BIOGRAPHICAL SKETCH

NAME: Judith A. James, MD, PhD

POSITION TITLE: OMRF: Vice President of Clinical Affairs; Member; Lou Kerr Chair in Biomedical Research; Program Chair, Arthritis & Clinical Immunology. OUHSC: Associate Vice Provost for Clinical & Translational Science; Professor of Medicine; Adjunct Professor of Pathology and of Micro & Immunology

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

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
Oklahoma Baptist University, OK	BS	05/1989	Chemistry, Math
University of Oklahoma Health Sciences Center, OK	PhD	05/1993	Micro & Immunology
University of Oklahoma Health Sciences Center, OK	MD	12/1994	Medicine

A. Personal Statement

My research group is focused on understanding the etiology and pathogenesis of systemic autoimmune diseases, such as systemic lupus erythematosus, as well as immune responses to select infections and vaccinations. Our group has over 25 years of experience in characterizing human humoral immune responses to autoantigens, deciphering etiologic triggers, defining early events in lupus autoimmunity, and identifying immune changes associated with disease flare and therapeutic response. In addition, I serve as principal investigator of the Oklahoma Autoimmunity Center of Excellence (NIAID), Oklahoma Rheumatic Disease Research Cores Center (NIAMS), Oklahoma Shared Clinical and Translational Resources (NIGMS), and a Native American Research Center for Health grant (NIGMS) to understand autoimmune rheumatic disease in Oklahoma tribal members**.** These grants support crucial resources for patient-oriented research in autoimmunity. Through these and philanthropic funds, we have built and grown a CAP-Certified Biorepository which serves the AMP RA/Lupus, multiple ACE clinical trials and other NIH-funded projects. I also have extensive experience in designing and analyzing mechanistic studies with trials. Through my senior leadership roles as a department head and with the aforementioned grants, I have extensive experience in collaborative research, and I have published >300 peer-reviewed publications. I have a broad background in clinical immunology, humoral autoimmunity, complex human genetics, rheumatology and patient-oriented investigation. In summary, I have a demonstrated record of successful and productive research projects in an area of high relevance for immunology and autoimmune disease research. I would be honored to apply this experience as a consultant for this project.

a. Slight-Webb S, Guthridge JM, Smith M… **James JA.** Autoantibody-positive healthy individuals with lower risk display a suppressive immune endotype. *J Allergy Clin Immunol.* 2020 May 22: S0091-6749(20)30675-8. PMCID: PMC6901719
b. **James JA**, Chen H, Young KA…Norris JM, Holers VM. Latent autoimmunity across disease-specific boundaries in at-risk first-degree relatives of SLE and RA patients. *EBioMedicine*. 2019 Apr; 42:76-85. PMCID: PMC6491794
c. Jog NR, Young KA, Munroe ME, Harmon MT, Guthridge JM…Norris JM, **James JA**. Association of Epstein-Barr virus serological reactivation with transitioning to systemic lupus erythematosus in at-risk individuals. *Ann Rheum Dis.* 2019 Sep; 78(9):1235-1241. PMCID: PMC6692217
d. Munroe ME, Young KA, Kamen DL, Guthridge JM…Norris, JM, **James JA**. Discerning risk of disease transition in relatives of systemic lupus erythematosus patients utilizing soluble mediators and clinical features. *Arthritis Rheumatol.* 2017; 69(3):630-642. PMCID: PMC5329053

B. Positions and Honors

Positions and Employment

1999-2001 Assistant Professor, Departments of Medicine and Pathology, OUHSC, OKC, OK
1998-2006 Assistant then Associate Member, Oklahoma Medical Research Foundation, OKC, OK
2001-2005 Associate Professor, Departments of Medicine and Pathology, OUHSC, OKC, OK
2005-Present Professor of Medicine and Adjunct Professor of Pathology, OUHSC, OKC, OK

