BIOGRAPHICAL SKETCH

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NAME: Liu, Dongfang

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

POSITION TITLE: Associate Professor/Director of Immunoassay Development Program

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 School of Hubei University for Nationalities & 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	NA.	08/2011	Immunology
Ragon Institute of MGH, MIT and Harvard	N.A.	06/2012	Immunology

A. Personal Statement

Dr. Dongfang Liu is a tenured Associate Professor at the Rutgers University- New Jersey Medical School (**NJMS**), Director of Immunoassay Development Program in the Department of Pathology, Immunology and Laboratory Medicine at NJMS, who is highly motivated to pursue academic research and translational research in immunobiology of immunological synapse and cancer therapy.

Specifically, Dr. Liu has a broad background in the 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 Communications, JACI, Proc. Natl. Acad. Sci.***, and others, as well as review articles in ***Annu. Rev. Immunol.***, ***Immunol. Cell Biol.***, et al. As a faculty at Baylor College of Medicine (**BCM**), Dr. Liu invented the ***Vertical Cell Paring*** device (**VCP**, 2015 ***J. Immunol.***) for high-resolution immunological synapse (**IS**) imaging and also discovered the molecular mechanisms of functional NK deficiency in partial DiGeorge Syndrome (P. Zheng, et al., 2015, ***J Allergy Clin Immun***). Dr. Liu invented a novel method using **IS** quality to predict the efficacy of chimeric antigen receptor (CAR)-modified immune cells (W. Xiong, et al., 2018, ***Molecular Therapy***), as well as AI-based CAR IS quantification from actual patient samples (Naghizadehm A., et al., ***PLoS Computational Biology***, 2022). As a faculty at Rutgers-NJMS, Dr. Liu invented a new method for NK and CAR-NK expansion (Y. Yang, et al., 2020, ***Molecular Therapy_Methods Clin. Dev.***) and discovered the efficacy of CD147-CAR-NK for Hepatocellular Carcinoma (H. Tseng, et al., 2020, ***Nature Communications***).

Dr. Liu's research includes studies of the cell biology of immunoreceptors, NK cell biology, immunotherapy, the immune synapse, and HIV-specific CTLs in chronic HIV and its related malignancies. As a PI for several government and private grants, Dr. Liu gained extensive experience in project administration (budgeting, establishing timelines, and evaluating progress).

In addition to grants, patents (> 10 submitted patents), and peer-reviewed publications, Dr. Liu made substantial academic progress, including attaining national and international distinction through scientific community service, professional memberships, presentations, teaching, and mentoring. Specifically, Dr. Liu has also served as a grant reviewer on several NIH study sections (R01, R03, F30/31/32, K99, U01/19/54, S10, and R21 study sections) and as a peer reviewer for the following journals: *Blood, PNAS, Journal of Allergy and Clinical Immunology, PLoS ONE, Journal of Clinical Immunology, Immunity, Immunology & Cell Biology, Scientific Reports, Cancers, Viruses, Science Translational Medicine, Signal Transduction and Target*

Therapy-Nature, and *Oncotarget, etc.* Meanwhile, Dr. Liu is actively participating in the graduate programs at Rutgers University.

Dr. Liu has strong experience in immunological synapse. Selected publications related to this R01 immunological synapse research are listed as follows:

1. **Dongfang Liu**, YT. Bryceson, T. Meckel, G. Vasiliver-Shamis, ML. Dustin, and E.O. Long. Integrin-dependent organization and bidirectional vesicular traffic at cytotoxic immune synapses. ***Immunity***. 2009, 31(1): 99-109 (Cover Article). (PMCID: PMC2740634)
2. 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, 26 (4): 963-975. (PMCID: PMC6080133)
3. **Dongfang Liu**[§]*, Badeti S, Dotti G, Jiang JG, Wang H, Dermody J, Soteropoulos P, Streck D, Birge RB, Liu C.* The Role of Immunological Synapse in Predicting the Efficacy of Chimeric Antigen Receptor (CAR) Immunotherapy, ***Cell Commun Signal***. 2020, Aug 25;18(1):134. doi: 10.1186/s12964-020-00617-7. (PMCID: PMC7446110)
4. **Naghizadeh, A.,** Tsao, W.C., Hyun Cho, J., Xu, H., Mohamed, M., Li, D., Xiong, W., Metaxas, D., Ramos, C.A., and **Liu, Dongfang**. In vitro machine learning-based CAR T immunological synapse quality measurements correlate with patient clinical outcomes. ***PLoS Computational Biology***, 2022, 18(3), p.e1009883. (PMCID: PMC8955962)

Ongoing and recently completed projects that I would like to highlight as follows:

Ongoing:

1R21CA267368-01 **Liu (PI)** 01/15/2022-12/31/2023
CD147-CAR-NK Cells for HCC Treatment. This project is to develop a CAR-NK therapy for HCC.
1R01AI130197-01A1 **Liu (PI)** 02/12/18 - 12/31/2023 (NCE)
The adaptor protein Crk in immune responses. This project is to understand the role of Crk in NK cells.

