

Duke Division of Allergy and Immunology Duke Division of Pulmonary and Sleep Medicine IMMUNOGRAM

February 2020 Newsletter



John William Sleasman, MD Chief, Division of Allergy and Immunology Chief, Division of Pulmonary and Sleep Medicine Dr. Glenn A. Kiser and Eltha Muriel Kiser Professor of Pediatrics

ALLERGY AND IMMUNOLOGY

Rebecca H. Buckley, MD James Buren Sidbury Professor of **Pediatrics** Bernard M. Fischer, DVM, PhD Associate Professor of Pediatrics Julie Joo Yeon Kim-Chang, MD Assistant Professor of Pediatrics Mary Louise Markert, MD, PhD Professor of Pediatrics Talal I. Mousallem, MD Associate Professor of Pediatrics Amanda Pratt, MD Clinical Associate Amy Stallings, MD Associate Professor of Pediatrics Xiaoping Zhong, MD, PhD Professor of Pediatrics Virginia Labelle, CPNP

PULMONARY & SLEEP MEDICINE

Richard M. Kravitz, MD
Professor of Pediatrics
Mai ElMallah, MBBCh
Associate Professor of Pediatrics
Jason Lang, MD
Associate Professor of Pediatrics
Susanne Meghdadpour, FNP

Message from the Chief

This year's edition of our *Immunogram* is bittersweet. While our division is basking in the success of the *2019 Susan Dees Symposium*, the passing of our friend, mentor, and colleague Dr. Michael Frank saddens it. Overall, the Duke Divisions of Allergy and Immunology and Pulmonary and Sleep Medicine have had another successful year. As you will see, we are continuing to stride forward in research and training missions. I would like to thank everyone for their continued support of our program.

2019 Susan Dees Symposium, April 26 - 28, 2019



The 2019 Susan Dees Symposium, held at the Washington Duke Inn and & Golf Club in Durham, NC, was a resounding success. Jointly sponsored by the Duke Division of Allergy, Immunology, and Pulmonary Medicine, the University of North Carolina Division of Rheumatology, Allergy and Immunology, and North Carolina Asthma, Allergy and Immunology Society the conference had over 124 registrants including 69 Duke Allergy and Immunology alumni. The three day conference included topics ranging from asthma therapy to current topics in food allergy, to a workshop on pulmonary function testing for office staff. On Saturday afternoon there was a special symposium related to primary immune deficiency disorders sponsored by Duke Jeffrey Modell Diagnostic and Research Center featuring Dr. Sergio Rosenzweig, Chief of the Infectious Disease Susceptibility Unit at NIH. Seven past presidents of the American Academy of Allergy, Asthma and Immunology were in attendance with talks given by Drs. William Busse, Hugh Sampson, Allen Kaplan, and Dennis Ledford. Dr. Allen Meadows, current President of the American College of Allergy, Asthma and Immunology spoke on Sunday. Several former Duke Alumni were featured speakers including: Dr. Tim Moran, Assistant Professor at the University of North Carolina Chapel Hill and Dr. Benjamin Wright, Assistant Professor at the Mayo Clinic in Scottsdale, AZ. The banquet on Saturday night included Dr. Buckley giving a retrospective on the career of Dr. Susan Dees and Dr. David Peden providing his thoughts on the challenges facing the next generation of Allergists and Immunologists. The Symposium included industry sponsors whose financial support made the event possible.



Advocacy, Programs and Outreach

American Lung Association Airways Clinical Research Center Network (ALA ACRC)

Under the direction of Jason Lang, MD, the Division of Pulmonary and Sleep Medicine continues to serve as a key site in the ALA ACRC network, a multi-center clinical research trial network dedicated to treating asthma, COPD and other chronic lung conditions.

Program in Cultured Thymus Tissue Implantation, CTTI, (formerly referred to as Thymus Transplantation)

Our unique CTTI program to treat infants with complete DiGeorge anomaly continues to work toward the goal of a Biologic License Application (BLA) approval from the FDA. Duke has been working with the company Enzyvant on the BLA. Hopefully, an approval will be obtained for CTTI in the next 12 to 18 months. In the meantime, CTTI will continue under Dr. Markert's Investigational New Drug (IND) agreement with the FDA. Dr. Markert, in collaboration with her surgery colleagues, continues research with CTTI in two different areas, 1) use of CTTI to induce tolerance to solid organs (in a monkey model) and 2) use of CTTI to cure Autoimmune Polyglandular Syndrome Type 1 using a rat model.

