

Rheumatology

Research highlight: Nelson lab & systemic sclerosis

Dr. J. Lee Nelson is a well-established autoimmunity researcher and rheumatologist at Seattle's Fred Hutchinson Cancer Research Center. Dr. Nelson completed her fellowship in rheumatology at the University of Washington and has been a faculty member with the Division since the 1980s.

Recent studies from Dr. Nelson's research group have documented distorted paternal versus maternal HLA inheritance observed in SSc patients, in contrast to healthy controls where inheritance was 50-50 as expected. Considering the important role of charge carried by the HLA-DR β 1 3rd hypervariable region in rheumatoid arthritis as precedent, they conducted analysis categorizing the 3rd hypervariable region amino acid sequence and associated charge irrespective of specific HLA-DRB1 alleles. Skewed parental HLA inheritance was observed, strongly implicating epigenetic modification of HLA. The importance of HLA molecules in SSc and other autoimmune diseases is well-established and although a central role of epigenetic modifications in SSc pathogenesis is supported by recent studies, an epigenetic effect on HLA has not previously been considered.



Dr. Whitney Harrington, MD, PhD, pediatric infectious disease fellow in Dr. Nelson's lab, was selected as an awardee by the Burroughs Wellcome Fund. Dr. Harrington is first author of a paper published in the Journal of Infectious Disease in which they investigated women who have malaria during pregnancy. Investigators found evidence for maternal cells in cord blood that significantly correlated with the probability that the neonate would get malaria but interestingly, decreased risk that the child would become symptomatic or hospitalized with malaria.

Dr. Sami Kanaan, PhD, post-doctoral research fellow in the Nelson lab, has a paper in press in OncoImmunology that investigated maternal cells in cord blood and found maternal cells were frequently present in immune cellular subsets including T cells, B cells, NK cells and monocyte/macrophages. They also showed in a patient who received a cord blood transplant for leukemia treatment that maternal cells could be detected post-transplantation in the patient.

Neutrophil activation & autoimmune disease



Dr. Christian Lood, Dr. Keith Elkon, Dr. Jeffrey Ledbetter, and visiting scientist Sabine Arve, MSc, recently published their paper *TLR7/8 activation in neutrophils impairs immune complex phagocytosis through shedding of Fc γ RIIA* in the Journal of Experimental Medicine.

Neutrophils are essential to host defense. However, in SLE circulating nucleic acid-containing immune complexes may engage neutrophils and contribute to chronic inflammation and tissue destruction. In the current investigation researchers asked how these RNA-containing lupus immune complexes are sensed by neutrophils, and the particular role of the RNA component of the immune

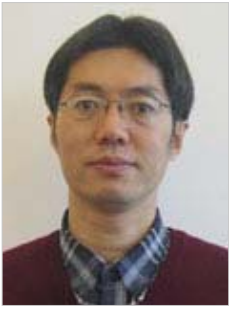
complexes in regulating subsequent neutrophil effector functions. In brief, they made the novel observation that activation of TLR7/8, the main RNA sensing receptors in neutrophils, shifted neutrophils from phagocytosis of immune complexes to the inflammatory neutrophil cell death process, NETosis, extruding its nuclear and cytosolic content causing marked inflammation and damage.

These observations extend our understanding of neutrophil function in regulation of autoimmunity and inflammation, and suggest that therapeutic interventions to prevent TLR7/8 activation would increase phagocytic clearance of immune complexes while limiting their ability to induce inflammatory NETosis.

Inside:

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FACULTY APPOINTMENTS & PROMOTIONS



Dr. Jie An, PhD, has been appointed as a Research Assistant Professor. Dr. An obtained a PhD degree in the field of Biochemistry & Cell Biology from the Chinese Academy of Sciences in Shanghai, China. His current research is focused on the role of interferon in SLE. In particular, he is studying the role of the cGAS-STING pathway and developing drugs to block

this pathway.

