BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person.

NAME: Dongfang Liu

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

POSITION TITLE: Associate Professor

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
Medical College of Wuhan University	MD equivalent	06/2001	Medicine
Huazhong University of Science and Technology	Ph.D.	06/2005	Immunology
NIAID, National Institutes of Health	Post-doc	08/2011	Immunology
Ragon Institute of MGH, MIT and Harvard	N.A.	06/2012	Immunology

A. Personal Statement

Dr. Dongfang Liu is an Associate Professor at the Rutgers University- New Jersey Medical School (NJMS), Director of Immunoassay Development Program in Department of Pathology, Immunology and Laboratory Medicine in NJMS, who is highly motivated to pursue an academic research career in immunology and immunotherapy.

Specifically, Dr. Liu has a broad background in cell biology of immune cells, with specific training and expertise in human natural killer (NK) cells and HIV-specific cytotoxic T lymphocytes (CTLs). Dr. Liu has published research papers in top-tier journals, including ***Nature Immunology, Immunity, Nature Genetics, JACI, Proc. Natl. Acad. Sci.***, and others, as well as review articles in ***Annu. Rev. Immunol.***, ***Immunol. Cell Biol.***, et al. As a junior faculty at Baylor College of Medicine (BCM), Dr. Liu invented the ***Vertical Cell Paring*** device (**VCP**, 2015 ***J. Immunol.***) for high-resolution synapse imaging and also discovered the molecular mechanisms of functional NK deficiency in partial DiGeorge Syndrome (P. Zheng, et al., 2015, ***J Allergy Clin Immun***), and a novel method using immunological synapse quality to predict the efficacy of chimeric antigen receptor (CAR)-modified immune cells (W. Xiong, et al., 2018, ***Molecular Therapy***).

Dr. Liu's research includes studies of the cell biology of immunoreceptors, NK cell biology, immunotherapy, the immunological synapse, and HIV-specific CTLs in chronic HIV and its related malignancies. As PI for several college- and private company- funded grants (such as **NIH** grants, and a ***Celgene*** research grant), Dr. Liu gained extensive experience in project administration (budgeting, establishing timelines, and evaluating progress). In addition, he has established active collaboration with other researchers.

In addition to the immunobiology background, Dr. Liu has strong experience on CAR-modified cell immunotherapy. Selected publications related to this CAR research are listed as follows:

1. Wei Xiong, Yuhui Chen, Joon Hee Jang, Hao Liu, Lidong Qin, Gianpietro Dotti, **Dongfang Liu**§. Immunological Synapse Predicts Effectiveness of Chimeric Antigen Receptor (CAR) T Cells. ***Molecular Therapy,*** 2018 (PMID: 29503199).

2. **Dongfang Liu**§, Shuo Tian, Kai Zhang, Wei Xiong, Ndongala Michel Lubaki, Zhiying Chen, Weidong Han§. Chimeric antigen receptor (CAR)-modified natural killer cell-based immunotherapy and immunological synapse formation in cancer and HIV. ***Protein Cell***, 2017 Dec;8(12):861-877. doi: 10.1007/s13238-017-0415-5. Epub 2017 May 9. (PMID: 28488245).

In summary, Dr. Liu's current research projects and collaborations successfully led to a number of new discoveries in the field of immunotherapy and immunology.

B. Positions and Honors

Positions and Employment

2018-present	Associate Professor, Rutgers-New Jersey Medical School, Newark, NJ
2018-2018	Associate Professor, Houston Methodist Research Institute, Houston, TX
2015-2018	Assistant Member, Houston Methodist Research Institute, Houston, TX
2012-2015	Assistant Professor, Baylor College of Medicine, Houston, TX
2011-2012	Postdoctoral Research Scientist, Ragon Institute of MGH, MIT and Harvard, Boston, MA
2005-2011	Postdoctoral Fellow, NIAID, National Institutes of Health, Rockville, MD
2001-2005	Ph.D. student, Tongji Medical College, Huazhong University of Science and Technology (Wuhan), and Institute of Biophysics, Chinese Academy of Sciences (Beijing), China

Other Experience and Professional Memberships

Mentoring:

2013-2015	Graduate Program Advisory Committee member
2012-2015	Scholarship Oversight Committee member
2012-2015	Qualifying and Candidacy Exam Standing Committee member
2012-2015	Graduate Program in Immunology Admissions Committee member
2012-2015	Molecular Immunology III teaching