Completed

1S10OD025182-01A1 **Liu (PI)** 07/10/2020 - 07/09/2021
Leica TCS SP8 STED 3x super-resolution microscope for the RBHS Newark campus
1 R21 AI124769-01 **Liu (PI)** 9/01/2016-6/30/2021
HIV-1-Specific CTL Exhaustion at Immune Synapse. This project explores the synapse of HIV-specific CTLs.
1 R21 AI129594-01 **Liu (PI)** 11/15/2016-10/31/2021
Targeting of Master Signaling Molecule to Restore Functions of Exhausted HIV-Specific CTLs.
1 R21 HL125018-01A1 **Liu (PI)** 07/01/2015-04/30/2019
Bispecific Cytotoxic Lymphocytes in HIV-related non-Hodgkin's lymphoma (NHL).
1R56AI130197-01 **Liu (PI)** 02/12/17 - 03/31/2018
The adaptor protein Crk in NK cells. This project aims to understand the role of Crk in NK cells.
NIH REACH program (part of U01HL150852) **Liu (site-PI)** 10/24/2020-03/01/2022
CD147 for Solid Cancer Treatment. This project explores a novel logCD147-CAR-NK therapy for HCC.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointment

2018-present	Associate Professor, Rutgers-New Jersey Medical School
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

Professional Memberships:

2022/2023	Ad hoc Reviewer NIH S10, U19, R21/R03, UH3/UH3
2021	Ad hoc Reviewer NIH PAR-20-292 (**02/2021**), Israel Science Foundation, Israel (**03/2021**), Rosetrees Trust Grant, UK (**05/2021**), CMIB study section (**11/2021**), Cancer Prevention and Immunotherapy-NCI (**12/2021**)

2020	Ad hoc Reviewer, F30/F31/F32 (**03/2020**), U54 (**07/2020**), SEP-2: NCI Clinical and Translational Exploratory/Developmental Studies (**10/2020**), F30/F31/F32- F09C Cancer Immunology and Immunotherapy (**07/2020**), ZRG1 F09C-Q (20) Fellowship panel, Cancer Immunology and Immunotherapy (**11/2020**).
2019	Ad hoc Reviewer, RFA-AI-18-058 (U19, ZAI1-JBS-A-S1, Genetic Engineering Technologies for HIV Cure Research, **2019**); PAR16-093-094-322 (R24, Improvement of Animal Models for Stem Cell-Based Regenerative Medicine, **2019**)
2018	Ad hoc Reviewer, PAR-16-093 (RG1 CB-F, Improvement of Animal Model for Stem Cell-based Regenerative Medicine, **2018**); RFA-CA-17-030 (HIV/AIDS and the Tumor Niche, **2018**); PA-16-040 (Cancer Immunopathology and Immunotherapy, **2018**); PA-18-484 (Innate Immunity and Inflammation, **2018**)
2017	Ad hoc Reviewer, NIH, AMCB (AIDS Molecular and Cellular Biology)
2016	Ad hoc Reviewer, NIH, ZRG1 IDM-W (51), ZRG1 IDM-W (50)
2015	Ad hoc Reviewer, NIH, ZHL1CSR-H Special Emphasis Panel (R01)
2015	Ad hoc Reviewer, NIH, ZHL1CSR-B, Special Emphasis Panel (R21)
2012-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, Science, Nat Commun.*, etc.
2011-present	Member, Clinical Immunology Society, Society of Chinese BioScientists in America, Society for Natural Immunity, American Association of Immunologists

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 (BCM)
2014	Texas Children's Hospital Pediatric Pilot Research Award
2014	National CFAR Symposium Travel Scholarship
2014	Celgene Corporation Research Grant Award, BCM
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. Contributions to Science

1. The first to use total internal reflection fluorescence (TIRF) microscopy to study cytotoxic lymphocyte functions. For Ph.D., Dr. Liu 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, Dr. Liu 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 and were recognized by one of **Top-10** graduate students awards and a highly competitive grant from the National Foundation for Natural Sciences of China (turned down because of postdoc training in the USA). In addition to NK cells, Dr. Liu 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 development of novel techniques to visualize vesicular traffic at the immunological synapse. During the postdoctoral training at the NIH, Dr. Liu continued to hone his microscopy and human NK cell manipulation skills, combining a unique lipid bilayer system with multiple imaging technologies to obtain live images of cytotoxic and inhibitory and inhibitory immunological synapses (**IS**). Dr. Liu gained extensive experience using fixed and live cell imaging techniques, including confocal and TIRF microscopy and fluorescence resonance energy transfer (FRET). At the NIH, Dr. Liu 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***)*. Dr. Liu has developed tools specifically to better understand lymphocyte cytotoxicity throughout his career. Using high-speed spinning disc confocal and TIRF microscopy to track the 3- and 2-dimensional movement of lytic granules, Dr. Liu 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). Dr. Liu has also developed a unique molecular probe to detect individual lytic granule fusion events in live cells (***Immunol Cell Biol***, 2011), allowing for a depth study of lytic granule exocytosis.