Primary Immune Deficiency Foundation (IDF)

Rebecca Buckley, MD, serves as the chair of the IDF Medical Advisory Committee. Over the past year, she has continued her research focused on the long-term clinical and immunologic outcomes of Severe Combined Immune Deficiency (SCID) patients following non-ablative bone marrow transplantation. She made a presentation on this subject at the IDF National Meeting in June of 2019 and Olga Hardin, MD, one of our current second year fellows, will present a poster on the long term clinical outcome of these transplants at the upcoming CIS meeting in Denver in April, 2020.

Faculty Awards and Updates



Rebecca Buckley, MD

Dr. Buckley continues to receive national accolades. In May, 2019 she was named a Distinguished Fellow by the American Association of Immunologists and in the same month received an Honorary Degree of Doctor of Science from the University of North Carolina at Chapel Hill.



John Sleasman, MD

Dr. Sleasman led a Grifols sponsored, multi-center clinical trial to achieve FDA approval of a new 20% subcutaneous immunoglobulin, Xembify®, used for the treatment of antibody deficiency disorders.



Jason Lang, MD

Dr. Lang along with other associates was part of a team supported by *National Heart, Lung, and Blood Institute to* determine the best asthma care for African American children with poorly controlled asthma. They

found differences in responses to commonly used treatments for the children enrolled in the study that will help shape the management of asthma in high-risk populations. Their findings were published in September 2019 in the New England Journal of Medicine.

New Faculty and Fellows



Amanda Pratt, MD

After growing up outside of Dallas in Plano, Texas, I attended the University of North Carolina at Chapel Hill and graduated with degrees in biology and Spanish. I then attended medical school at Georgetown University in Washington, DC, but returned

to Chapel Hill to do my Pediatrics Residency at UNC. After that I completed my Allergy & Immunology Fellowship at Vanderbilt University in Nashville, Tennessee. I spent a year working in primary care while my husband was finishing his Internal Medicine Residency at Vanderbilt before joining Duke in the Pediatric Allergy Department on October 1st, 2019. My clinical interest is in food allergy. My husband Elias is a first year Pulmonary and Critical Care Medicine Fellow here at Duke. We have two children-Josiah is 2 ½ and Lorelei is 6 months old. We are excited to be back in the triangle area and part of the Duke Family!



Pooja Purswani, MD

Dr. Purswani is a native of Greensboro, North Carolina. She completed her undergraduate education at UNC Chapel Hill, and graduated from medical school at The Brody School of Medicine at ECU. She is coming to Duke from residency in Pediatrics at Johns

Hopkins All Children's Program in St. Petersburg, Florida. She is a former participant in the AAAAI Chrysalis Program, and is currently in the Clinical and Translational Research (CTRT) Program in St. Petersburg. We are so excited to bring Dr. Purswani back home to North Carolina!



Alex Wonnaparhown, MD

Dr. Wonnaparhown is a native of Las Vegas, Nevada. He completed his undergraduate work at UCLA and is a graduate of the University of Nevada-Reno School of Medicine. He is coming to Duke from Internal Medicine Residency at UCLA. His research experience and inter-

ests include rhinosinusitis in immunodeficient patients, as well as hypersensitivity to radiocontrast media. We are thrilled to welcome Dr. Wonnaparhown to Duke!

Fellowship Corner





After completion of her T32 training in genomics program in June 2019, Dr. Baloh remained at Duke in the Pediatric Division of Allergy Immunology and Pulmonary Medicine to have an additional year of research time as a 4th year advanced research

fellow. She is continuing to build her research portfolio in the genomics of primary immunodeficiency diseases. She is currently interviewing for faculty positions.



Anusha Vadlamudi, MD

After completion of her fellowship in July 2019, Dr. Vadlamudi began working as a private practice allergist at Allergy Partners in Wilmington, NC. She provides comprehensive Allergy, Asthma, and Immunology care for children and adults in a clinic setting and also serves as a consultant for

the New Hanover Regional Medical Center.