2006-Present Member and Lou Kerr Chair in Biomedical Research, OMRF, Oklahoma City, OK
2009-Present Member and Chair, Arthritis & Clinical Immunology, OMRF, Oklahoma City, OK
2010-Present George Lynn Cross Research Professor, OUHSC, OKC, OK
2013-Present Associate Vice Provost for Clinical & Translational Science, OUHSC, OKC, OK
2017-Present Vice President of Clinical Affairs, OMRF, OKC, OK

Selected Honors and National Service

2001 AAI Young Investigator Travel Award, Orlando, FL; FOCIS Young Investigator Travel Award, Boston, ME; NIAID Roundtable Planning Session, Boston, ME; NIAMS Strategic Planning Session, Bethesda, MD; Study Section, NIAMS, R03 Projects, Bethesda, MD. **2002** Henry Kunkel Society Membership; Rheumatology Regional Consultants Meeting Chair, Dallas, TX; Aesculapian Outstanding Medical Student Teaching Award Finalist. **2003** American Society of Clinical Investigation Election. **2003-07** NIAMS AMS Study Section. **2004** Edward L. & Thelma Gaylord Prize for Scientific Achievement. **2005** OU Health Sciences Center Regent's Award for Superior Research and Creative Activity. **2005-06** NIH NIAMS Lupus Strategic Planning Panel Member. **2007** American College of Rheumatology Dubois Lectureship for Outstanding Lupus Research, Boston, MA. **2008-10** National Association of IDeA PI Council, Central Region Elected Member. **2008-10** Kirkland Scholar, Hospital for Special Surgery, NY. **2010** George Lynn Cross Research Professor, OUHSC. **2008-12** NIAID AITRC Study Section. **2009-19** Autoimmunity Centers of Excellence Steering Committee. **2010-14** NIH/NIAMS Board of Scientific Counselors. **2012-15** Secretary-Treasurer, American Society for Clinical Investigation. **2013** Edward L. & Thelma Gaylord Prize for Scientific Achievement. **2014-Present** NIAMS Intramural Research Program Planning Committee. **2015-16** Chair NIH/NIAMS Board of Scientific Counselors; **2016-present** NIAMS Scientific Advisory Council Member; **2019-Present** Chair NIAMS Council Planning Committee; **2019-Present** NIAID Autoimmunity Center of Excellence Clinical Co-Chair, ACE Steering Committee; **2019** Paul Klemperer, MD, Memorial Lectureship, ACR; **2019**: Evelyn V. Hess Award, Lupus Res Found; **2020** Stanley J. Korsmeyer Award, American Society for Clinical Investigation; **2021:** Member, American Association of Physicians

C. Contribution to Science

1. Provided Critical Understanding of Early Preclinical Events in Systemic Autoimmunity. A major focus of my research career is understanding early autoantibody production to provide insights for treating or preventing autoimmune diseases. My work has documented the timing and possible mechanisms of autoantibody development in preclinical SLE. We showed that autoantibodies are present years before SLE diagnosis; anti-dsDNA antibodies are associated with renal disease and typically precede signs of nephritis; and antibodies to Ro/SSA appear years before SLE classification and cross-react with Epstein-Barr nuclear antigen 1, a suspected etiological factor for SLE. We identified unique inflammatory mediator profiles associated with anti-nuclear autoantibodies, delineated a progression of immune dysregulation in individuals moving from initial autoimmunity to SLE classification, and defined combinations of autoantibodies and soluble mediators that may predict SLE risk (see below and section A). I served as senior or co-senior investigator on these studies.

a. Arbuckle MR, McClain MT…**James JA**, et al. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. *N Engl J Med.* 2003; Oct 16; 349(16):1526-33. PMID: 14561795
b. McClain MT, Heinlen LD, Dennis GJ, Roebuck J…**James JA**. Early events in lupus humoral autoimmunity suggest initiation through molecular mimicry. *Nat Med.* 2005 Jan; 11(1):85-9. PMID: 15619631
c. Munroe ME, Young KA, Kamen DL, Guthridge JM…**James JA**. Discerning risk of disease transition in relatives of systemic lupus erythematosus patients utilizing soluble mediators and clinical features. *Arthritis Rheumatol.* 2017; 69(3):630-642. PMCID: PMC5329053
d. Lu R, Munroe ME, Guthridge JM, Bean KM…**James JA**. Dysregulation of innate and adaptive serum mediators precedes systemic lupus erythematosus classification and improves prognostic accuracy of autoantibodies. *J Autoimmun.* 2016;Nov; 74:182-193. PMCID: PMC5079766

