a renal transplant and am the Medical Director of the Pediatric Kidney Transplant Program. This program is the busiest pediatric kidney transplant program in the USA. We have a history of cutting-edge research and innovation in clinical practice. These include innovative urological techniques, use of routine kidney transplant biopsies for early diagnosis, use of steroid free immunosuppression, desensitization programs, aggressive surveillance for the development and treatment of Donor Specific Antibodies. The propensity for pediatric patients to develop devastating viral complications is driving our current research to reduce immunosuppression and improve response to episodes of viral disease. However the specter of smoldering rejection to shorten graft survival prevents us from substantial immunosuppression adjustments. Based on my previous and current basic science and clinical trial experience and my current position as medical director I am optimally situated and have the clinical skills to collaborate with investigators to ensure a successful clinical study with excellent center enrollment.

B. Positions and Honors

Positions and Employment

1991-1996 Assistant Professor, Department of Pediatrics and Child Health, University of Manitoba
1996-1999 Associate Professor, Department of Pediatrics and Child Health, University of Manitoba
1996- 2000 Associate Professor, Department of Immunology, University of Manitoba
1999-2005 Associate Clinical Professor, Department of Pediatrics, University of California at San Diego
2005-2007 Professor of Clinical Pediatrics, Department of Pediatrics, University of California at San Diego
1998-2010 Consultant (Special Gov't Employee) to Biological Response Modifiers Advisory Committee, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration (FDA)
2007-present Professor of Pediatrics, Dept. of Pediatrics, Stanford University School of Medicine
2007-present Director of Stanford Pediatric Nephrology Fellowship Program
2012-present Medical Director, Stanford/LPCH Pediatric Kidney Transplant Program

Other Experience and Professional Memberships

1991-present American Society of Transplant Physicians
1991-present International Pediatric Nephrology Association
1991-present International Society of Nephrology
2000-present International Pediatric Transplantation Association
2008-present National Kidney Foundation
2015-present Member, Medical Advisory Board. Cystinosis Research Foundation

Honors

1993 & 99 Most Outstanding Teacher Award by Pediatric Residents, U. of Manitoba
1995-96 Nathan Block Research Award, Kidney Foundation of Canada
2001 Visiting Professor. 2nd Med Sch, Charles University, Prague. 1st Dept. of Pediatrics. Mar 20-21.
2001, 3 & 6 Voted Outstanding Faculty Teacher of the Year by UCSD Pediatric Resident House staff
2001-present Listed in "The Best Doctors in America"
2011-2017 Board Member, American Board of Pediatrics, Subboard of Pediatric Nephrology
2015-2017 Councilor, International Pediatric Transplant Association
2016 Robert J. Gorlin Lectureship, University of Minnesota, Aug 23-4, 2016
2017 8th Cornfield Lectureship, Children's Hospital of Philadelphia. October 4, 2017
2020 Stanford Dept. of Pediatrics Mid-Senior Career Clinical Excellence Award

C. Contribution to Science

A major contribution of my research has been the development of and continued discernment of the usefulness of **protocol renal allograft biopsies** in the care of patients after kidney transplantation. At the start of my career in Winnipeg, Canada, I was part of the original team that introduced protocol renal biopsies to diagnose subclinical rejection. This technique has now achieved worldwide use and recognition, and was being utilized at Stanford prior to my arrival. Now that we have changed immunosuppressive medication protocols and reduced the incidence of transplant rejection I'm actively involved in the ongoing dialogue about the usefulness and indications of continued protocol renal biopsies in this current immunosuppressive epoch.

These articles were important for the clinical and basic evaluation of the protocol renal allograft biopsy used as a standard of care in the majority of transplant programs.

1) **Grimm** P, McKenna R, Nickerson P, Russell ME, Gough J, Gospodarek E, Liu B, Jeffery J, Rush D. Clinical rejection is distinguished from subclinical rejection by increased infiltration by a population of activated macrophages. (feature article) J Am Soc Nephrol 1999;10(7):1582-1589
2) Rush D, Nickerson P, , Gough J, McKenna R, **Grimm** PC, Cheang M, Trpkov K, Solez K and Jeffery J. beneficial effects of treatment of early subclinical rejection: A randomized study. J. of American Soc. of Nephrology, 1998 ; 11: 2129-2134

This article showed for the first time that a subpopulation of cells involved in laying down fibrous tissues that result in renal allograft scarring actually come from the recipient. What this means is the cells that have the potential to cause scarring circulate in the blood stream in normal people and invade a transplanted organ setting up the process of scarring. This opened the door for the development of tests to recognize this invasion of scarring cells and the development of treatments to prevent the invasion and growth of the scarring cells. This publication was the basis of a large research endeavor by multiple laboratories to understand the mechanism of circulating mesenchymal precursors (i.e., "stem cells") that is still ongoing.

