BIOGRAPHICAL SKETCH
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NAME: Dutta, Partha

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

POSITION TITLE: Assistant Professor of Medicine and Immunology

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
West Bengal University of Animal and Fishery Science, India	DVM	06/2003	Veterinary Medicine and Surgery
Wichita State University, KS, USA	MS	05/2006	Biological Science
University of Wisconsin-Madison, WI, USA	PhD	08/2010	Immunology of heart transplantation
MGH/ Harvard Medical School, MA, USA	Postdoctoral	12/2013	Immunology of cardiovascular disease

A) Personal Statement

My current research interests focus on immunology of cardiovascular disease. I am investigating how myeloid cells, such as monocytes and macrophages, induce inflammation in metabolic disease such as type II diabetes and cardiovascular disease such as myocardial infarction. My ultimate goal is to develop potential therapeutic avenues to check generation of myeloid cells in the bone marrow and spleen, and recruitment of myeloid cells to sites of inflammation such as adipose tissue and the myocardium. I am keenly interested to investigate differential functions of tissue resident and monocyte-derived macrophages in steady state and disease. In this vein, my laboratory has published expertise using a mouse model of myocardial infarction to test novel treatment approaches. In the proposed fellowship application, I will serve as a collaborator. Josh will receive extensive training in the surgical technique used for the model and will complete the hemodynamics measurements, cardiac imaging, and histology experiments he is proposing through my group.

B. Positions and Honors

Positions:

2002-2003 Intern, Veterinary Medicine and Surgery, WB University of Animal and Fishery Science, India
2004-2005 Teaching Assistant, Department of Biology, Wichita State University, KS, USA
2005-2006 Research Assistant, Department of Biology, Wichita State University, KS, USA
2006-2010 Research Assistant, Department of Surgery, University of Wisconsin-Medical School, WI, USA
2010-2013 Research Fellow, Center for Systems Biology, Massachusetts General Hospital, MA, USA
2013-2015 Instructor, Center for Systems Biology, MGH, Harvard Medical School, MA, USA
2015- Assistant Professor of Medicine, Division of Cardiology, University of Pittsburgh, PA, USA

Honors:

1996 National Merit Scholarship
2009 University of Wisconsin-Madison Vilas Travel Grant
2012 American Society of Transplantation Basic Science Fellowship Grant (Application ID AST-129)
2012 American Heart Association Fellowship Grant (Founder Affiliates, Application ID 12POST12050471)
2014 Keystone Symposia Future of Science Fund Scholarship

2014 Featured Scientist in Fall 2014 TPEN newsletter
2014 NIH Pathway to Independence (PI) Award (K99)
2015 NIH Pathway to Independence (PI) Award (R00)
2016 VMI/ HVI Fellow Award
2017 HVI/VMI Innovator Award

C. Contribution to Science
Complete list of published work:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/50252537/?sort=date&direction=descending

1. Immunology of Organ Transplantation: During my doctoral thesis work, I investigated the role of maternal cells present in offspring in inducing tolerance to heart transplantation. Since family members frequently serve as organ donors, it was important to know how presence of maternal cells or antigen in offspring affects outcome of maternal antigen expressing allografts. We found that there was a strong correlation between number of maternal cells and degree of tolerance to maternal antigen expressing allograft.

a. **Dutta, P**., Molitor-Dart, M. J., Bobadilla, L., Roenneburg, D. A., Yan, Z., Torrealba, J. R. , and Burlingham, W. J. Microchimerism is strongly correlated with tolerance to noninherited maternal antigens in mice. *Blood* 2009. 114: 3578-3587. PMCID: PMC2766676
b. **Dutta, P**., Dart, M., Roenneburg, D. A., Torrealba, J. R. and Burlingham. W. J. Pretransplant immune-regulation predicts allograft tolerance. *Am J Transplant* 2011. 11: 1296-1301. PMCID: PMC3110527
c. **Dutta, P**., Hullett, D. A., Roenneburg, D. A., Torrealba, J. R., Sollinger, H. W., Harn, D. A. and Burlingham, W. J.. Lacto-N-fucopentaose III, a pentasaccharide, prolongs heart transplant survival. *Transplantation* 2010. 90: 1071-1078. PMID: 20885339

2. The Role of Sympathetic Activation in Exacerbation of Cardiovascular Disease: During my postdoctoral training, I investigated the sympathetic activation in metabolic and cardiovascular disease. We found that acute myocardial infarction activation the sympathetic system in the bone marrow, resulting in hematopoietic stem cell mobilization to extramedullary sites. This accelerates ongoing atherosclerosis, which may trigger a second heart attack. We demonstrated that atherosclerotic plaques become more vulnerable after myocardial infarction. Not only myocardial infarction but also stroke exacerbates ongoing atherosclerosis by increasing sympathetic tone. We also found that accumulation and proliferation of hematopoietic stem and progenitor cells in the spleen give rise to inflammatory monocytes that are responsible for worsening atherosclerosis. This can be blocked with chemical sympathetic ablation and a selective beta 3 antagonist resulting in less inflamed atherosclerotic plaques, thereby reducing chances of a second heart attack. This body of work discovered several therapeutic targets to reduce hostile inflammation in cardiovascular disease.

