### Division Data Summary

#### Research and Training Details

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#### Clinical Activities and Training

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<tr>
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<td>Outpatient Encounters</td>
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### Significant Publications


Significance: The many quality improvement initiatives and extensive experience of the Division physicians in caring for patients with systemic lupus erythematosus has led to better management of these patients, which is summarized in this review.


Significance: A deeper and much more fundamental understanding of the potentially deadly hemophagocytic lymphohistiocytosis is emerging. The division faculty is making a major contribution to the aggregate of this knowledge with the identification of critical elements in the pathophysiology of this condition. This study is the first genome wide study of gene expression in this syndrome.


Significance: The toll-like receptors are an important component of the innate immune response. TLR7 is a
gene on the X chromosome. Since women and girls have systemic lupus erythematosus much more frequently than men and boys (~10-fold), we would expect that genes on the X chromosome would be more important in women than it is in men. Surprisingly, variants in TLR7 are much more strongly associated with male lupus than female lupus in Asians.


Significance: These represent the first evidence based treatment guidelines for children with Juvenile Idiopathic Arthritis and due to the rigor of the development process they have been officially endorsed and adopted by the American College of Rheumatology. Three members of the CCHMC Division of Rheumatology (Esi Morgan Dewitt, Janalee Taylor and Daniel Lovell) were key participants in the effort.


Significance: These represent the first nationally developed quality measures for the care of children with juvenile idiopathic arthritis. Five members of the CCHMC Division of Rheumatology (Janalee Taylor and Drs. Giannini, Henrickson, Lovell and Morgan Dewitt) initiated and lead this national effort. These quality measures are being used by an international quality improvement network, PR-COIN, being led by a CCHMC Division of Rheumatology faculty member, Esi Morgan Dewitt, in collaboration with the CCHMC Anderson Center.

Division Highlights

Edward Giannini, MSc, DrPH

Dr. Giannini is the recipient of a Life-Time Achievement Award which was bestowed upon him at the Pediatric Rheumatology Symposium (PRSYM) that was held in Miami, Florida in June 2011. The Life-Time Achievement awardees are selected by a Committee representing the American Academy of Pediatrics and the American College of Rheumatology. Recipients are considered those whose career has demonstrated a sustained and lasting contribution to the field of rheumatology and rheumatology health professionals.

Esi Morgan DeWitt, MD, MSCE

PR-COIN - The Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) is a multi-center quality improvement learning collaborative formed to improve the outcomes of care of children with juvenile idiopathic arthritis and to accelerate adoption of evidence into medical practice. Our collaborative approach is based on the Institute of Healthcare Improvement (IHI) Breakthrough Series Collaborative Model and utilizes the Model for Improvement to guide performance improvement activities. Using the American College of Rheumatology Rheumatology Clinical Registry (ACR RCR), PR-COIN is designed to aggregate data from participating pediatric rheumatology practices to study performance of sites on both process measures of care delivery and measures of patient outcomes to better understand which disease management approaches are optimal. In the past year we formed our project team with leadership from the Division of Rheumatology in partnership with the Anderson Center for Health Systems Excellence with expertise in QI science and project management. After project launch, we customized and piloted the electronic data capture system. Twelve centers in the US and Canada have joined the collaborative. Initial project activities include collection of baseline data and training teams in performance improvement methodology, prior to testing change strategies
at team sites that are based on a chronic illness care model. Teams convene during three Learning Sessions over a 12 month period where QI experts offer intensive training and coaching. Sessions were held June 2011, and planned for September 2011 and March 2012. Site and aggregate data feedback reports are provided monthly to enable teams to assess progress on quality measures.

**Division Collaboration**

**Allergy** » Marc Rothenberg

- John Harley and Marc Rothenberg collaboration: Candidate gene study of Eosinophilic esophagitis

**Human Genetics** » Greg Grabowski; Mehdi Keddache; Sarah Zimmerman

- John Harley, Sarah Zimmerman, Mehdi Keddache, and Greg Grabowski collaboration: Genome wide association study of height from routine clinical samples

**Molecular Immunology** » Chris Karp

- John Harley and Chris Karp collaboration: PXK association with lupus

**Immunobiology** » Marsha Wills Karp

- John Harley and Marsha Wills Karp collaboration: Genome wide study of asthma in an isolated population

**Bioinformatics** » John Hutton ; Michael Wagner

- John Harley Michael Wagner and John Hutton collaboration: Genetic association analysis of systemic lupus erythematosus

**Anderson Center for Health Systems Excellence** » Peter Margolis; Carole Lannon

- Esi Morgan DeWitt, Peter Margolis and Carole Lannon collaboration: PR-COIN

**Behavioral Medicine ; Pain Management; Pulmonary; Rehabilitation** » Susmita Kashikar-Zuck; Kenneth Goldschneider; Michael Seid; Jilda Vargus-Adams