1) Grimm P, et al Neointimal and tubulointerstitial Infiltration by recipient mesenchymal cells in chronic renal allograft rejection. *New England Journal of Medicine***.** 2001;345(2):93-7.

My translational research focuses on using **innovative computerized image analysis techniques** to obtain highly quantitative data from human biopsy tissue. Especially in renal allograft pathology, human assessment has been shown to be poorly reproducible and prone to error. Combining my interest in computer programming and my clinical experience in Pediatric Nephrology, this research attempts to provide quantitative measurements to augment the human pathologist's analysis and ultimately provide a better tool for both research and patient care.

1) **Grimm P**, et al. Computerized Image Analysis of Sirius Red Stained Renal Allograft Biopsies as a Surrogate Marker to Predict Long Term Allograft Function. *J. Am Soc Nephrol*, 2003;14:1662-1668.

2) Farris AB, Adams CD, Brousaides N, Della Pelle PA, Collins AB, Moradi E, Smith RN, **Grimm PC**, and Colvin RB. Morphometric and Visual Evaluation of Fibrosis in Renal Biopsies. *J. Am Soc Nephrol*, 2011; 22: 176–186.
3) Sund S, **Grimm P**, Reisaeter AV, Hovig T. Computerized image analysis vs semiquantitative scoring in evaluation of kidney allograft fibrosis and prognosis. Nephrol Dial Transplant. 2004 Nov;19(11):2838-2845
4) Arjang Djamali, Shannon R. Reese, Nancy A. Wilson, Elizabeth A Sadowski, Wei Zha, David Niles, Sean B Fain, Omeed Hafez, Justin Dorn, Tom Mehner, **Paul C. Grimm**, F. Michael Hoffmann, Weixiong Zhong, Konrad Famulski, Philip Halloran. Nox2 is a Mediator of Calcineurin-Inhibitor-Induced Renal Hypoxia. Transplantation, 2016; 100(6):1198-210. NIHMSID: NIHMS753241

Clinical Care of Pediatric Renal Allograft Recipients. As medical director of the largest pediatric kidney transplant program in the USA, I am in a position to rapidly evaluate and implement changes in clinical practice to improve the outcome of pediatric transportation, both as a large single center and as part of collaborative groups. The following articles are examples of the work we are doing and disseminating in this area. Steroid free immunosuppression in pediatrics was innovated and spearheaded here. We are currently spearheading assessment of long-term allograft dysfunction and influence of donor specific antibodies in pediatric patients.

1) Ryan, CM, Chaudhuri A, Concepcion W, and **Grimm PC**. Immune cell function assay does not identify biopsy-proved pediatric renal allograft rejection or infection Pediatr Transplant. 2014 Aug;18(5):446-52, PMID:24930482
2) Robert Ettenger, Hyunsook Chin, Karen Kesler, Nancy Bridges, **Paul Grimm**, Elaine F. Reed, Minnie Sarwal, Richard Sibley, Eileen Tsai, Barry Warshaw, Allan D. Kirk. Relationship between viremia/viral infection, alloimmunity and nutritional parameters in the first year after pediatric kidney transplantation. Am J Transplantation, 2017;17:1549-1562. DOI: 10.1111/ajt.14169, PMID: 27989013
3) Andrew M. South, Lynn Maestretti, Neeraja Kambham, **Paul C. Grimm** and Abanti Chaudhuri. Persistent C4d and antibody-mediated rejection in pediatric renal transplant patients. Pediatric transplantation. 2017, DOI: 10.1111/petr.13035
4) Maryam Aghighi, Laura Pisani, Ashok J. Theruvath, Anne M. Muehe, Jessica Donig, Ramsha Khan, Samantha Holdsworth, Neeraja Kambham, Waldo Concepcion, **Paul C. Grimm**, Heike E. Daldrup-Link. Ferumoxytol is not retained in kidney allografts in patients undergoing acute rejection. *Molecular Imaging and Biology.* 2018; 20(1):139-149 PMID: 28411307
5) Brian I Shaw, Hui-Jie Lee, Cliburn Chan, Robert Ettenger, **Paul Grimm,** Meghan Pearl, Elaine F Reed, Mark A Robien, Minnie Sarwal, Linda Stempora, Barry Warshaw, Congwen Zhao, Olivia M Martinez, Allan D Kirk,, Eileen T Chambers. Relationship Between Antithymocyte Globulin, T Cell Phenotypes and Clinical Outcomes in Pediatric Kidney Transplantation. American Journal of Transplantation. http://dx.doi.org/10.1111/ajt.16263