Dr. Christian Lood, PhD, has been appointed as an Assistant Professor effective April 16th 2017. Under this new title Dr. Lood's extensive teaching and service contributions to our fellowship program as well as his research productivity are recognized. In addition, Dr. Lood will continue his research at our South Lake Union campus where his primary focus is to identify the causes of neutrophil mediated inflammation and to find methods to block the inflammation. Dr. Lood obtained his PhD degree in the field of Biomedicine-Rheumatology from Lund University, Sweden. He has significant research experience in Immunology/Autoimmune disease. He worked with internationally renowned research scientists, Drs. Bengtsson and Sturfelt at the University of Lund.



Dr. Jenna Thomason, MD, MPH, has been appointed as an Acting Instructor. She obtained her MD from Emory University School of Medicine and her MPH from the Emory University Rollins School of Public Health. Dr. Thomason completed an Internal Medicine Residency and Rheumatology Fellowship at the University of Washington.

Dr. Thomason will see patients primarily at HMC and participate in the division's ACGME Fellowship Training Program.

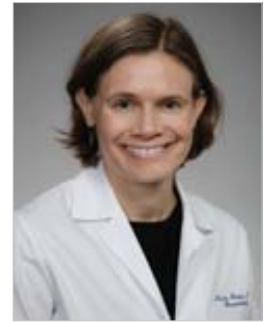
NEW DIVISION WEBSITE

The Division has launched a new website that matches the University of Washington Department of Medicine's website. The new site is hosted on Drupal and now contains updated information such as news and events in addition to our entire conference schedule in a more user friendly format.

The new website can be accessed at www.rheumatology.uw.edu.

NEW FELLOWSHIP ASSOCIATE PROGRAM DIRECTOR

Dr. Alison Bays, MD, MPH, has been appointed Associate Director of the Rheumatology Fellowship Program. Dr. Bays obtained her MD and MPH from Tulane University School of Medicine and School of Public Health. Dr. Bays completed an internal medicine residency at the University of Washington followed by a fellowship in rheumatology at the University of California, San Francisco.



She is a clinician-educator interested in medical education, quality improvement, musculoskeletal ultrasound and is currently researching the effects of TNF inhibitors on viral loads. She sees patients at Harborview Medical Center and will be bringing her expertise as a clinician-educator to the fellowship program.

DR. POLLOCK APPOINTED EMERITUS PROFESSOR



Dr. Scott Pollock, MD, has been appointed as a Clinical Emeritus Professor. Dr. Pollock has been a member of the Division since completing his residency and fellowship at the University of Washington in the 1980s.

Dr. Pollock was pivotal in developing the fellowship program's ultrasound and musculoskeletal training curriculums. He has presented on ultrasound at the American College of Rheumatology Annual Meeting and internationally. Dr. Pollock's many years of service are appreciated. The Division will recognize this new title with a celebration at the annual ACR Meeting in November 2017.

LANE LECTURE 2017



In March 2017 the Division held the annual James J. Lane Jr. Endowed Lecture Series. The Lane Lecturer this year was Dr. Martin Herrmann, Professor of Experimental Medicine at the Friedrich-Alexander University and researcher at the Erlangen-

Nurnberg Institute for Clinical Immunology spoke. His talk was entitled *Neutrophils & NETs Orchestrate Initiation and Resolution on Gout and Other Inflammatory Diseases*.



OPPORTUNITIES FOR GIVING

You can support programs and initiatives in the Division of Rheumatology. We have established four Professorships and eight endowments through generous donations. In addition, several gift funds target specific programs such as the Rheumatology Fellowship Fund, the Rheumatology Discretionary Fund, and the Rheumatology Research Fund for Junior Faculty.

Send Checks to:

Division of Rheumatology, Campus Box 356428,
1959 NE Pacific St, Seattle, WA 98195

To learn more about these opportunities for giving, please visit: <http://depts.washington.edu/rheum>

DIVISION GRANTS

Dr. Jie An received a \$10,000 award through the Institute of Translational Health Sciences Research Scholars Program. The one-year program supports research and career development.