Tyler Yates, MD

After completion of his fellowship in June of 2019, Dr. Yates was appointed Assistant Professor of Pediatric Allergy and Immunology at Oregon Health and Sciences University in Portland, Oregon. He established the first pediatric Aller-

gy/Immunology subspecialty clinic at this institution, is the site principal investigator for the Primary Immune Deficiency Treatment Consortium and is the immunologist consultant for the Northwest Regional Newborn Screening Program in addition to his responsibilities as an educator at the medical school and pediatric residency program.





research in asthma mechanisms of disease and novel treatments.



Duke/UNC T32 Research Training in Allergy and Clinical Immunology Updates

Carolyn Baloh, MD

4th year Duke Al fellow; her research area of genomics primary the of immunodeficiency diseases, with current work focusing on the genomics of 22q11.2 deletion syndrome. Dr. Baloh is supported by Duke's Allergy Immunology T32.

John W. Sleasman MD, Vandana Shashi MBBS, MD, & Louise Markert PhD, MD

Johanna Smeekens, PhD

3rd Year Post-Doc with the UNC Food Allergy Initiative. Research focuses on understanding the factors influencing sensitization in the gut of CC027/GeniUnc mice by quantifying peanutspecific IgA, and Tregs in Peyer's patches and mesenteric lymph nodes, and manipulating the microbiome.

Mentors: Wesley Burks, MD and Mike Kulis, PhD

Edward Iglesia, MD, MPH

2nd Year UNC Allergy/Immunology Fellow Research focuses on food allergy prevention in clinical and public health practice.

Mentors: Michelle Hernandez, MD and Edwin Kim,

MD, MS

Mark Ihrie, PhD

2nd year Postdoc in the Duke Department of Medicine, Division of Pulmonary, Allergy and Critical Care Medicine; research focuses on how metabolic changes in obesity influence inflammation and airway remodeling in asthma.

Mentor: Jennifer Ingram, PhD

Jacob T. Kilgore, MD 3rd year Duke Pediatric Infectious Diseases fellow and May 2020 MPH candidate at the UNC Gillings School of Global Public Health; research focus is antimicrobial stewardship within immunecompromised hosts with specific emphasis on thymic hypoplasia patients.

Mentors: Michael J. Smith, MD, MSCE and John Sleasman, MD

AAAAI Highlights for Faculty and Fellows

Carolyn Baloh, MD:

Abstract: Predicting Autoimmunity Devel-

opment in 22g11.2DS

Session: Clinical Presentation of Immuno-

deficiency Disorders

Date: Saturday, March 14, 2020

Time: 3:00 pm—3:15 pm

Suzanne Barshow, MD:

Case Report: Complexity of Hypererosinophilia Evaluation in a Patient with Chronic

Eosinophilic Pneumonia

Location: Pennsylvania Convention Cen-

ter, 200 Level, Halls D-E

Date: Saturday, March 14, 2020

John W. Sleasman, MD:

Abstract: "Immune globulin subcutaneous, human – klhw 20% solution (Xembify®, IGSC-C 20%) is effective in primary humoral immunodeficiency (PI): results from a prospective, open-label, multi-

center, phase 3 study"

Location: Convention Center, 200 Level, Hall D

Date: Saturday, March 14, 2020

Time: 10:45 am



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New Grant Awards

1R01HD099486-01 (PI Elmallah) National Institute of Health

Targeted Therapy for Pompe Disease

The goal is to comprehensively examine smooth muscle involvement with and without ERT and target the global disease – cardiac, skeletal and smooth muscle as well as respiratory neurons - using adeno-associated virus gene therapy. 09/01/2019 – 05/31/2020

Sarepta Thearapeutics (PI Elmallah)

Respiratory Characterization of DMD Mouse Models

The goal is to impact the clinical treatment of DMD because respiratory failure is the leading cause of death in DMD.

