Rheumatology

Division Photo

First Row: T. Griffin, M. Henrickson, D. Lovell
Third Row: M. Flick, D. Glass, S. Thompson, E. Giannini, A. Grom

Division Data Summary

<table>
<thead>
<tr>
<th>Research and Training Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Faculty</td>
</tr>
<tr>
<td>Number of Support Personnel</td>
</tr>
<tr>
<td>Direct Annual Grant Support</td>
</tr>
<tr>
<td>Direct Annual Industry Support</td>
</tr>
<tr>
<td>Peer Reviewed Publications</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Clinical Activities and Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Clinical Staff</td>
</tr>
<tr>
<td>Number of Clinical Fellows</td>
</tr>
<tr>
<td>Inpatient Encounters</td>
</tr>
</tbody>
</table>

Significant Publications


This and the next publication represent the results of over 20 years of dedicated work of a team of investigators within the CCHMC Division of Rheumatology who have combined careful description of the clinical course of many children with JIA and extensive characterization of genetic markers. This study demonstrated JIA subtype differences in the genetic markers expressed on peripheral blood mononuclear white blood cells demonstrating the immunobiologic differences between JIA subtypes.


Even very soon after the development of the disease, subsets of children with Polyarticular JIA (arthritis in more than 4 joints) differ from each other in the gene expression on mononuclear cells in the peripheral blood allowing for a molecular classification of disease and identification of discrete disease processes even within this one JIA subtype.


This manuscript is one of several from this Division focused on understanding the causes of disease for children with the most severe form of JIA – Systemic JIA. This paper showed an association with variations in the gene MUNC 13-4 with the severe complication of systemic JIA called macrophage activation syndrome.


This manuscript presented results of a large international, double-blind, randomized clinical trial to assess the efficacy and safety of a new class of therapy – i.e., biologic that blocks the stimulation of T-cells in children with severe JIA. Therapy was both efficacious and safe in over 85% of the patients. The clinical trials unit within the Division of Rheumatology directed this entire study.


This is one of a series of publications from a very productive team of investigators in the CCHMC Divisions of Rheumatology and Nephrology. This manuscript demonstrated proteins found in the urine that can serve as biomarkers in children and adolescents with SLE of the activity of kidney involvement and also can help anticipate the future course of kidney involvement.

Faculty Members

Hermine Brunner, MD, MSc, Associate Professor
Matthew Flick, PhD, Research Instructor
Edward H. Giannini, MSc, DrPH, Professor
David N. Glass, MD, Professor
Thomas Griffin, MD, PhD, Research Assistant Professor
Alexei A. Grom, MD, Research Associate Professor
Jennifer Huggins, MD, Assistant Professor Clinical ; Fellowship Director
Daniel Joe Lovell, MD, MPH, Professor ; Interim Division Director
Susan Thompson, PhD, Associate Professor
Sherry Thornton, PhD, Research Assistant Professor

Clinical Staff Members

- Janalee Taylor, MSN, RN, CNP

Trainees
Significant Accomplishments
Clinical and Translational Research Accomplishments

The Division of Rheumatology continues to move forward in a very productive fashion in both clinical and translational research areas. This last year saw the completion of three large international multi-centered Phase III interventional trials that were developed and led by Clinical Trials Unit within the Division of Rheumatology. Results of these trials were published in the *New England Journal of Medicine*, *Lancet* and *Arthritis & Rheumatism*. In addition, these studies led to the approval by the FDA and the European EMEA of two new treatments for children with Juvenile Idiopathic Arthritis (JIA). Each of these treatments represents a powerful and extremely effective treatment option for children with severe JIA. In addition, studies are being developed to provide focused pathogenic driven treatments for children with a form of chronic arthritis for which we have very poor treatments at the current time – Systemic JIA.

Translational laboratory-based investigations in the Division of Rheumatology have been directed towards the goal of understanding the molecular basis of JIA, a heterogeneous disease with several subtypes. Work has focused on defining the basis for genetic risk and identifying distinct molecular profiles related to the various subtypes using gene expression profiling. In the past year genomic JIA datasets, of unprecedented scope, have been completed. The data includes high resolution HLA allele types, single nucleotide polymorphisms (SNP) and copy number variant genotypes for about 1000 patients and 1000 controls and gene expression profiles for a subset of about 200 patients. Genetic association studies have revealed a set of risk factors common with other autoimmune diseases such as Lupus and Crohn’s disease as well as risk factors that are unique to JIA and its various subtypes. HLA associations have been defined with greater precision than previously possible. Gene expression studies, using blood samples obtained from patients at onset of disease, have revealed an increased presence and function of various immature cell types including B-cells, monocytes and macrophages. Of importance and supported in each of our datasets, are results suggesting that patients who develop disease at a young age share a common biological basis for disease which is different in patients that develop disease later in life. Together these genomic studies provide evidence for a fundamental shift toward molecular definitions for disease and may lead to a reevaluation of the present clinical criteria for defining subtypes as well as provide insight into disease origins and pathogenesis.