Professional Memberships:

2019-present	Ad hoc Reviewer, NIH, ZAI1-JBS-A-S1(Genetic Engineering Technologies for HIV Cure Research)
2018-present	Ad hoc Reviewer, NIH, ZRG1 CB-F (Improvement of Animal Model for Stem Cell-based Regenerative Medicine)
2018-present	Ad hoc Reviewer, NIH, NCI, (HIV/AIDS and the Tumor Niche)
2018-present	Ad hoc Reviewer, NIH, III (Innate Immunity and Inflammation)
2018-present	Ad hoc Reviewer, NIH, CII (Cancer Immunopathology and Immunotherapy)
2017-present	Ad hoc Reviewer, NIH, AMCB (AIDS Molecular and Cellular Biology)
2016-present	Ad hoc Reviewer, NIH, ZRG1 IDM-W (51)
2016-present	Ad hoc Reviewer, NIH, ZRG1 IDM-W (50)
2015-present	Ad hoc Reviewer, NIH, ZHL1CSR-H Special Emphasis Panel (R01)
2015-present	Ad hoc Reviewer, NIH, ZHL1CSR-B, Special Emphasis Panel (R21)
2014-present	Member, Clinical Immunology Society
2014-present	Member, Society of Chinese BioScientists in America
2012-present	Member, Society for Natural Immunity
2011-present	Member, American Association of Immunologists
2011-present	Reviewer for Journals: *Blood, J Allergy Clin Immunol*, *PLoS ONE, J Clin Immunol, Immunol Cell Biol, Oncotarget, Experimental and Molecular Pathology, Immunity, Inflammation and Disease, PNAS, etc.*

Honors and Awards

2017	Houston Methodist Research Institute NIH Competitiveness Award
2016	Career Cornerstone Award (Houston Methodist Research Institute, HMRI)
2015	Bridge to Independence Award (Baylor College of Medicine, BCM)
2014	Texas Children's Hospital Pediatric Pilot Research Award
2014	National CFAR Symposium Travel Scholarship
2014	Celgene Corporation Research Grant
2013	Lymphoma SPORE Developmental Research Program Award, BCM
2013	Center for AIDS Research Development Award at Baylor-UT Houston
2013	Caroline Weiss Law Fund for Research in Molecular Medicine
2011	Ragon Institute of MGH, MIT and Harvard Fellow Award

C. Contribution to Science

1. Use total internal reflection fluorescence (TIRF) microscopy to study cytotoxic lymphocyte functions. For my Ph.D., I studied the formation and directed exocytosis of cytolytic granules in human natural killer (NK) cells. This work utilized several types of microscopy, including total internal reflection fluorescence (TIRF) and de-convolution wide-field fluorescence microscopy, in conjunction with patch-clamp electrophysiological recordings to obtain quantitative data on granule biogenesis and degranulation (**Liu et al., *PNAS*, 2005**). With this publication, I was the first to use TIRF to study cytotoxic lymphocyte function. Now, TIRF is widely used in many immunological research laboratories worldwide. These efforts led to the discovery of a new and rapid pathway for replenishing granules during cytotoxicity. In addition to my studies on NK cells, I investigated degranulation in other cell types, including mast cells (***Allergy*, 2008**) and neutrophils (***Int Arch Allergy Immunol*, 2004**).

1. **Dongfang Liu***, L. Xu*, F. Yang, D. Li, F. Gong, T. Xu. Rapid biogenesis and sensitization of secretory lysosomes in NK cells mediated by target cell recognition. ***Proc Natl Acad Sci USA***. 2005, 102, 123-127. (PMCID: PMC544047) (*, Co-first author)
2. **Dongfang Liu**, J. Zhang, J. Wu, C. Zhang, T. Xu. Altered calcium-induced exocytosis in neutrophils from allergic patients. ***Int Arch Allergy Immunol***. 2004, 134, 281-287. (PMID: 15205559)
3. J. Zhou*, **Dongfang Liu***, C. Liu, Z. Kang, X. Shen, Y. Chen, T. Xu, C. Jiang. Glucocorticoids inhibit degranulation of mast cells in allergic asthma via nongenomic mechanism. ***Allergy***. 2008, 63, 1177-1185. (PMID: 18699934) (*, Co-first author)
4. Y. Ma, H. Yang, J. Qi, **Dongfang Liu**, P. Xiong, Y. Xu, W. Feng, G. Zheng, P. Li, M. Fang, Z. Tan, F. Zheng, F. Gong. CD2AP is indispensable to multistep cytotoxic process by NK cells. ***Mol Immunol***. 2010, 47, 1074-82. (PMID: 19945749)