Clinical Care of Patients (adult and pediatric) with Cystinosis. As medical director of the Stanford cystinosis clinic, we provide a valuable service to patients and an opportunity to perform research in this rare but important disease. This clinic has assessed more than 15% of all the known patients with this disease in North America. We participate, in collaborative group research and as an individual center.

1) Craig B Langman, Larry A Greenbaum, Minnie Sarwal, Paul **Grimm**, Patrick Niaudet, Georges Deschênes, Elisabeth Cornelissen, Denis Morin, Pierre Cochat, Debora Matossian, Segolene Gaillard, Mary Jo Bagger, and Patrice Rioux., A Randomized Controlled Crossover Trial with Delayed-Release Cysteamine Bitartrate in Nephropathic Cystinosis: Effectiveness on White Blood Cell Cystine Levels and Comparison of Safety. Clin J Am Soc Nephrol 2012;7 1112-1120
2) Langman,CB, Greenbaum LA, **Grimm** PC, Sarwal M, Niaudet P, Deschênes G, Cornelissen EAM, Morin D, Cochat P, Elenberg E, Hanna C, Gaillard S, Bagger MJ, and Rioux P. Quality of Life and Status are Improved and Kidney Function Preserved in Patients with Nephropathic Cystinosis Treated for Two Years with Delayed-release Cysteamine Bitartrate. J of Pediatrics J Pediatr. 2014 Sep;165(3):528-533. PMID:24948347
3) Berryhill A, **Grimm PC**. Cysteamine in renal transplantation: A report of two patients with nephropathic cystinosis and the successful re-initiation of cysteamine therapy during the immediate post-transplant period. Pediatr Transplant. 2015 Oct 19. doi: 10.1111/petr.12617
4) Langman CB, Barshop BA, Deschênes G, Emma F, Goodyer P, Lipkin G, Midgley JP, Ottolenghi C, Servais A, Soliman NA, Thoene JG, Levtchenko EN; Conference Participants. Controversies and research agenda in nephropathic cystinosis: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference. Kidney Int. 2016 Jun;89(6):1192-203.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1Zm7DV0ZFm6QF/bibliography/47187772/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIDDK 07/01/2019-05/31/2024
Metagenomic shotgun microbial sequencing in post-transplant lymphoproliferative disorders (PTLD-MSMS)
(1R01AI142135-01A1)
Role: Co-PI

Cystinosis Research Foundation 01/01/2019-10/31/2020
The effect of resistance exercise on muscle dysfunction in cystinosis
Role: Co-PI

NIH-NIAID 03/01/17 – 02/28/21
VIRTUUS Children's Study: Validating Injury to the Renal Transplant Using Urinary Signatures in Children
(1R01HD091185 – 01)
Role: PI

Alexion Pharmaceutical 11/01/2016 - 10/31/2020
ALXN1210-aHUS-312 SINGLE ARM STUDY OF ALXN1210 IN COMPLEMENT INHIBITOR TREATMENT-NAÏVE Pediatric AND ADOLESCENT PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME (aHUS)
Role: PI

Completed Research Support

Horizon Pharmaceutical 11/12/2010 – 11/10/2017
A Long-Term, Open-Label, Safety and Superior Effectiveness Study of Cysteamine bitartrate Delayed-release Capsules (RP103) in Patients with Cystinosis. RP103-07
Role: PI

Bristol-Myers Squibb Company (277) (BMS) 5/15/2013 – 5/14/2019
A Phase 2 Multi-Center, Randomized Conversion Study to Evaluate the Pharmacokinetics, Efficacy, and Safety of Belatacept Administered to Pediatric Subjects with a Stable Renal Transplant (IM103144)
Goal: To investigate the use of once monthly IV Belatacept to prevent kidney transplant rejection in potentially noncompliant youth.
Role: PI