a. Leuschner, F*., **Dutta, P.***, Gorbatov, R., Novobrantseva, T. I., Donahoe, J. S., Courties, G., Lee, K. M., Kim, J. I., Markmann, J. F., Marinelli, B., Panizzi, P., Lee, W. W., Iwamoto, Y., Milstein, S., Epstein-Barash, H., Cantley, W., Wong, J., Cortez-Retamozo, V., Newton, A., Love, K., Libby, P., Pittet, M. J., Swirski, F. K., Koteliansky, V., Langer, R., Weissleder, R., Anderson, D. G. and Nahrendorf, M. Therapeutic siRNA silencing in inflammatory monocytes in mice. *Nature Biotechnology* 2011. 29: 1005-1010. PMCID: PMC3212614 ***Equal contribution authors**
b. **Dutta, P**., Courties, G., Wei, Y., Leuschner, F., Gorbatov, R., Robbins, C. S., Iwamoto, Y., Thompson, B., Carlson, A. L., Heidt, T., Majmudar, M. D., Lasitschka, F., Etzrodt, M., Waterman, P., Waring, M. T., Chicoine, A. T., van der Laan, A. M., Niessen, H. W., Piek, J. J., Rubin, B. B., Butany, J., Stone, J. R., Katus, H. A., Murphy, S. A., Morrow, D. A., Sabatine, M. S., Vinegoni, C., Moskowitz, M. A., Pittet, M. J., Libby, P., Lin, C. P., Swirski, F. K., Weissleder, R. and Nahrendorf, M. Myocardial infarction accelerates atherosclerosis. *Nature* 2012. 487: 325-329. PMCID: PMC3401326
c. Sager HB*, **Dutta P***, Dahlman JE, Borodovsky A, Fitzgerald K, Heidt T, Courties G, Wojtkiewicz GR, Iwamoto Y, Sebas M, Khan OF, Xing Y, Shaw TE, Libby P, Swirski FK, Langer R, Weissleder R, Anderson DG, Nahrendorf M. RNAi targeting multiple cell adhesion molecules reduces immune cell recruitment and vascular inflammation after myocardial infarction. *Science Translational Medicine* 2016. 8: 342ra80. PMCID: PMC5125383 * **Equal contribution authors**
d. **Dutta P**, Hoyer FF, Sun Y, Iwamoto Y, Tricot B, Weissleder R, Magnani JL, Swirski FK, Nahrendorf M. E-selectin inhibition mitigates splenic HSC activation and myelopoiesis in hypercholesterolemic mice with

myocardial infarction. *Atheroscler Thromb Vasc Biol* 2016. 36: 1802-8. PMCID: PMC5001901

3. Hematopoiesis in Cardiovascular Disease: Since inflammatory myeloid cells can determine disease pathogenesis, one of the major research interests in our lab is to understand the mechanisms of inflammatory myeloid cell production from hematopoietic stem and progenitor cells in cardiovascular disease. We found that myocardial infarction releases danger associated molecular patterns, such as HMGB1, which activates $CCR2^+$ hematopoietic stem cells (HSC) and drive them into the cell cycle. As a result, HSC differentiate into inflammatory myeloid cells. Generation of $CCR2^+$ HSC from $CCR2^-$ HSC in the bone marrow depends on the myeloid translocation gene 16. Because splenic myeloipoiesis is insidious to the progression of atherosclerosis, we investigated splenic HSC maintenance. We found that VCAM-1+ macrophages play a crucial role in splenic HSC maintenance and myelopoiesis.

a. **Dutta P***, Sager H, Stengel K, Naxerova K, Libby P, Hiebert S, Scadden D, Swirski FK, Weissleder R, Nahrendorf M. Myocardial infarction activates $CCR2^+$ hematopoietic stem cells. *Cell Stem Cell* 2015. 16: 477-87. PMCID: PMC4426344. *Correspondence: **Partha Dutta** and Matthias Nahrendorf

b. **Dutta, P***., Hoyer, F. F., Grigoryeva, L. S., Sager, H. B., Leuschner, F., Courties, G., Borodovsky, A., Novobrantseva, T., Ruda, V. M., Fitzgerald, K., Iwamoto, Y., Wojtkiewicz, G., Sun, Y., Da Silva, N., Libby, P., Anderson, D. G., Swirski, F. K., Weissleder, R. and Nahrendorf, M. Macrophages retain hematopoietic stem cells in the spleen via VCAM-1 in atherosclerosis. *Journal of Experimental Medicine* 2015. 212: 497-512. PMCID: PMC4387283. *Correspondence: **Partha Dutta** and Matthias Nahrendorf

D. Research Support

Ongoing Research Support

4R00HL121076-03 Dutta (PI) 10/01/2015-09/31/2018
Effect of diabetes on myelopoiesis and atherosclerosis
The goal of this study is to investigate the role of inflammatory myeloid cells in diabetic atherosclerosis.
Role: PI

CMRF Dutta (PI) 07/17/2017-07/16/2019
The mechanisms of disappearance of visceral adipose tissue resident macrophages in obesity
The goal of this study is to investigate the dynamics of visceral adipose tissue macrophages in inflammation
Role: PI

HVI/VMI Innovator Award Dutta (PI) 07/31/2017-07/30/2019
Role of visceral adipose tissue macrophage apoptosis in insulin resistance after myocardial infarction
The goal of this study is to investigate the role of adipose tissue resident macrophages in insulin resistance after myocardial infarction
Role: PI

Completed Research Support

K99-HL121076 Dutta (PI) 12/13/2013-12/12/2015
Effect of diabetes on myelopoiesis and atherosclerosis
The goal of this study is to investigate role of inflammatory myeloid cells in diabetic atherosclerosis.
Role: PI