



October 16, 2007

Richard M. Green, MD
Associate Professor of Medicine
Director, Medical Student Summer Research
and Research Thesis Programs

Dear Dr. Green: *Rich*

I am writing to express my interest in continuing my involvement as a mentor in the Medical Student Summer Research Program. I have had the pleasure of mentoring many (9) students in the past.

I am interested to be a mentor for many reasons. The research environment in my laboratory is excellent for the MSSRP. The work environment is very much geared toward mentoring students. I am involved in all of the projects and devote several hours per week at laboratory meetings going over the projects and ensuring that the student has a good experience. The laboratory has very experienced technical personnel, also, Hermann Kissler, a transplant research fellow, as well as research associate professor Jan Chen, PhD, have worked effectively with the MSSRP students in the past. The students have learned very rapidly and have quickly become independent in their defined laboratory project.

The project described is designed with the student in mind. This project has several component parts and also includes bioluminescent imaging of transplanted islets of a transgenic mouse strain expressing luciferase under control of a rat insulin promoter. Thus, this work fits in well with previous studies done in our lab using the bioluminescence technology and will be a novel molecular approach to track the islet fate. As our lab has also started to develop the components of this mRNA profiling assay for type I diabetic patients to track the fate of their islet transplants, the student will gain an appreciation of how the basic science and clinical science aspects intersect and complement one another on this project.

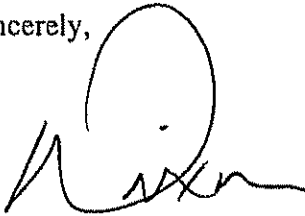
This laboratory is very well structured for the student to effectively learn new concepts in transplantation science that can be translated into the clinical context. We have had several first year medical students in the laboratory and they have flourished in this environment. The laboratory itself is attractive and spacious. It is located in the Tarry building on the 11th floor and occupies approximately 4000 square feet that is shared with other members of the transplant division. It is a very well-equipped laboratory that has all the appropriate space and equipment to successfully conduct the experiments.

Before choosing a student, I interview each about their prior research experience and the nature of the work being performed to determine if it will be an excellent match. Only students that are highly motivated and serious about the research project are accepted.

Students that are accepted for the MSSPR are involved in a structured program. Importantly, the projects are chosen so they can be completed during the allotted period of time. The first week of the summer student research program will emphasize training and safety. Next, the students will be taught how to perform the necessary technical assays that will be applied to the project. The student will also be given specific reading assignments, and encouraged to peruse current literature for new information pertinent to the project. As a guide they are encouraged to use the book entitled "Surgical Research: Basic principles in clinical practice". This is an excellent guide with chapters that discuss organization of the research, effective presentation, experimental design, etc. This is also very good resource to learn to write abstracts and manuscripts and present formal oral presentations. A weekly meeting will bring students together to report progress to lab members. This is the time for critical evaluation, troubleshooting, and new ideas. I also make it a point to have an extra meeting with every student each week or so, one-on-one, to discuss her particular project as well as to be sure she understands the relevance of this work to the clinical issues of transplantation.

I am confident that the environment is excellent and this will be a very rewarding experience for the MSSPR students.

Sincerely,

A handwritten signature in black ink, appearing to read "Dixon", written over a large, light-colored circular mark.

Dixon B. Kaufman, MD, PhD
Professor and Vice Chair, Research
Department of Surgery
Division of Transplantation

**Medical Student Summer Research Program (MSSRP)
Mentor Information**

**Dixon B. Kaufman, MD, PhD
Department of Surgery
Division of Transplantation**

1). Research description

Our ultimate goal is to contribute in a meaningful way to the cure of diabetes through islet transplantation. Certain immunologic variables (host rejection) impact on the fate of the implanted cells. The standard methods for monitoring islet graft function after transplantation rely on blood sugar measurements and occasional metabolic tests that are relatively insensitive or untimely to detect rejection early enough to rescue the graft by adjusting the immunosuppressive regime. Thus, better methods to track the fate of the graft are urgently needed. One of the projects will define how the immune responsiveness of the host effect cellular viability and function. We hypothesize that: combined profiling of islet mass in vivo and islet hormone and cytotoxic lymphocyte mRNA in peripheral blood will be useful surrogate biomarkers of allograft rejection that prompts timely initiation of intensive immunosuppression to rescue the graft by preserving viability and function. The specific aims are: 1. To use real-time bioluminescent imaging as a modality to monitor the fate of transplanted 'tagged' islets from transgenic RIP-luciferase donor strain mice. 2. To use advanced molecular technology to detect ongoing graft damage and islet rejection, and to correlate to the changes in signal intensity via bioluminescent imaging. The aims will be accomplished by applying the general methods of real-time, non-invasive bioluminescent imaging to the specific field of islet transplantation. This imaging modality will permit visualization of 'tagged' transplanted islets in the living mouse. Through serial post-transplant monitoring it will be possible to define how the fate of the viable islet mass is affected by immunologic considerations that directly relate to transplant functional outcome. We will also investigate whether combined profiling of islet hormone and cytotoxic lymphocyte mRNAs in peripheral blood will allow us to detect islet graft rejection before recurrence of diabetes and prompt timely initiation of intensive immunosuppression to rescue the graft by preserving viability and function..