Dr. Keith Elkon was awarded an NIH R21 award entitled "Link between Retroelements, Ro and Interferon Biology in Lupus". This will support a two year project in collaboration with Dr. Michael Gale of the Department of Immunology.

Dr. Keith Elkon also received an Co Motion Innovation Fund grant in support of his project titled "cGAS-STING".

Dr. Natalia Giltiay has been awarded a grant from the Lupus Research alliance in the amount of \$300,000 to research anit-BDCA2-targeted therapy for SLE. This grant will last three years.

Rheumatology fellow **Dr. Judy Juo** has been awarded the Institute of Translational Health Sciences (ITHS) Early Investigator Award. This award will supply \$2,000 for biostatistical support for the project Perioperative management of synthetic disease-modifying anti-rheumatic drugs and biologics in Rheumatoid arthritis.

Dr. Christian Lood was also awarded a grant from the Lupus Research Alliance in the amount of \$300,000 to research impaired mitochondrial clearance in systemic lupus erythematosus. This grant will last three years.

Dr. Christian Lood has been awarded an Investigator Initiated grant from Pfizer, Inc. The project entitled, "Neutrophil-Derived Biomarkers in Rheumatic Diseases" is funded for two years with a total budget of \$150,000.

DIVISION AWARDS

We congratulate **Drs. Gregory Gardner, Julie Carkin, Mark Wener,** and **Philip Moberg** for being listed as Top Doctors in Seattle Met for 2017.

Dr. Grant Hughes was nominated for American College of Rheumatology Distinguished Program Director Award.

Dr. Mark Wener was nominated as a American College of Rheumatology Master to honor his decades of work as a rheumatologist.

Program Operations Specialist and Fellowship Program Administrator **Kat McGhee** was nominated for the 2017 University of Washington Distinguished Staff award.

NEW ACGME RHEUMATOLOGY FELLOWS

Dr. Sarah Chung attended medical school at Georgetown School of Medicine. She completed her residency at the University of Washington in Seattle, WA.



Dr. Jean Liew attended medical school at the University of Texas Medical Branch School of Medicine, Galveston. She completed her residency Oregon Health & Science University in Portland, OR.



Dr. Muhsen Al-ani attended medical school at the University of Baghdad College of Medicine in Iraq. He completed his most recent residency at Maricopa Integrated Health Systems, AZ. He also completed a Fellowship in Nuclear & Radiation Medicine in Iraq.

DIVISION PUBLICATIONS

Expression of Cyclic GMP-AMP Synthase in Patients With Systemic Lupus Erythematosus. An J, Durcan L, Karr RM, Briggs TA, Rice GI, Teal TH, Woodward JJ, **Elkon KB**. *Arthritis Rheumatol*. 2017 Apr;69(4):800-807. doi: 10.1002/art.40002. Epub 2017 Mar 7. PMID: 27863149

Antimalarial Drugs as Immune Modulators: New Mechanisms for Old Drugs. An J, Minie M, Sasaki T, Woodward JJ, **Elkon KB**. *Annu Rev Med*. 2017 Jan 14;68:317-330. doi: 10.1146/annurev-med-043015-123453. Epub 2016 Oct 21. PMID: 27813878

Tartrate-Resistant Acid Phosphatase Deficiency in the Predisposition to Systemic Lupus Erythematosus. An J, Briggs TA, Dumax-Vorzet A, Alarcón-Riquelme ME, Belot A, Beresford M, Bruce IN, Carvalho C, Chaperot L, Frostegård J, Plumas J, Rice GI, Vyse TJ, Wiedeman A, Crow YJ, **Elkon KB**. *Arthritis Rheumatol*. 2017 Jan;69(1):131-142. doi: 10.1002/art.39810. Epub 2016 Dec 2.