2. Discovery of 'Bidirectional Vesicular Traffic' at the cytotoxic immunological synapse and the development of novel techniques to visualize vesicular traffic at the immunological synapse. I continued to hone my microscopy skills and human immune cell manipulation skills at the NIH as a postdoctoral fellow, this time combining a unique lipid bilayer system with multiple imaging technologies to obtain live images of cytotoxic and inhibitory immunological synapses (IS). I gained extensive experience in the use of fixed and live cell imaging techniques, including confocal and TIRF microscopy and fluorescence resonance energy transfer (FRET). At the NIH, I made *the first observation of bidirectional vesicular traffic at the center of the NK cell cytotoxic synapse*, and discovered that binding of integrin LFA-1 to ICAM-1 controls cytotoxic synapse organization and prevents diffusion of lysosomal protein LAMP-1 at the plasma membrane. This work was featured on the cover of the July 2009 issue of ***Immunity* (Liu, et al., *Immunity*, 2009)**. Throughout my career, I have developed tools specifically to better understand lymphocyte cytotoxicity. Using high-speed spinning disc confocal and TIRF microscopy to track the 3- and 2-dimensional movement of lytic granules, I found a distinct role for Rab27a (***PLoS ONE***, 2010) on lytic granule trafficking and discovered that lateral diffusion of integrin ligands is an important determinant of susceptibility to lysis by cytolytic lymphocytes (***J Immunol.*** 2010), by developing an automated image analysis algorithm (MATLAB). I have also developed a unique molecular probe to detect individual lytic granule fusion events in live cells (***Immunol Cell Biol***, 2011), allowing for in depth study of lytic granule exocytosis. More recently, I have optimized the use of single molecule FRET for use in live lymphocytes. This cutting-edge imaging modality, which allows visualization of live phosphorylation events at the single molecule level, has never before been applied to the study of live cytotoxic cells. Given my expertise in sophisticated imaging techniques, familiarity with and ability to code complex algorithms required for image analysis, robust publication record, and strong background in the cell biology and immune regulatory mechanisms governing both the NK and CTL synapse, I consider myself to be an ideal candidate to bring new concepts and technologies to the field of immunology.

1. **Dongfang Liu**, YT. Bryceson, T. Meckel, G. Vasiliver-Shamis, ML. Dustin, and EO. Long. Integrin-dependent organization and bidirectional vesicular traffic at cytotoxic immune synapses. ***Immunity***. 2009, 31(1): 99-109 (**Cover Article**). (PMCID: PMC2740634)
2. **Dongfang Liu***, T Meckel*, EO. Long. Distinct role of Rab27a in granule movement at the plasma membrane and in the cytosol of NK cells. ***PLoS ONE***. 2010, 5(9), e12870. (PMCID: PMC2943471) (*, co-first author)
3. **Dongfang Liu***, JA. Martina, XS. Wu, JA. Hammer III, EO. Long*. Two modes of lytic granule fusion during degranulation by natural killer cells. ***Immunology and Cell Biology***. 2011, 1-11. (PMCID: PMC3257049) (*, co-corresponding author)

4. CC. Gross, JA. Brzostowski, **Dongfang Liu**, EO. Long. Tethering of ICAM on target cells is required for LFA-1-dependent NK cell adhesion and granule polarization. ***J. Immunol***. 2010, 185, 2918-26. (PMCID: PMC3867939)

3. Crk functions as a two-way molecular switch to control NK cell-mediated cytotoxicity. In further studies, I determined that a small adaptor protein, CT10 regulator of kinase (Crk), plays an essential upstream regulatory role at the immunological synapse (IS), influencing signaling events required for both activation and inhibition (**Liu et al., *Immunity*, 2012**). Using primary human cells, cutting-edge microscopy, small interfering RNA (siRNA), and lipid bilayer systems, I demonstrated that Crk controls both NK cell activation and inhibition. Meanwhile, I also demonstrated that inhibitory receptor alone (in the absence of an activating receptor) is sufficient to induce phosphorylation of Crk (pCrk). This runs counter to prevailing thoughts that posit, first, that activation, not inhibition, is synonymous with phosphorylation, and second, that phosphorylation in the presence of inhibitory receptors requires the presence of activating receptors. Therefore, I propose the following working hypothesis: Crk serves as an upstream two-way switch in controlling NK cell-mediated cytotoxicity. This work was featured on F1000 (http://f1000.com/prime/714147801).