There are also complementary opportunities for involvement on the clinical service related to islet and pancreas transplantation. A new study in clinical islet transplantation will be ongoing. The objective is to determine the incidence and duration of achieving insulin independence after islet transplantation in type I diabetic recipients using a new immunosuppressive approach. The modality of islet replacement by transplantation of the whole pancreas is the most successful method to control glycemia and halt or reverse the secondary complications of diabetes. We are participants in a multicenter study examining the efficacy of a new immunosuppressive protocol for recipients of simultaneous pancreas/kidney transplants.

2.) Cover letter (separate document)

3.) Current Biosketch (separate document)

4.) Previous Trainees:

1994: *Ellis Nam

1995: *David Rosenfeld, *Boyd Lumsden

1998: *Conrad Cheung

1999: *Jashin Wu

2000: Marshall Baker, *Rajesh Gupta,

2001: Marshall Baker, *David Chen

2002: Marshall Baker

2003: Justin Braverman

2005: Hermann Kissler, Jonathan Rink

2006: Hermann Kissler, Jonathan Rink, *Eapen Mathew

2007: Hermann Kissler, *Jean Park

*: MSSRP students

Research areas:

X Basic,

X Translational,

X Clinical

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	Dixon Blake Kaufman			POSITION TITLE	Professor, Surgery		
eRA COMMONS USER NAME	DIXONKAUFMAN						
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)							
INSTITUTION AND LOCATION				DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY	
University of Minnesota, Minneapolis				BS	1979	Biology	
University of Minnesota, Minneapolis				MD	1983	Medicine	
University of Minnesota, Minneapolis				PhD	1994	Surgery	

A. Employment.Dates Institution Position

1983 - 1991 University of Minnesota, Minneapolis, MN Resident, General Surgery
 1991 - 1992 University of Minnesota, Minneapolis, MN Fellow, Transplantation
 1992 - 1996 Northwestern University, Chicago, IL Assistant Professor
 1996 - 2004 Northwestern University, Chicago, IL Associate Professor
 2001 - present Northwestern University, Chicago, IL Tenure
 2004 - present Northwestern University, Chicago, IL Professor

Honors/Awards.

1983 Undergraduate Research Award, University of Minnesota Medical School, Minneapolis.
 1983 National Student Research Forum, Galveston, Texas:
 -- 1st place The James W. McLaughlin Award in Infectious Disease and Immunology.
 -- 2nd place Roche Laboratories Award in Basic Sciences.
 1986-1989 National Research Service Award. University of Minnesota
 1990 David Gaiser Award for Outstanding Surgical Research, University of Minnesota, Mpls.
 1993 Baxter Faculty Scholarship Award, Northwestern University
 1994 American Society of Transplant Surgeons Research Career Development Award
 2002 Associate Editor, American Journal of Transplantation
 2003 Editorial Board, Transplantation Journal
 2007 American Society of Transplant Surgeons (ASTS), Councillor, 2007-present

Federal government public advisory committees

United Network for Organ Sharing (UNOS)

Pancreas and Kidney Committee, Region 7 representative 1994-1996
 Membership and Professional Standards Committee, ad hoc member, 1994-1996
 Kidney Committee, Region 7 representative 2005-2007
 Pancreas Committee, Region 7 representative 2005-2007
 Vice chair 2007-2010
 Policy Oversight Committee representative 2007-2010

National Institutes of Health

NIDDK Board of Scientific Counselors Review, 11/03

NIDDK Scientific panel member: Special Statutory Funding Program for Type 1 Diabetes Research, 1/2005

NIDDK External Advisory Committee Review of Contracts, 4/2000

National Institutes of Health grant review

Surgery, Anesthesiology, Trauma (S.A.T.) study section, ad hoc member, 1999

NCRR, GCRC site-visitor, 2001.