1. **Dongfang Liu**, YT. Bryceson, T. Meckel, G. Vasiliver-Shamis, ML. Dustin, and E.O. 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***, J.A. Martina, XS. Wu, JA. Hammer III, E.O. 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, Dr. Liu 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, Dr. Liu demonstrated that Crk controls both NK cell activation and inhibition. Meanwhile, Dr. Liu also demonstrated that the 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 that activation, not inhibition, is synonymous with phosphorylation and, second, that phosphorylation in the presence of inhibitory receptors requires activating receptors. Therefore, Dr. Liu proposes the following working hypothesis: Crk serves as a two-way upstream 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 the 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. E.O. 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 molecular mechanisms of functional NK deficiency in patients with partial DiGeorge syndrome. After joining Baylor College of Medicine (BCM) in 2012, Dr. Liu continues to investigate the role of Crk in immune responses through multidisciplinary approaches, focusing on cutting-edging super-resolution stimulated emission depletion (STED) microscopy. For the first time, Dr. Liu demonstrated 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 in the Journal of Allergy and Clinical Immunology's 'The Editors' Choice' (http://www.jacionline.org/article/S0091-6749(15)00416-9/pdf). In addition to NK cell immunobiology in pDGS, Dr. Liu also invented the ***Vertical Cell Paring*** device for high-resolution immunological synapse (**IS**) imaging, as well as the role of PD-1 on NK cell IS.

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. Joon Hee Jang, Yu Huang, Peilin Zheng, Myeong Chan Jo, Grant Bertolet, Lidong Qin, **Dongfang Liu**§. Imaging of Cell-Cell Communication in a Vertical Orientation Reveals High-Resolution Structure of Immunological Synapse and Novel PD-1 Dynamics. ***Journal of Immunology.*** 2015 Aug 1; 195(3):1320-30. doi: 10.4049/jimmunol.1403143. Epub 2015 Jun 29. (PMID: 26123352).
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)

5. Development of superior NK and CAR-NK expansion technologies and CD147 as a valid target for tumors using CD147-CAR-NK cell therapy and CAR-NK for SARS-CoV-2 treatment. After joining Rutgers University-New Jersey Medical School (NJMS) in 2018, Dr. Liu continues investigating CAR-NK's role in cancers and infections. Dr. Liu developed a novel approach to rapidly expand primary NK and CAR-NK cells with superior expansion capability and *in vivo* cytotoxicity from various sources (including peripheral, cord blood, and tumor tissue). Meanwhile, Dr. Liu reports that both T and NK cells transduced with a CAR targeting the hepatocellular carcinoma (HCC) surface marker, CD147, also known as Basigin (BSG) or Extracellular Matrix MetalloProteinase Inducer (EMMPRIN), can be expanded long-term *ex vivo*. This study supports the therapeutic potential of 'off-the-shelf' CD147-CAR-NK cells in patients with HCC. In addition to CAR-NK cells for cancers and infections (e.g., SARA-CoV-2), Dr. Liu also developed a computational tool (e.g., machine learning) to study the IS of CAR cells by quantifying the quality of IS.

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. Tseng HC, Xiong W, Badeti S, Yang Y, Ma M, Liu T, Ramos CA, Dotti G, Fritzky L, Jiang JG, Yi Q, Guarrera J, Zong WX, Liu C, **Liu Dongfang**§. *Efficacy of anti-CD147 chimeric antigen receptors targeting hepatocellular carcinoma*. ***Nat Commun.*** 2020 Sep 23;11(1):4810. doi: 10.1038/s41467-020-18444-2. (PMID: 32968061).
3. Yan Yang, Aditya Badeti, Minh Ma, **Dongfang Liu**§. *Superior Expansion and Cytotoxicity of Human Primary NK and CAR-NK Cells from Various Sources via Enriched Metabolic Pathways*, ***Molecular Therapy-Methods and Clinical Development***, 2020, 18, 428-445. (PMID: 32695845).
4. **Naghizadeh, A.,** Tsao, W.C., Hyun Cho, J., Xu, H., Mohamed, M., Li, D., Xiong, W., Metaxas, D., Ramos, C.A., and **Liu, Dongfang**, 2022. In vitro machine learning-based CAR T immunological synapse quality measurements correlate with patient clinical outcomes. ***PLoS Computational Biology***, 18(3), p.e1009883. (PMCID: PMC8955962).

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