2. Initial and Confirmatory Description of Humoral Epitope Spreading in Human Autoimmune Disease. The spliceosome is a major target of SLE autoimmunity, and responses recognizing Sm antigens of the spliceosome progress to recognize the structurally related nuclear ribonucleoprotein (nRNP) autoantigen. These seminal studies provided direct evidence of epitope spreading in the humoral responses to Sm and nRNP, and linked epitope spreading in the Ro/SSA and La/SSB system to Sm and nRNP responses. Rabbits immunized with antigenic 60 kDa Ro/SSA peptides develop diverse responses against Sm and nRNP, which reflect those seen in humans. Rabbits immunized with antigenic Sm peptides develop autoantibodies to other spliceosomal proteins, as well as lupus-like pathology. Various strains of mice immunized with antigenic Sm

peptides develop autoantibodies that react with additional regions of Sm B/B' and Sm D, followed by additional epitope spreading with specificities directed against dsDNA. Together with our analyses of autoimmunity progression in humans, our contributions in this area provided the first description of human humoral epitope spreading, which has served as the premise for new work in other lupus autoantigens (see SciENCV and below) and by others in autoimmune diseases like type 1 diabetes and rheumatoid arthritis. I served as primary or senior investigator on all of these studies.

a. **James JA**, Gross T, Scofield RH, Harley JB. Immunoglobulin epitope spreading and autoimmune disease after peptide immunization: Sm B/B'-derived PPPGMRPP and PPPGIRGP induce spliceosome autoimmunity. *J Exp Med.* 1995; 181(2):453-61. PMCID: PMC2191871
b. **James JA**, JB Harley. A model of peptide-induced lupus autoimmune B cell epitope spreading is strain specific and is not H-2 restricted in mice. *J Immunol.* 1998; 160(1):502-8. PMID: 9552009
c. Poole BD, Schneider RI, Guthridge JM…**James JA**. Early targets of nuclear RNP humoral autoimmunity in human systemic lupus erythematosus. *Arthritis Rheumatol.* 2009; 60(3):848-59. PMCID: PMC2653589
d. Jog N, McClain MT, Heinlen LD…**JA James**. Epstein Barr Virus Nuclear Antigen 1 (EBNA-1) peptides recognized by adult multiple sclerosis patient sera induces neurologic symptoms in a murine model. *J Autoimmun.* 2020 Jan; 106:102332. PMCID: PMC6930324

3. Dissecting Molecular Heterogeneity in Systemic Autoimmune Rheumatic Diseases. The molecular heterogeneity of systemic autoimmune rheumatic diseases hinders diagnosis, management, and treatment development. We have identified multi-dimensional molecular and immune profiles that distinguish unique subsets of autoimmune disease patients through machine learning on detailed clinical, autoantibody, soluble mediator, and molecular phenotyping data. Interestingly, clinical features commonly used for clinical trial selection were seen across multiple clusters with distinct patterns of immune activation. In a pSS cohort with relatively homogenous disease activity scores, three molecular clusters were characterized by differences in IFN, inflammation, and leukocyte transcriptional module signatures. In SLE, inflammation, IFN, T cell, B cell, monocyte, and neutrophil signatures distinguished seven patient clusters, with certain immunologically distinct clusters enriched for more severe disease manifestations or higher disease activity. In an SLE cohort where disease activity was transiently suppressed with depomedrol after withdrawing background immuno-suppressants, three subsets of patients with early flare could be distinguished by greater baseline frequencies of aCD11b+ monocytes, or $CD86^{hi}$ B naïve B cells, or both, pointing towards an overlapping spectrum of lymphoid and myeloid mechanisms contributing to SLE disease activity in different patients. Further, mass cytometry, bead-based assays, and ELISAs revealed effects of MMF on various immune pathways in SLE patients, including reduction of STAT3 phosphorylation and reduced numbers of transitional B cells, plasmablasts, and T cells. Ongoing studies address use of such profiles to inform patient selection for clinical trials and guide treatment decisions. I served as primary or senior investigator on all of these studies.