Surgery, Anesthesiology, Trauma (S.A.T.) study section, ad hoc member, 5/2002

NIAID Special Emphasis Panel (ZAI1 PTM-I (J1)) 10/02

NIAID Special Emphasis Panel (ZAI1 PTM-I (M2)) 12/02

Clinical Trial for Pediatric Transplantation" 12/2002

Surgery, Anesthesiology, Trauma (S.A.T.) study section, ad hoc member, 2/2003

Surgery, Anesthesiology, Trauma (S.A.T.) study section, ad hoc member, 10/2003

NIDDK Study section for RFA DK-021 (ZDK GRB (M1)) 4/03

B. Publications.

Select Publications (of 130+ peer reviewed manuscripts and book chapters)

1. **Kaufman DB**, Rabe F, Platt J, Stock PG and Sutherland DER. 1988. On the variability of outcome of islet allo-transplantation. *Transplantation*. 45:1153.
2. **Kaufman DB**, Platt JL, Rabe FL, Dunn DL, Bach FH and Sutherland DER. Differential roles of Mac1+ cells, and CD4+ and CD8+ T lymphocytes in primary nonfunction and classic rejection in islet allografts. 1990. *J Exp Med* 172:291.
3. **Kaufman DB**, Morel P, Field MJ, Munn SR and Sutherland DER. Purified canine islet autografts: functional outcome as influenced by islet number and implantation Site. 1990. *Transplantation*. 50:385.
4. **Kaufman DB**, Morel P, Condie R, Field MJ, Roney M, Tzardis P, Stock P and Sutherland DER. Beneficial and detrimental effects of RBC-adsorbed antilymphocyte globulin and prednisone on purified canine islet autograft and allograft function. 1991. *Transplantation*. 51:37.
5. **Kaufman DB**, Gores PF, Field MJ, Farney A, Stephanian E and Sutherland DER. 1994. Effect of 15-deoxyspergualin on immediate function and long-term survival of transplanted islets in murine recipients of a marginal islet mass. *Diabetes* 43: 778.
6. **Kaufman DB**, Kaplan B, Kanwar Y, Abecassis M, and Stuart FP. 1995. Successful use of tacrolimus (FK506) in a pancreas/kidney transplant recipient with recurrent cyclosporine-associated hemolytic uremic syndrome. *Transplantation* 59: 1737.
7. **Kaufman DB**, Gores PF, Kelley S, Grasela DM, Nadler SG, and Ramos E. 1996. 15-Deoxyspergualin: Immunotherapy in solid organ and cellular transplantation. *Transplantation Reviews* 10:160.
8. **Kaufman DB**. Chapter 17.3. Experience with DSG in Experimental Models of Transplantation, pp 389-395. in Principles of Drug Development in Transplantation and Autoimmunity. Ed. R. Lieberman and A. Mukherjee. R. G. Landes Company. 1996.
9. **Kaufman DB**, Naidu Y, Norman JG, Fink G, Rosenfeld D, Lumsden B, Nam E, Abecassis MM, Fryer J, and Stuart FP. 1997. Functional significance of donor islet IL-1 receptor type 1 (IL-1Rt1) expression in islet transplantation. *Trans Proc*. 29: 772.
10. **Kaufman DB**, Leventhal JR, Koffron AJ, Abecassis MM, Fryer JP, and Stuart FP. 2000. Simultaneous pancreas-kidney transplantation in the mycophenolate mofetil / tacrolimus era: evolution from induction therapy with bladder drainage to non-induction therapy with enteric drainage. *Surgery* 128: 726.
11. Wu JJ, Chen J, Cao X-C, Baker MS and **Kaufman DB**. 2001. Cytokine-induced dysfunction of MIN6 β -cells is nitric oxide independent. *J Surg Res* 101: 190-5.