1. **Dongfang Liu,** ME. Peterson, EO. Long. The adaptor protein Crk controls activation and inhibition of natural killer cells. ***Immunity***. 2012, 36(4): 600-11. (PMCID: PMC3355982)
2. **Dongfang Liu.** The adaptor protein Crk in immune response. ***Immunology and Cell Biology***. 2014, 92 (1): 80-9. (PMCID: PMC4065865)
3. EO. Long, HS. Kim, **Dongfang Liu,** ME. Peterson, S. Rajagopalan. Controlling NK cell responses: integration of signals for activation and inhibition. ***Annual Review of Immunology***. 2013, 31:227-58. (PMCID: PMC3868343)
4. Tsukasa Nabekura, Zhiying Chen, Taeju Park, Tom Curran, Eric Vivier, Lewis Lanier, **Dongfang Liu**. Crk adaptor proteins regulate NK cell expansion and differentiation during mouse cytomegalovirus infection. ***Journal of Immunology***, 2018 (PMC5940538).

4. Discovery of the superior quality of immunological synapses formed by HIV-specific CTLs from elite controllers. At the end of my postdoctoral fellowship at the NIH, I successfully competed for a Ragon Fellowship award to extend my microscopy-based studies of immunological synapses to those formed by HIV-specific CTL cells from elite controllers and chronic progressors (Ragon Institute of MGH, MIT and Harvard). Comparing synapse formation and function, we observed TCR clonotype-specific differences in antiviral efficacy; controllers demonstrate superior control of HIV-1 replication in vitro, greater cross-reactivity to epitope variants, and enhanced loading and delivery of perforin (**Chen et al., *Nat Immunol*, 2012**), as well as molecular mechanisms of CTL dysfunction in chronic HIV infection (**Gaiha et al., *Immunity*, 2014**). Importantly, this award was instrumental in launching my career as an independent investigator, providing me a chance to develop active collaborations with other researchers. This experience will be invaluable as I continue my independent faculty position in academia.

1. **Dongfang Liu** and Huabiao Chen. Structured illumination microscopy improves visualization of lytic granules in HIV-1 specific cytotoxic T-lymphocyte immunological synapse. ***AIDS Res Hum Retroviruses***. 2015 Apr 1. [Epub ahead of print] (PMID: 25831465)
2. H. Chen*, ZM. Ndhlovu*, **Dongfang Liu**, LC. Porter, JW. Fang, S. Darko, MA. Brockman, T. Miura, ZL. Brumme, A. Schneidewind, A. Piechocka-Trocha, KT. Cesa, J. Sela, I. Toth, F. Pereyra, XG. Yu, DC. Douek, DE. Kaufmann, TM. Allen, BD. Walker. T cell receptor clonotypes modulate the protective effect of HLA class I alleles in HIV-1 infection. ***Nature Immunology***. 2012, 13 (7): 691-700. (PMCID: PMC3538851) (*, co-first author)
3. Gaurav D. Gaiha, Kevin J. McKim, Matthew Woods, Thomas Pertel, Janine Rohrbach, Natasha Barteneva, Christopher R Chin, **Dongfang Liu**, Damien Z Soghoian, Kevin Cesa, Shannon Wilton, Michael T. Waring, Adam Chicoine, Travis Doering, E. John Wherry, Daniel E. Kaufmann, Mathias Lichterfeld, Abraham L. Brass, Bruce D. Walker. Dysfunctional HIV-specific CD8+ T cell proliferation is associated with increased caspase-8 activity and mediated by necroptosis. ***Immunity.*** 2014, 41(6): 1001-120 (PMCID: PMC4312487)

5. Discovery of molecular mechanisms of functional NK deficiency in patients with partial DiGeorge syndrome. After joining Baylor College of Medicine (BCM) in 2012, I continue to investigate the role of Crk in immune responses by multidisciplinary approaches, with a focus on cutting-edging super-resolution stimulated emission depletion (STED) microscopy. I demonstrated, for the first time, functional NK cell deficiency in

patients with partial DiGeorge syndrome (pDGS) and dissected the molecular mechanisms of functional NK deficiency in pDGS. This work was featured on the Journal of Allergy and Clinical Immunology's 'The Editors' Choice' (http://www.jacionline.org/article/S0091-6749(15)00416-9/pdf).