11/25/2019 - 11/24/2022

Enzyvant (PI Markert)

Use of cultured thymus tissue implantation to treat APECED in a rat model. Show that CTTI can cure APECED in a rat model. 1/1/2020 to 12/31/2020

Jeffrey Modell Foundation (PI Markert)
Use of cultured thymus tissue implantation to treat
APECED in a rat model. Major Goals: Show that
CTTI can cure APECED in a rat model.
1/1/2020 to 12/31/2020

Pfizer-NC Biotech Distinguished Postdoctoral Fellowship in Gene Therapy (Pl Angela McCall) A Novel Vector to Treat Smooth Muscle Pathology in Pompe Disease.

CCRX011-19 (PI Elmallah) Cystic Fibrosis Foundation

Award for a Pharmacist

The goal is to support a clinical pharmacist who provides care to the pediatric CF patients, allowing the pharmacist to be present in every CF clinic for the full clinic time and committing dedicated time to implementing outpatient clinical pharmacy services for all pediatric CF patients at DUHS. 04/01/2019 - 03/31/2020

Publications

M.E. Wechsler, S.J. Szefler, V.E. Ortega, J.A. Pongracic, V. Chinchilli, J.J. Lima, J.A. Krishnan, S.J. Kunselman, D. Mauger, E.R. Bleecker, L.B. Bacharier, A. Beigelman, M. Benson, K.V. Blake, M.D. Cabana, J.-C. Cardet, M. Castro, J.F. Chmiel, R. Covar, L. Denlinger, E. DiMango, A.M. Fitzpatrick, D. Gentile, N. Grossman, F. Holguin, D.J. Jackson, H. Kumar, M. Kraft, C.F. LaForce, **J. Lang,** S.C. Lazarus, R.F. Lemanske, Jr., D. Long, N. Lugogo, F. Martinez, D.A. Meyers, W.C. Moore, J. Moy, E. Naureckas, J.T. Olin, S.P. Peters, W. Phipatanakul, L. Que, H. Raissy, R.G. Robison, K. Ross, W. Sheehan, L.J. Smith, J. Solway, C.A. Sorkness, L. Sullivan-Vedder, S. Wenzel, S. White, and E. Israel, for the NHLBI AsthmaNet* . Step-Up Therapy in Black Children and Adults with Poorly Controlled Asthma . N Engl J Med 2019;381:1227-39. DOI: 10.1056/NEJMoa1905560 Copyright © 2019 Massachusetts Medical Society.

Lang JE., Obesity and childhood asthma. Curr Opin Pulm Med. 2019 Jan;25(1):34-43.

Amatuni GS, Currier RJ, Church JA, Bishop T, Grimbacher E, Nguyen AA, Agarwal-Hashmi R, Aznar CP, Butte MJ, Cowan MJ, Dorsey MJ, Dvorak CC, Kapoor N, Kohn DB, **Markert ML**, Moore TB, Naides SJ, Sciortino S, Feuchtbaum L, Koupaei RA, Puck JM. Newborn Screening for Severe Combined Immunodeficiency and T-cell Lymphopenia in California, 2010-2017. Pediatrics. 2019 Feb;143(2). pii: e20182300. doi: 10.1542/peds.2018-2300. PMID: 30683812

Lang JE., The impact of exercise on asthma. Curr Opin Allergy Clin Immunol. 2019 Apr;19(2):118-125.



Publications (Cont'd)

Farmer JR, Foldvari Z, Ujhazi B, De Ravin SS, Chen K, Bleesing JJH, Schuetz C, Al-Herz W, Abraham RS, Joshi AY, Costa-Carvalho BT, Buchbinder D, Booth C, Reiff A, Ferguson PJ, Aghamohammadi A, Abolhassani H, Puck JM, Adeli M, Cancrini C, Palma P, Bertaina A, Locatelli F, Di Matteo G, Geha RS, Kanariou MG, Lycopoulou L, Tzanoudaki M, **Sleasman JW**, Parikh S, Pinero G, Fischer BM, Dbaibo G, Unal E, Patiroglu T, Karakukcu M, Al-Saad KK, Dilley MA, Pai SY, Dutmer CM, Gelfand EW, Geier CB, Eibl MM, Wolf HM, Henderson LA, Hazen MM, Bonfim C, Wolska-Kuśnierz B, Butte MJ, Hernandez JD, Nicholas SK, Stepensky P, Chandrakasan S, Miano M, Westermann-Clark E, Goda V, Kriván G, Holland SM, Fadugba O, Henrickson SE, Ozen A, Karakoc-Aydiner E, Baris S, Kiykim A, Bredius R, Hoeger B, Boztug K, Pashchenko O, Neven B, Moshous D, Villartay JP, Bousfiha AA, Hill HR, Notarangelo LD, Walter JE. Outcomes and Treatment Strategies for Autoimmunity and Hyperinflammation in Patients with RAG Deficiency. *J Allergy Clin Immunol Pract*. 2019 Jul - Aug;7 (6):1970-1985.e4. doi: 10.1016/j.jaip.2019.02.038. Epub 2019 Mar 12.