12. Baker MS, Chen J, Cao X-C and **Kaufman DB**. 2001. Expression of a Dominant Negative Inhibitor of NF- κ B Protects MIN6 β -Cells From Cytokine Induced Apoptosis. *J Surg Res* 97:117-22.
13. **Kaufman DB**, Leventhal JR, Koffron AJ, Gallon LG, Parker MA, Fryer JP, Abecassis MM, and Stuart FP. 2002. A prospective study of rapid corticosteroid elimination in simultaneous pancreas-kidney transplantation: Comparison of two maintenance immunosuppression protocols: tacrolimus/mycophenolate mofetil versus tacrolimus/sirolimus. *Transplantation* 73: 169-77.
14. **Kaufman DB**, Baker MS, Chen X, Leventhal JR, and Stuart FP. 2002. Sequential kidney/islet transplantation using prednisone-free immunosuppression. *American Jour of Transplantation* 2: 674-7.
15. Baker MS, Chen X, Rotramel, A, Nelson J, **Kaufman DB**. 2003. Pro-inflammatory Cytokines Induce NF- κ B-Dependent/NO-Independent Chemokine Gene Expression in MIN6 β -Cells. *J Surg Res* 110: 295-303.
16. **Kaufman DB**. 2003. Editorial. Life lies waiting. *American J Transplantation*. 3:769-70.
17. **Kaufman DB**, Burke GW, Bruce DS, et al. 2003. A Prospective, randomized, multi-center trial of antibody induction therapy in simultaneous pancreas-kidney transplantation. *American J Transplantation*. 3:855-864.
18. Baker MS, Chen X, Rotramel AR, Nelson JJ, **Kaufman DB**. 2003. Interferon regulatory factor-1 (IRF-1) down-regulates cytokine-induced IP-10 expression in pancreatic islets. *Surgery* 134: 124-41.
19. Baker MS, Chen X, Rotramel AR, Nelson, JJ, **Kaufman DB**. 2003. Genetic deletion of chemokine receptor CXCR3 or antibody blockade of its ligand IP-10 modulates effector cell infiltrates and prolongs functional graft survival in pancreatic islet allograft recipients. *Surgery* 134: 126-33.
20. **Kaufman DB**, Lowe W. 2003. Clinical Islet Transplantation, *CURRENT DIABETES REPORTS*. 3;344-350.
21. **Kaufman DB**, and Hering B. Chapter 8. Islet Transplantation, pp 183-204, in Organ Transplantation, 2nd edition. Ed. F. Stuart, M. Abecassis and **D.B. Kaufman**. Landes Bioscience. 2003.
22. **Kaufman DB**, Shapiro R, Lucey MR, Cherikh WS, Bustami RT, and Dyke, DB. 2004. SRTR Report on the State of Transplantation. Immunosuppression: Practice and Trends. *American J Transplantation* 4 (Suppl. 9):38-53.
23. **Kaufman DB**, Leventhal JR, Axelrod D, Gallon LG, Parker MA, and Stuart FP. 2005. Alemtuzumab induction and prednisone-free maintenance immunotherapy in kidney transplantation. Comparison with Basiliximab Induction: Long-term results. *American J Transplantation*. 5: 2539-48.
24. **Kaufman DB**, Leventhal JR, Gallon LG, and Parker MA. 2006. Alemtuzumab induction and prednisone-free maintenance immunotherapy in simultaneous pancreas-kidney transplantation. Comparison with Rabbit Antilymphocyte Globulin Induction: Long-term results. *American J Transplantation*. 6: 331-9.
25. Chen X, Zhang X, Baker MS and **Kaufman DB**. 2006. Visualization of islets after transplant and early detection of graft rejection by in vivo bioluminescence imaging. *Transplantation*, 81: 1421-7.

26. Blomeier H, Zhang X, Rives C, Brissova M, Hughes E, Baker M, Powers AC, **Kaufman DB**, Shea LD, Lowe WL 2006. Polymer scaffolds as synthetic microenvironments for extrahepatic islet transplantation. *Transplantation*, 82: 452-9.
27. Smith SJ, Zhang H, Clermont AO, Powers AC, **Kaufman DB**, Purchio AF, and West DB. 2006. In vivo monitoring of pancreatic beta-cells in a transgenic mouse model. *Mol Imaging*. 5:65-75.
28. Chen X, Zhang X, Larson C, Chen F, Kissler H and **Kaufman DB**. 2007. The epididymal fat pad as a transplant site for minimal islet mass. *Transplantation* 84: 122-5.

C. Research Support

National Institutes of Health. "Chicago Islet Consortium ICR at Northwestern"

U42 RFA-RR-05-003 2006-2009 (PI: Kaufman) Percent effort: 15%

Northwestern University subcontract from UIC (PI: Oberholzer)

9/1/06-8/31/09

Total direct costs: \$1,050,000. Annual 2006 direct costs: \$350,000

The major goal of this award is to develop new techniques of human islet isolation and to be a provider of isolated, purified human islets for investigators' studies

Co-investigator

National Institutes of Health. "Regenerative Scaffold technologies for CNS and Diabetes"

R01 EB003806-0 (PI: Stupp) 9/1/04-8/31/09

Requested total direct costs: \$6,506,754. Annual 2004 direct costs: \$1,174,254 Effort: 2.5%

National Institutes of Health. "Advancing islet transplants for the treatment of type 1 diabetes care "

U01-DK070459-01 (PI: Hering) 9/30/04-7/31/09

Requested total direct costs: \$3,371,216. Annual 2006 direct costs: \$1,439,869

Per cent effort: 10%