1. Peilin Zheng, Lenora M. Noroski, Imelda C. Hanson, Yuhui Chen, Michelle Eugene Lee, Yu Huang, Pinaki Banerjee, George Makedonas, Jordan S. Orange, William T. Shearer, **Dongfang Liu**. Molecular mechanisms of functional natural killer deficiency in patients with partial DiGeorge syndrome. ***J Allergy Clin Immun.*** 2015 March 3, doi: 10.1016/j.jaci.2015.01.011 (PMID: 25748067)
2. Peilin Zheng, Grant Bertolet, Yuhui Chen, Shengjian Huang, **Dongfang Liu**. Super-resolution imaging of the natural killer cell immunological synapses on a glass-supported planar lipid bilayer. ***Journal of Visualized Experiments***. 2015 Feb 11, doi: 10.3791/52502. (PMCID: PMC4354632)
3. Egest J. Pone, Tonika Lam, Zhang Lou, Rui Wang, Yuihui Chen, **Dongfang Liu**, Aimee L. Edinger, Zhenming Xu, Paolo Casali. B cell rab7 mediates induction of activation-induced cytidine deaminase expression and class-switching in T-dependent and T-independent antibody responses. ***Journal of Immunology***. 2015 Apr 1; 194(7): 3065-78. (PMID: 25740947)
4. Yu Huang, Joon Hee Jang, Mirza S. Baig, Grant Bertolet, Xi Kang, Shengjian Huang, Qian Hu, Yong Zhao, Lidong Qin, Michael Xi Zhu, **Dongfang Liu**. PD-1 Blocks Lytic Granule Polarization in Natural Killer Cell Immunological Synapse via Impairing Integrin 'Outside-in' Signaling. ***J Allergy and Clinical Immunology***, 2018 (PMID: 29679656)

Link to full list of publications:

http://www.ncbi.nlm.nih.gov/sites/myncbi/1HYcc8TCT6Z58/bibliograpahy/40356891/public/?sort=date&direction=ascending

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

Ongoing:

1R01AI130197-01A1 Liu (PI) 02/12/18 - 03/31/2023
The adaptor protein Crk in immune responses. The major goals of this project are to understand the role of Crk in NK cells.

1 R21 AI124769-01 Liu (PI) 9/01/2016-6/30/2020 (NCE)
HIV-1-Specific CTL Exhaustion at Immune Synapse. The major goals of this project are to explore the role of PD-1 in regulating the immunological synapse of HIV-specific CTLs.

1 R21 AI129594-01 Liu (PI) 11/15/2016-10/31/2019 (NCE)
Targeting of Master Signaling Molecule to Restore Functions of Exhausted HIV-Specific CTLs. The major goals of this project are to explore the role of phosphorylated Crk inhibitors in regulating the functions of HIV-specific CTLs.

Completed:

2531319101 Liu (PI) 07/01/13 - 6/30/2014
The Caroline Weiss Law Fund for Research in Molecular Medicine
The adaptor molecule CrkL in NK inhibition. The goal of this project is to determine the role of adaptor protein CrkL in NK cell inhibition.

2531319301 Liu (PI) 05/01/13 - 4/30/2014
Center for AIDS Research (CFAR) at Baylor- UT Houston
Bi-specific CTL in HIV-related malignancy. The goal of this project is to develop bi-specific T cells for HIV immunotherapy.

1 R21 HL125018-01A1 Liu (PI) 07/01/2015-04/30/2019
Bispecific Cytotoxic Lymphocytes in HIV-related non-Hodgkin's lymphoma (NHL).
The goal of this project is to develop (Aim 1) and characterize (Aim 2) these bispecific cells with the ultimate goal of administering them to HIV-infected patients with NHL as part of a future clinical trial.