- Esi Morgan DeWitt, Susmita Kashikar-Zuck, Kenneth Goldschneider, Michael Seid, and Jilda Vargus-Adams collaboration: The Patient Reported Outcomes Measurement Information System (PROMIS) - Cincinnati Children's Hospital Medical Center (CCHMC) is a research site in the NIH Roadmap PROMIS (Patient-Reported Outcomes Measurement Information System) cooperative network which mission is to use measurement science to create a state-of-the-art assessment system for self-reported health. The CCHMC PROMIS research project has two aims. The first aim is to perform longitudinal validation of current PROMIS pediatric PRO measures in the domains of physical function (upper extremity, mobility), pain interference, fatigue, anger, anxiety, depressive symptoms, and peer relationships in pediatric patients with chronic pain conditions, juvenile idiopathic arthritis, or cerebral palsy. An extensive qualitative interview study in children with these conditions was conducted as an initial step. The longitudinal portion of the study is well underway. The second aim is to develop new PRO item banks to measure pain behavior, and pain quality, including pain severity, in pediatric patients. Candidate items for testing have been created following a rigorous standard PROMIS methodology and are ready for large scale cross-sectional validation. The validation sample for the new pain assessment tools includes children with chronic and recurrent pain, including juvenile idiopathic arthritis, widespread musculoskeletal or regional pain syndromes, and sickle cell anemia. Use of IRT based PROMIS measures will allow for efficiency of PRO measurement, potential for increased sensitivity to measure change in health status over time, and facilitate comparison of an individual’s results to population norms in patients with rheumatic diseases and other chronic disease cohorts.

**Experimental Hematology ; Human Genetics** » Matthew Flick ; Xiaoyang Qi

- Sherry Thornton Collaboration: with Dr. Matthew Flick in Experimental Hematology and Dr. Xiaoyang Qi, Division of Human Genetics CCHMC and now Division of Hematology-Oncology-UC College of Medicine on a
project funded by the local CTSA entitled SapC-DOPS Agents: Imaging in Arthritis. This project involves assessment of the ability of SapC-DOPS fluorescently labeled agent to localize to arthritic joints. A manuscript will be submitted in the very near future describing our findings that SapC-DOPS localizes to arthritic joints. In addition a revision of an R21 has been submitted which determines whether SapC-DOPS can detect subclinical arthritis and can be used as a clinical marker to assess response to therapy in arthritis models.

Experimental Hematology » Matthew Flick
Sherry Thornton and Matthew Flick Collaboration: assessment of hemostatic factors in arthritis which generated a manuscript

Faculty Members

John Harley, MD, PhD, Professor
Division Director
Research Interests

Hermine Brunner, MD, MSc, Associate Professor
Research Interests

Edward H. Giannini, MSc, DrPH, Professor
Research Interests

David N. Glass, MD, Professor
Research Interests

Thomas Griffin, MD, PhD, Associate Professor
Research Interests

Alexei A. Grom, MD, Associate Professor
Research Interests

Michael Henrickson, MD, MPH, Associate Professor
Clinical Director
Research Interests

Jennifer Huggins, MD, Assistant Professor
Fellowship Director
Research Interests

Daniel Joe Lovell, MD, MPH, Professor
Joseph E. Levinson Endowed Chair in Pediatric Rheumatology
Research Interests

Esi Morgan DeWitt, MD, MSCE, Assistant Professor
Research Interests

Susan Thompson, PhD, Associate Professor
Associate Director
Research Interests

Sherry Thornton, PhD, Assistant Professor
Research Interests

Tracy Ting, MD, Assistant Professor
Research Interests
Clinical Staff Members

- Janalee Taylor, MSN, RN, CNP

Trainees

- Lu Pai-Yue, MD, PGY-IV, Cincinnati Children's Hospital Medical Center
- Moussa El-Hallak, MD, PGY-IV, Memorial University Medical Center
- Rina Mina, MD, PGY-VI, Downstate Medical Center New York
- Annette Lopez-Martinez, MD, PGY-VI, University of Puerto Rico Pediatric Hospital
- David Moser, DO, PGY-V, United States Army, Pediatrics
- Keith Sikora, MD, PGY-V, Johns Hopkins Hospital

Significant Accomplishments

**Division and CAGE Achieve Milestones**

The Division of Rheumatology and the Center for Autoimmune Genomics and Etiology (CAGE) achieved many milestones this past year.