Kim-Chang JJ, Wilson L, Chan C, **Fischer B, Venturi G,** Goodenow MM, Aldrovandi G, Weber TJ, **Sleasman JW**; Adolescent Medicine Trials Network for HIV/AIDS Interventions. Tenofovir Has Minimal Effect on Biomarkers of Bone Health in Youth with HIV Receiving Initial Antiretroviral Therapy. *AIDS Res Hum Retroviruses.* 2019 Aug;35(8):746-754. doi: 10.1089/AID.2018.0270. Epub 2019 Jun 27.

Bosticardo M, Yamazaki Y, Cowan J, Giardino G, Corsino C, Scalia G, Prencipe R, Ruffner M, Hill DA, Sakovich I,Yemialyanava I, Tam JS, Padem N, Elder ME, **Sleasman JW**, Perez E, Niebur H, Seroogy CM, Sharapova S, Gebbia J, Kleiner GI, Peake J, Abbott JK, Gelfand EW, Crestani E, Biggs C, Butte MJ, Hartog N, Hayward A, Chen K, Heimall J, Seeborg F, Bartnikas LM, Cooper MA, Pignata C, Bhandoola A, Notarangelo LD. Heterozygous FOXN1 Variants Cause Low TRECs and Severe T Cell Lymphopenia, Revealing a Crucial Role of FOXN1 in Supporting Early Thymopoiesis. *Am J Hum Genet*. 2019 Sep 5;105(3):549-561. doi: 10.1016/j.ajhg.2019.07.014. Epub 2019 Aug 22.

Du Q, Huynh LK, Coskun F, Molina E, King MA, Raj P, Khan S, Dozmorov I, Seroogy CM, Wysocki CA, **Padron GT, Yates TR**, **Markert ML**, de la Morena MT, van Oers NS. FOXN1 compound heterozygous mutations cause selective thymic hypoplasia in humans. *J Clin Invest.* 2019 Nov 1;129 (11):4724-4738. doi: 10.1172/JCI127565. PMID: 31566583

Sleasman JW, Lumry WR, Hussain I, Wedner HJ, Harris JB, Courtney KL, Mondou E, Lin J, Stein MR. Immune globulin subcutaneous, human - klhw 20% for primary humoral immunodeficiency: an open-label, Phase III study. *Immunotherapy*. 2019 Nov;11(16):1371-1386. doi: 10.2217/imt-2019-0159. Epub 2019 Oct 17.

Pan Y, Deng W, Xie J, Zhang S, Wan CK, Li L, Tao H, Hu Z, Chen Y, Ma L, Gao J, and **Zhong XP**. Graded diacylglycerol kinases a and z activities ensure mucosal-associated invariant T cell development. (2019) *Eur J Immunol*. 2019 Nov 11. doi: 10.1002/eji.201948289

Dvorak CC, Haddad E, **Buckley RH**, Cowan MJ, Logan B, Griffith LM, Kohn DB, Pai S-Y, Notarangelo LD, Shearer W, Prockop S, Kapoor N, Heimal J, Chaudhury S, Shyr D, Chandra S, Cuvelier G, Moore T, Shenoy S, Goldman F, Smith AR, Sunkersett G, Vander Lugt, Caywood E, Quigg T, Torgerson T, Chandrakasan S, Craddock J, Saidana BJD, Gillio A, Shereck E, Aquino V, DeSanto K, Knutsen A, Thaker M, Yu L, Puck JM.: The genetic landscape of SCID in the US and Canada in the current era (2010-2018). *Allerg. Clin. Immunol.* 143: 405-407, 2019. PM: 30193840