a. Guthridge JM, Lu R, Tran LT…**James JA**. Adults with systemic lupus exhibit distinct molecular phenotypes in a cross-sectional study. *EClinicalMedicine.* 2020 Mar 4; 20:100291. PMCID: PMC7058913
b. Slight-Webb S, Guthridge JM, Chakravarty EF… **James JA**. Mycophenolate mofetil reduces STAT-3 phosphorylation in systemic lupus erythematosus patients. *JCI Insight.* 2019 Jan 24;4(2):e124575. [Online ahead of print]. PMCID: PMC6413783
c. Lu R, Guthridge JM, Chen H, Bourn RL, Kamp S…**James JA**. Immunologic findings precede rapid lupus flare after transient steroid therapy. *Sci Rep.* 2019 Jul; 9(1):8590. PMCID: PMC6565690.
d. **James JA**, Guthridge JM, Chen H, Lu R, et al. Unique Sjögren's syndrome patient subsets defined by molecular features. *Rheumatology.* 2020 Apr 1; 59(4):860-868. PMCID: PMC7188221

4. Described Mechanisms of Systemic Autoimmune Disease Pathogenesis and Flare. SLE typically follows a waxing and waning disease course where organ damage accumulates during periods of elevated disease activity, called flares. My group has explored risk factors, possible predictors, and pathogenetic mechanisms for impending SLE onset and flare. We have demonstrated that proinflammatory adaptive cytokines are elevated prior to disease flare, while regulatory mediators are elevated during stable disease. Levels of B lymphocyte stimulator (BLyS), which is linked to autoantibody production and SLE onset, are higher in African American patients than European American patients, and increase after influenza vaccination in African American patients with low BLyS at baseline. Early pathogenic changes appear to influence the later disease course, as patients with anti-cardiolipin antibodies prior to diagnosis typically experience a more severe clinical course. Disease activity may be enhanced by poor resolution of inflammation after infections such as influenza. I served as senior investigator on all of these studies.

a. Munroe ME, ES Vista, JT Merrill… **JA James**. Pathways of impending disease flare in African-American systemic lupus erythematosus patients. *J Autoimmun*. 2017 Mar; 78:70-78. PMCID: PMC5340190

b. Ritterhouse LL, Crowe SR…**James JA**. B lymphocyte stimulator levels in systemic lupus erythematosus: higher circulating levels in African American patients and increased production after influenza vaccination in patients with low baseline levels. *Arthritis Rheumatol.* 2011; 63(12):3931-41. PMCID: PMC3234134
c. Munroe ME, Vista ES, Guthridge JM, Thompson LF…**James JA**. Proinflammatory adaptive cytokine and shed tumor necrosis factor receptor levels are elevated preceding systemic lupus erythematosus disease flare. *Arthritis Rheumatol.* 2014;66(7):1888-99. PMCID: PMC4128244
d. Merrill JT, Immermann F, Whitley M…**James JA**, Sridharan S. The Biomarkers of Lupus Disease Study: A bold approach may mitigate interference of background immunosuppressants in clinical trials. *Arthritis Rheumatol.* 2017 Jun;69(6):1257-1266. PMCID: PMC5501389