Ultraviolet B Irradiation Causes Stimulator of Interferon Genes-Dependent Production of Protective Type I Interferon in Mouse Skin by Recruited Inflammatory Monocytes. Sontheimer C, Liggitt D, **Elkon KB**. *Arthritis Rheumatol*. 2017 Apr;69(4):826-836. doi: 10.1002/art.39987. PMID: 27863141

Targeting CD22 with the monoclonal antibody epratuzumab modulates human B-cell maturation and cytokine production in response to Toll-like receptor 7 (TLR7) and B-cell receptor (BCR) signaling. Giltiay NV, Shu GL, Shock A, **Clark EA**. *Arthritis Res Ther*. 2017 May 15;19(1):91. doi: 10.1186/s13075-017-1284-2. PMID: 28506291

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Be green!

Receive newsletters by email: rheum@uw.edu



RECENT DIVISION PUBLICATIONS (CONTINUED)

Decreased platelet size is associated with platelet activation and anti-phospholipid syndrome in systemic lupus erythematosus. **Lood C**, Tydén H, Gullstrand B, Nielsen CT, Heegaard NH, Linge P, Jönsen A, Hesselstrand R, Kahn R, Bengtsson AA. *Rheumatology (Oxford)*. 2017 Mar 1;56(3):408-416. doi: 10.1093/rheumatology/kew437. PMID: 28031442

Neutrophil extracellular traps as a potential source of autoantigen in cocaine-associated autoimmunity. **Lood C, Hughes GC**. *Rheumatology (Oxford)*. 2017 Apr 1;56(4):638-643. doi: 10.1093/rheumatology/kew256. PMID: 27354687

TLR7/8 activation in neutrophils impairs immune complex phagocytosis through shedding of FcγRIIA. **Lood C, Arve S, Ledbetter J, Elkon KB**. *J Exp Med*. 2017 Jul 3;214(7):2103-2119. doi: 10.1084/jem.20161512. Epub 2017 Jun 12. PMID: 28606989

Juvenile idiopathic arthritis in relation to perinatal and maternal characteristics: a case control study. Bell SW, Shenoi S, **Nelson JL**, Bhatti P, Mueller BA. *Pediatr Rheumatol Online J*. 2017 May 11;15(1):36. doi: 10.1186/s12969-017-0167-z. PMID: 28494794

Maternal microchimerism predicts increased infection but decreased disease due to *P. falciparum* during early childhood. Harrington WE, Kanaan SB, Muehlenbachs A, Morrison R, Stevenson P, Fried M, Duffy PE, **Nelson JL**. *J Infect Dis*. 2017 Mar 15. doi: 10.1093/infdis/jix129. [Epub ahead of print] PMID: 28329160

Characterization of the HLA-DRβ1 third hypervariable region amino acid sequence according to charge and parental inheritance in systemic sclerosis. Gentil CA, Gammill HS, Luu CT, Mayes MD, Furst DE, **Nelson JL**. *Arthritis Res Ther*. 2017 Mar 7;19(1):46. doi: 10.1186/s13075-017-1253-9. PMID: 28270189

Autocrine Loop Involving IL-6 Family Member LIF, LIF Receptor, and STAT4 Drives Sustained Fibroblast Production of Inflammatory Mediators. Nguyen HN, **Noss EH**, Mizoguchi F, Huppertz C, Wei KS, Watts GF, Brenner MB. *Immunity*. 2017 Feb 21;46(2):220-232. doi: 10.1016/j.immuni.2017.01.004. PMID: 28228280

Cadherin-11 Is a Cell Surface Marker Up-Regulated in Activated Pancreatic Stellate Cells and Is Involved in Pancreatic Cancer Cell Migration. Birtolo C, Pham H, Morvaridi S, Chheda C, Go VL, Ptasznik A, Edderkaoui M, Weisman MH, **Noss EH**, Brenner MB, Larson B, Guindi M, Wang Q, Pandolfi SJ. *Am J Pathol*. 2017 Jan;187(1):146-155. doi: 10.1016/j.ajpath.2016.09.012. Epub 2016 Nov