Buckley RH: SCID: A pediatric emergency. *North Carolina Medical Journal* 80: 55-56, 2019. PM: 30622209

Keeler A.M, Zieger M., Semple C., Pucci L., Veinbachs A., Brown Jr, R.H., Meuller C., **ElMallah M.K.** (2019) MIntralingual and Intrapleural AAV Gene Therapy Prolongs Survival in a SOD1 ALS Mouse Model. Molecular Therapy Methods and Clinical Development. 17: 246-257



Publications (Cont'd)

- Han S.-O., Li S., McCall A.L., Arnson B., Everitt J., Zhang H., Young S., **ElMallah M.K.,** Koeberl D. (2019) Comparisons of infant and adult mice reveal age effects for liver depot gene therapy in Pompe disease. Molecular Therapy Methods and Clinical Development. 17: 133-142
- **McCall A.L. and ElMallah M.K**. Macroglossia, Motor Neuron Pathology and Airway Malacia Contribute to Respiratory Insufficiency in Pompe Disease: A Commentary on Molecular Pathways and Respiratory Involvement in Lysosomal Storage Diseases. (2019) In J Mol Sci 20: 751
- **Kim-Chang JJ,** Donovan K, Loop MS, Hong S, **Fischer B, Venturi G,** Garvie PA, Kohn J, Rendina HJ, Woods SP, Goodenow MM, Nichols SL, **Sleasman JW**; Adolescent Medicine Trials Network for HIV/AIDS Interventions. Higher soluble CD14 levels are associated with lower visuospatial memory performance in youth with HIV. Adolescent Medicine Trials Network for HIV/AIDS Interventions. *AIDS*. 2019 Dec 1;33(15):2363-2374. doi: 10.1097/QAD.00000000000002371.
- Byrne B.J., Fuller D.D., Smith B.K., Clement N., Coleman K., Cleaver B., Vaught L., Falk D.J., **McCall A.L.,** Reduction of Autophagic Accumulation in a Pompe Disease Mouse Model Following Gene Therapy. Corti M. (2019). *Current Gene Therapy*.19(3): 197-207
- Byrne B.J., Fuller D.D., Smith B.K., Clement N., Coleman K., Cleaver B., Vaught L., Falk D.J., **McCall A.L.**, Corti M. Pompe Disease Gene Therapy: Neural Manifestations Require Consideration of CNS Therapy. (2019). *Annals of Translational Medicine*. 7(13): 290
- Chen P, Deng W, Li D, Zeng T, Huang L, Wang Q, Wang J, Zhang W, Yu X, Duan D, Wang J, Xia H, Chen H, Huang W, Li J, Zhang D, **Zhong XP*** Gao J. Circulating Mucosal-Associated Invariant T Cells in a Large Cohort of Healthy Chinese Individuals From Newborn to Elderly. (2019) Front Immunol. 10:260. doi: 10.3389/fimmu.2019.00260.
- Xie J, Pan Y, Tao H, Wang P, Chen Y, Gao J, and **Zhong XP** (2019). Deficiency of Mucosal-Associated Invariant T Cells in TCRJα18 Germline Knockout Mice. ImmunoHorizons 3 (6) 203-207; DOI: https://doi.org/10.4049/immunohorizons.1900035
- Chen P, Wang S, Janardhan KS, Zemans RL, Deng W, Karmaus P, Shen S, Sunday M, Que LG, Fessler MB, and **Zhong XP** Efficient CD4-Cre mediated conditional KRas expression in alveolar macrophages and alveolar epithelial cells causes fatal hyperproliferative pneumonitis. (2019) J Immunol 203(5):1208-1217. doi: 10.4049/jimmunol.1900566. PMID: 3131588
- Hu S, Fu Y, Zhan X, Wang Y, Jiang X, Liu M, Yang Y, Huang Y, Du X, **Zhong XP**, Li L, and Ma L. NLRC3 expression in dendritic cells attenuates CD4+ T cell response and autoimmunity. (2019) EMBO J. 38 (16):e101397. doi: 10.15252/embj.2018101397.
- Zieger M., Keeler A.M., Flotte T.R., **ElMallah M.K**. AAV9 Gene Replacement Therapy for Respiratory Insufficiency in Very Long Chain acyl-CoA Dehydrogenase Deficiency. J. Inherit Metab Dis. 42(5): 870-877
- **McCall A.L.,** Stankov S.G., Cowen G., Cloutier D., Zhang Z., Yang Y., Clement N., Falk D.J., Byrne B.J Reduction of Autophagic Accumulation in a Pompe Disease Mouse Model Following Gene Therapy. (2019) *Current Gene Therapy*. 19(3): 197-207
- **McCall A.L.,** Stankov S.G., Cowen G., Cloutier D., Zhang Z., Yang Y., Clement N., Falk D.J., Byrne B.J Reduction of Autophagic Accumulation in a Pompe Disease Mouse Model Following Gene Therapy. (2019) *Current Gene Therapy*. 19(3): 197-207
- Tao H, Li L, Gao Y, Wang Z, and **Zhong XP** Differential control of iNKT cell effector lineage differentiation by the Forkhead Box Protein O1 (Foxo1) transcription factor. (2019) Front. Immunol. 10:2710. doi: 10.3389/fimmu.2019.02710