5. Identification of Genetic and Environmental Triggers of Systemic Autoimmune Disease. Autoimmune diseases arise from a complex but poorly understood combination of genetic and environmental factors. My work has helped uncover genetic risk factors in lupus, Sjogren's syndrome, and other diseases. In addition, we have provided extensive evidence that Epstein-Barr virus (EBV) is an important etiologic agent in SLE. These publications demonstrate a high incidence of EBV exposure and confirmed infection in SLE patients and posit that EBV infection stimulates SLE autoimmunity through molecular mimicry and interferon induction. My collaborative work has identified 59 genetic risk loci for systemic autoimmune diseases (please see SciENCV). Finally, Vitamin D deficiency is more common among SLE patients and in controls who have high levels of autoantibodies. I served as primary, senior or co- investigator on these studies.

a. **James JA**, Kaufman KM, Farris AD, Taylor-Albert E, Lehman TJ, et al. An increased prevalence of Epstein-Barr virus infection in young patients suggests a possible etiology for systemic lupus erythematosus. *J Clin Invest.* 1997;100(12):3019-26. PMCID: PMC508514
b. Young KA, Munroe ME, Guthridge JM…**James JA**, Norris JM. Combined role of vitamin D status and CYP24A1 in the transition to systemic lupus erythematosus. *Ann Rheum Dis*. 2017 Jan;76(1):153-158. PMCID: PMC5360632
c. Langefeld CD, Ainsworth HC…**James JA**, et al. Transancestral mapping and genetic load in systemic lupus erythematosus. *Nature Commun.* 2017 Jul 17;8:16021. PMCID: PMC5520018
d. Jog NR, Chakravarty EF…**James JA**. Epstein Barr Virus Interleukin 10 Suppresses Anti-inflammatory Phenotype in Human Monocytes. *Frontiers Immunol.* 2018 Oct 9; 9:2198. PMCID: PMC6189329

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/judith.james.1/bibliography/public/

D. Research Support

Ongoing Research Support

NIH/NIGMS **5 U54 GM104938-09** (PI James) 08/03/18 – 06/30/23
Oklahoma Shared Clinical and Translational Resources
The OSCTR will provide clinical and translational research infrastructure which fosters clinically relevant discoveries and translates findings into improved health and launches the careers of junior investigators.

NIH/NIGMS **3 U54 GM104938-08S1** (PI James) 09/25/20 – 06/30/22
Oklahoma Shared Clinical and Translational Resources
Supplement: Community-engaged Approaches to Testing in Community and Healthcare settings for Underserved Populations in Oklahoma (CATCH UP OK)
The practice-based intervention will utilize our existing research infrastructure to assist 50 small primary care practices to implement guidelines-based testing and patient education about COVID-19 and risk mitigation strategies.

NIH/NIAMS **5 P30 AR073750-03** (PI James) 09/07/18 – 08/31/23
Oklahoma Rheumatic Disease Research Cores Center
This infrastructure project provides pilot project and core support for all rheumatic disease researchers in Oklahoma, including senior investigators from 6 departments and other institutions. Dr. James serves as Administrative Core PI and assists with the Phenotyping and Clinical Characterization/Biorepository Cores.

NIH-NIAID **5 UM1 AI144292-03** (PI James) 05/01/19 – 04/30/24
Oklahoma ACE: Molecular Deconstruction of Autoimmune Disease to Aid Clinical Trial Success
The Oklahoma ACE will pursue a novel, comprehensive theme of accelerating discovery and translation by deconstructing molecular heterogeneity to enrich for patients with common molecular pathways, partnered with repurposed therapies from other fields and novel trial designs which eliminate confounding background polypharmacy, to address these unmet needs.

NIH/NIAID **5 U19 AI062629-17** (PI Coggeshall) 09/01/19 – 08/31/24

Molecular and Immunologic Analysis of the Pathobiology of Human Anthrax
Project 3: **Mechanisms of humoral immune protection induced by anthrax vaccine adsorbed**
The goals of this study are to identify mechanisms of poor neutralization after AVA vaccination and to facilitate protection against anthrax by identifying optimal neutralizing PA epitopes and the cellular immune responses that support neutralization

NIH-NIAID **3 U19 AI062629-17S2** (PI Coggeshall) 06/08/20 – 08/31/22 NCE
Molecular and Immunologic Analysis of the Pathobiology of Human Anthrax
Supplement: The Immune Response to SARS-CoV-2 Infection in Native Americans
The goals of this supplement are: Aim 1. Identify biomarkers and mechanisms of severe Covid-19 disease pathogenesis; Aim 2. Characterize the humoral immune response to SARS-CoV-2 infection; Aim 3. Characterize the T cell immune response to SARS-CoV-2 infection.