Work led by Alexei Grom, MD, identified a pathway that is important for the development of the sometimes deadly macrophage activation syndrome. Susan Thompson, PhD, led work that provided deep genetic insight into the variations of DNA that predispose to juvenile onset idiopathic arthritis. Dan Lovell, MD, MPH, Ed Giannini, DrPH, and Hermine Brunner, MD, MSc, have shown that the new biological therapies are spectacularly successful; their critically important work has become the new standard of therapy and is helping many thousands of afflicted children avoid the life-long disability of chronic destructive arthritis.

Esi Morgan DeWitt, MD, MSc, has achieved better compliance and therapeutic outcomes in juvenile onset rheumatoid arthritis by applying quality-improvement interventions. DeWitt and Brunner are co-leading efforts to effectively align research, clinical care and quality improvement to provide high-value care locally and are leading international initiatives to develop quality indicators and benchmarks for pediatric rheumatology care with focus on systemic lupus erythematosus and juvenile idiopathic arthritis.

Biomarker development efforts are synergistic with development of clinical trial outcome measures that set the stage for testing novel medications for children with SLE. John Harley, MD, PhD, has led an effort to identify the genes that cause systemic lupus erythematosus, now numbering more than 40, followed by progress in discovering the mechanisms and pathways through which they cause lupus.

Division Publications


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### Grants, Contracts, and Industry Agreements

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<td><strong>Early Aggressive Therapy in Juvenile Idiopathic Arthritis</strong> National Institutes of Health(Children's Hosp &amp; Reg Med Ct-Seattle)</td>
<td><strong>R01 AR 049762</strong> 07/01/10-06/30/11 $12,859</td>
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<td><strong>Family Study of Pediatric Autoimmunity</strong> Children's Hosp &amp; Reg Med Ct-Seattle</td>
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<td><strong>Myositis Registry</strong> Centers for Disease Control and Prevention(The Myositis Association)</td>
<td><strong>H75 DP 001743</strong> 09/01/10-08/31/11 $78,536</td>
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<td><strong>Towards Measures of Lupus Nephritis Activity &amp; Damage in Children</strong> National Institutes of Health</td>
<td><strong>U01 AR 059509</strong> 08/08/10-05/31/13 $135,002</td>
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GIANNINI, E

Early Aggressive Therapy in Juvenile Idiopathic Arthritis
National Institutes of Health (Children's Hosp & Reg Med Ct-Seattle)
R01 AR 049762 05/01/10-09/22/11 $113,924

GRiffin, T

HLA-B27 Misfolding an the UPR in Spondyloarthritis
National Institutes of Health
R01 AR 046177 09/01/06-06/30/11 $273,473

HARLEY, J

Genetic Linkage in Lupus
National Institutes of Health
R37 AI 024717 09/07/10-02/28/15 $207,939

Genetic Linkage in Lupus
National Institutes of Health
R37 AI 024718 09/16/10-08/31/11 $153,900

Genetic Linkage in Lupus
National Institutes of Health
R37 AI 024719 09/07/10-02/28/15 $258,680

Illumina iScan System for the OMRF Microarray Research Facility
National Institutes of Health
S10 RR 027190 06/10/10-06/09/11 $413,350

Genome-Wide Association Study in African-Americans with Systemic Lupus Erythematosus
Department of Defense
09/01/10-08/31/13 $269,095

HUGGINS, J

ACR REF/Amgen/Wyeth Rheumatology Fellowship Training Award
American College of Rheumatology Research & Education Foundation
07/01/10-06/30/11 $25,000

LOVELL, D

Multidisciplinary Clinical Research Center
National Institutes of Health
P60 AR 047784 08/18/08-07/31/13 $847,406

Lovell, D Administrative Core $70,938
Giannini, E Methodology Core $112,710
Brunner, H Project 1 $179,060
Lovell, D Project 2 $178,593
Grom, A Project 3 $163,409
Seid, M Project 4 $142,696

MORGAN DEWITT, E

Enhancing PROMIS in Pediatric Pain, Rheumatology, and Rehabilitation Research
National Institutes of Health
U01 AR 057940 02/01/11-07/31/13 $72,262

Enhancing PROMIS in Pediatric Pain, Rheumatology, and Rehabilitation Research
National Institutes of Health
U01 AR 057940 09/30/09-07/31/13 $367,410

Juvenile Arthritis Improvement Network for Clinical Excellence & Safety
Arthritis Foundation
07/01/10-06/30/12 $92,593

THOMPSON, S
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<td>CARRA: Accelerating Toward an Evidence Based Culture in Pediatric Rheumatology</td>
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<td>Strait, R</td>
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<td>Genetics of Juvenile Idiopathic Arthritis and Subtypes</td>
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**Current Year Direct** $4,090,159

**Industry Contracts**

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**Current Year Direct Receipts** $669,616

**Total** $4,759,775