Publications (Cont'd)

Pan Y, Deng W, Xie J, Zhang S, Wan CK, Li L, Tao H, Hu Z, Chen Y, Ma L, Gao J, and **Zhong XP**. Graded diacylglycerol kinases a and z activities ensure mucosal-associated invariant T cell development. (2019) Eur J Immunol. 2019 Nov 11. doi: 10.1002/eji.201948289

Yang J, Wang HX, Xie J, Li L, Wang J, Wan ECK, and **Zhong XP** (2019). DGK α and ζ Activities Control TH1 and TH17 Cell Differentiation. Front Immunol. doi:10.3389 /fimmu.2019.03048



In Memorandum Dr. Michael M. Frank



Michael Frank, MD, passed away with his family at his side on Thursday, August 1, 2019. Dr Frank was born in Brooklyn, New York, in 1937. In one of his recollections, he pointed out that his interest in immunology began before he was 10 years old when he read Paul de Kraif's Microbe Hunters. This early fascination set the stage for his lifelong interest in how antibody and

complement control microorganisms can contribute to tissue damage. Mike's brilliance and potential were recognized early on when he received a Ford Foundation Scholarship to attend the University of Wisconsin–Madison at age 15 years. There he met the microbial biologist and future Nobel Laureate Joshua Lederberg, Lederberg suggested that Mike get a PhD in microbiology; however, Mike decided to go to medical school. He graduated from Harvard Medical School in 1960 and did an internship in medicine at Boston City Hospital and later an internship in pediatrics at Johns Hopkins. Mike came to the National Institutes of Health (NIH) for 2 years, working in the laboratories of Herb Rapp and Tibor Borsos in the National Institute of Mental Health, where he discovered the dependence of complement components on divalent cations and their sensitivity to reducing agents. Mike then spent a year at the Mill Hill Medical Research Laboratories in London, England, where he worked with Dr. J. H. Humphrey, studying the distribution of antigens in draining lymph nodes, the structure of IgM, and electron microscopic imaging of complement lysis of red cells.

Mike returned to the NIH as a senior investigator and quickly became Head of the Clinical Immunology Section in the Laboratory of Clinical Investigation at the National Institute of Allergy and Infectious Diseases (NIAID). In 1977, he was appointed Clinical Director of the NIAID and Chief of the NIAID's Laboratory of Clinical Investigation, positions he held for 13 years. It was during this time that Mike began the groundbreaking work for which he is best known. He collected a cohort of patients with hereditary angioedema (HAE), which at the time had a mortality rate of 20%. In a series of landmark articles, he identified multiple strategies to treat HAE caused by C1 esterase inhibitor deficiency using epsilon-aminocaproic acid, fresh frozen plasma, the androgen derivative danazol, and C1 inhibitor concentrates. Said John Atkinson, "Mike was largely responsible for the development of two successful therapies for HAE at a time when we had no treatment." His approach became used worldwide for prophylaxis and for treatment of acute HAE attacks.