NIH/NIAMS **5 UM2 AR067678-05** (PI Utz) 09/24/14 – 05/31/22 NCE
Accelerating Medicines Partnership (AMP) in Rheumatoid Arthritis & Lupus: Network Leadership Center
Project: AMP Coalition Tissue Acquisition Research Network (ACTARN) (Consortium PI James)
ACTARN provides the protocols, infrastructure, quality control and sample management services which will enable optimal sample procurement, processing, interim storage and appropriate shipping of high-quality specimens to collaborative AMP sites for interrogation, experimental data generation and analytic evaluation.

NIH/NIAMS **3 UM2 AR067678-05S2** (PI Utz) 08/09/19 – 05/31/22 NCE
Accelerating Medicines Partnership (AMP) in Rheumatoid Arthritis & Lupus: Network Leadership Center
Project: AMP Coalition Tissue Acquisition Research Network (ACTARN) (Project PI James)
This will enable optimal sample procurement, processing, interim storage and appropriate shipping of high-quality specimens to collaborative AMP sites.

NIH/NIGMS **5 S06 GM127983-03** (PI Khan) 09/12/18 – 07/31/22
Native American Research Centers for Health (NARCH)
Project 3: Molecular Phenotyping of Autoimmunity in Tribal Members: Aiding Precision Medicine and Tribal Student Training (Consortium PI James)
This project studies biomarkers in AI tribal members to find potentially targeted, early interventions to help prevent autoimmunity and improve outcomes in OK tribal patients with rheumatic diseases.

NIH/NIGMS **3 S06 GM127983-03S1** (PI Khan) 09/23/20 – 07/31/22
Native American Research Centers for Health (NARCH)
RAD-X UP NARCH Supplement: A Cherokee Nation Community-Driven Program for Testing and Contact Tracing (Cherokee PROTECT)
This supplement unites tribal, academic, and community partners to solve a dire need for COVID-19 testing, contact tracing, and culturally informed education in underserved and vulnerable rural populations.

NIH/NIAMS **5 U01 AR071077-04** (Olsen) 02/01/17 – 01/31/22
Study of Anti-Malarials in Incomplete Lupus Erythematosus
The goal of this project is to determine the ability of hydroxychloroquine (HCQ) treatment in incomplete lupus erythematosus (ILE) patients to prevent acquisition of additional clinical and immunologic features that define systemic lupus erythematosus (SLE).

NIH/NIAMS **5 R01 AR072401-04** (James) 09/01/17 – 06/30/22 NCE
Mechanisms of Lupus Disease Transition and Hydroxychloroquine Immune Modulation
This project will establish mechanisms of how HCQ modifies the dysregulated immune system in preclinical lupus in (a) Adaptive Autoimmune responses and (b) Innate Immune activation.

NIH/NIAID **5 U19 AI110483-08** (PI Sanz) 05/01/19 – 04/30/22 NCE
Autoimmunity Center of Excellence Collaborative Project
ARA08 Clinical and Mechanistic Studies
The James lab assists with this trial through the ACE consortium.

NIH/NIAID **5 U19 AI110483-08** (PI Sanz) 05/01/19 - 04/30/24
Autoimmunity Center of Excellence Collaborative Project
Molecular Dissection of Disease Heterogeneity in SLE
Our collaborative project deconstructs molecular heterogeneity and associated pathogenic mechanisms of disease in subsets of SLE patients.

<u>Completed</u>: 9 grants and subawards from 2017 - 2020