As described above, in the last year research in the CCHMC Division of Rheumatology has resulted in real advances in understanding both the molecular basis of the inflammation but also treatment of JIA- the most common chronic arthritis in children and one of the more common chronic childhood illnesses.

Division Publications


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Grants, Contracts, and Industry Agreements

**Grant and Contract Awards**

| BRUNNER, H | Efficacy Measures for Pediatric Lupus Studies |
| National Institutes of Health | U01 AR 055054 | 08/17/07 - 07/31/10 | $130,219 / $401,754 |
| | Mechanisms of Tolerance to Renal Maternal Microchimerism |
| National Institutes of Health (Children's Hospital and Regional Medical Center-Seattle) | R01 AR 051545 | 09/13/07 - 07/31/10 | $4,540 / $6,520 |
| | Early Aggressive Therapy in Juvenile Idiopathic Arthritis ( Per Patient) |
| National Institutes of Health (Children's Hospital and Regional Medical Center-Seattle) | R01 AR 049762 | 09/01/06 - 08/31/11 | $28,846 / $156,750 |
| | Biomarkers for Diagnosis, Monitoring, and Prognosis in Pediatric SLE |
| Lupus Foundation of America (University of Pittsburgh) | 10/01/08 - 09/30/09 | $52,311 / $52,311 |

| GLASS, D | Hematopoietic Cell Transplantation |
| National Institutes of Health (Fred Hutchinson Cancer Research Center) | U01 AI 069197 | 09/15/08 - 02/28/09 | $210,000 / $210,000 |
Research Registry For Juvenile Rheumatoid Arthritis
National Institutes of Health
N01 AR 042272 09/30/04 - 09/29/09 $826,858 / $4,255,695

HLA/KIR Region Genetics in Pediatric Arthritis
National Institutes of Health
U01 AI 067150 09/30/05 - 03/31/10 $264,468 / $1,297,617

Hematopoietic Cell Transplantation
National Institutes of Health
U01 AI 069197 09/15/08 - 02/28/09 $210,000 / $315,000

GRAFFIN, T
Pediatric Rheumatology Training Grant
National Institutes of Health
T32 AR 007594 05/01/05 - 04/30/10 $282,840 / $1,464,420

HLA-B27 Misfolding and the UPR in Spondyloarthritis
National Institutes of Health
R01 AR 046177 09/01/06 - 06/30/11 $262,864 / $1,409,806

Role of Type I Interferons in a Self-Sustaining Murine Model of Myositis
National Institutes of Health
R21 AR 055702 09/14/07 - 08/31/09 $126,420 / $236,500

Role of Immunoproteasomes in Activated T Cell Apoptosis
National Institutes of Health
R21 AI 073584 09/20/07 - 08/31/09 $147,150 / $275,000

LOVELL, D
Early Aggressive Therapy in Juvenile Idiopathic Arthritis
National Institutes of Health (Children's Hospital and Regional Medical Center-Seattle)
R01 AR 049762 09/01/06 - 08/31/11 $87,814 / $719,397

Rituximab in the Treatment of Refractory Adult and Juvenile Dermatomyositis
National Institutes of Health (University of Pittsburgh)
N01 AR 042273 09/01/06 - 09/29/09 $56,674 / $170,022

Cincinnati Multidisciplinary Clinical Research Center
National Institutes of Health
P60 AR 047784 08/18/08 - 07/31/13 $825,653 / $4,210,600
Lovell, D Administrative Core 66,866
Giannini, E Methodology Core 105,190
Brunner, H Project 1 160,309
Lovell, D Project 2 184,861
Grom, A Project 3 164,492
Seid, M Project 4 143,935

Dynamic Outcome Assessment in Multicenter Trials
National Institutes of Health (Duke University)
U01 AR 052186 08/01/08 - 07/31/09 $18,333 / $18,333

THOMPSON, S
Cincinnati Rheumatic Diseases Core Center
National Institutes of Health
P30 AR 047363 09/01/06 - 06/30/11 $388,400 / $2,000,000
Thompson, S Administrative Core 56,586
Thompson, S Core 1 - Tissue 43,042
Degen, J Core 2 - Animal Models of 67,299
Prevention of Cardiovascular Complications of Pediatric Lupus  
National Institutes of Health (Duke University)  
N01AR022265  
9/30/02 - 8/31/08  
$26,873 / $134,367

Early Agressive Therapy in JIA  
National Institutes of Health (Seattle Children's)  
R01AR049762  
05/01/08 - 04/30/11  
$42,809 / $85,619

Industry Contracts

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Current Year Direct Receipts  
157,923

Total  
$4,150,995