Working with Baruch Benacerraf, Ira Green, and Lenny Ellman, Mike's laboratory identified C4 deficiency in the guinea pig, a model in which there was no detectable classical complement pathway function. John Atkinson noted, "I joined Mike Frank's laboratory at a great time." Mike's model provided many insights into the role of alternative versus classical complement pathways in immunopathologic settings. These insights delineated the function of complement and Fcy receptors in human

subjects; Mike showed in animals and then in human subjects that IgG-sensitized red blood cells are removed by Fc receptors in the spleen. In another landmark study he demonstrated impaired Fc receptor-mediated clearance in patients with systemic lupus erythematosus and dermatitis herpetiformis and performed a prospective study of serum sickness in patients treated with antithymocyte globulin; the latter provided an in-depth immunologic analysis of a disease identified in the early 20th century. Reflecting on his experience, Tom Lawley said, "Mike was a wonderful person and a great mentor." Mike also identified impaired immune responses of splenectomized patients to pneumococcal vaccination. Tony Fauci summed up Mike's years at the NIH, saying, "It was such a pleasure to have Mike as a colleague for so many years at NIAID. He was an extraordinarily creative basic and clinical investigator and a devoted mentor to so many future stars in biomedical research." An NIAID colleague, Warren Strober concluded, "Straightforward, sturdy and serious; you know where you stood with Mike Frank. The perfect complement to NIAID."

Mike was recruited to be Chair of the Department of Pediatrics at Duke, where he served from 1990 to 2004. Rebecca Buckley noted, "In the 14 years he was Chairman, Mike accomplished an amazing number of things, including doubling the number of faculty, building a new Children's Health Center (for which he had to raise all of the money through his Pediatric Development office), improving enormously the fiscal situation in the department, and advancing the level of NIH research funding in the Department so that we were ranked 10th in the nation among pediatric departments in that regard." Duke Children's Health Center is widely regarded as a top children's hospital and remains a legacy to his perseverance and drive.

Mike was a consummate physician-scientist. He followed his childhood dream spurred by de Kraif's book and substantially advanced our basic understanding of the biology of the complement system. Equally important, he contributed substantially to treating HAE and understanding complement and Fc receptors in human subjects. Throughout his career, Mike was a wonderful mentor to many young investigators who have gone on to major leadership roles in academia. John O'Shea pointed out how fortunate he was to be in Mike's laboratory, learning serious biochemistry with a group of dedicated rigorous scientists. Notably, the American Academy of Allergy, Asthma & Immunology Foundation recently honored his life's work with the creation of the Michael M. Frank, MD, FAAAAI, Lectureship.

Another NIH colleague, Dean Metcalfe, summed it up as follows: "Mike was a true gentleman with unrivaled sincerity and compassion for medical education and research and will be greatly missed." John Gallin echoed these sentiments: "Mike set a very high bar for excellence in science for everyone around him. Those of us who collaborated with Mike benefited tremendously from his extraordinary insight and talent. It was a privilege to work with him.



J Allergy Clinical Immunology 2019 John J. O'Shea, MD and John I. Gallin, MD

Upcoming Events

Duke/UNC Joint AAAAI Alumni Dinner Sunday, March 15, 2020 Maggiano's Little Italy **1201 Filbert Street** Philadelphia, PA 19107 (215) 567-2020

Dinner: 6:00 - 9:00 pm

Cash Bar

Payment of \$50.00 if Paid by March 3, 2020 Payment of \$70.00 if Paid On-Site Cash and Checks Accepted (No Credit Cards) **RSVP Soon - Seats Are Limited**

Make Checks Payable to: Duke University

Mail to: **Debbie Preddy**

Duke University Medical Center

Box 2644

Durham, NC 27710

April 14, 2020 Rebecca Buckley Lectureship **Grand Rounds** Harry L. Malech, MD **Chief, Genetic Immunotherapy Section** Deputy Chief, Laboratory of Clinical Immunology and Microbiology National Institute of Allergy and Infectious Diseases, NIH

August 2020 Jeffrey Modell Kidd's Day Durham Bulls Ball Park Stadium

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