

Division of Rheumatology

DIVISION PROFILE	
Number of Faculty	12
Number of Fellows	
Clinical Fellows	6
Research Fellows	4
Number of Graduate Students	3
Number of Other Students (full and part-time)	3
Number of Support Personnel	57
Annual Total Grant Support (direct)	5,067,576
Annual Total Industry Contracts (direct)	553,232
Number of Peer Reviewed Publications	22
Patient Encounters	
Outpatient	4,098
Inpatient	276

FACULTY LISTING

David N. Glass, MD, Professor of Pediatrics, Director, William S. Rowe Division of Rheumatology

Hermine I. Brunner, MD, MSc, Assistant Professor of Pediatrics

Robert A. Colbert, MD, PhD, Professor of Pediatrics, Associate Director, William S. Rowe Division of Rheumatology; Associate Director, Physician Scientist Program, University of Cincinnati College of Medicine

Edward H. Giannini, MSc, Dr. PH, Professor of Pediatrics, Co-Director, Clinical Trials Unit

T. Brent Graham, MD, Associate Professor of Pediatrics

Thomas A. Griffin, MD, PhD, Assistant Professor of Pediatrics

Alexei A. Grom, MD, Associate Professor of Pediatrics

Joseph E. Levinson, MD, Professor Emeritus of Pediatrics

Daniel J. Lovell, MD, MPH, Professor of Pediatrics, Associate Director, William S. Rowe Division of Rheumatology; Joseph E. Levinson Chair in Pediatric Rheumatology; Co-Director, Clinical Trials Unit

Murray H. Passo, MD, Professor of Pediatrics, Director, Clinic and Fellowship Training Program, William S. Rowe Division of Rheumatology

Susan D. Thompson, PhD, Associate Professor of Pediatrics

Sherry Thornton, PhD, Assistant Professor of Pediatrics, Director, Summer Undergraduate Research Fellowship Program

OVERVIEW

The past year has witnessed considerable effort toward the renewal of center grants that support the division's academic efforts including clinical, translational, and basic research. The NIH/NIAMS-funded Rheumatic Diseases Core Center Grant (P30) was renewed in FY 2006, and a revised Multidisciplinary Clinical Research Center Grant (P60) was submitted in May.

The clinic in Treatment Center 14 is the site of most of the division's patient care and patient-oriented research activities. Five Clinical Research Coordinators are continually recruiting and enrolling patients in clinical and translational research studies. The clinical service continues to expand, particularly with outreach efforts. Drs. Griffin and Brunner evaluate patients at Toledo Children's Hospital, where over 300 outpatients patients were seen in FY 2006. Dr. Passo attends at the outreach clinic at Dayton Children's Medical Center, where close to 300 patients were seen. Expanded outreach efforts in FY 2006 include a clinic run by Dr. Griffin at St. Vincent Children's Hospital in Indianapolis, and in FY 2007 will include a clinic in Northern Kentucky and at the Shriner's Hospital in Lexington, KY attended by Dr. Graham.



Left to Right: (seated) H. Brunner, D. Glass, T.B. Graham, (standing) S. Thornton, R. Colbert, S. Thompson, D. Lovell, T. Griffin, E. Giannini, M. Passo

The division has expanded its educational efforts with a newly recruited training and education specialist, Jill Segerman, MEd, who is developing web-based training modules. Several members of the division play important roles at CCHMC and the University of Cincinnati, as well as at the national and international level. Sherry Thornton, PhD, is now the Director of the Summer Undergraduate Research Fellowship (SURF) Program that places approximately 75 undergraduates in various laboratories to obtain hands-on research experience. Janalee Taylor, RN, MSN, CNS, has been serving as Chair of the American Juvenile Arthritis Organization (AJAO) for the last two years, in addition to ongoing efforts on the Executive Committee and Board of Trustees of the National Arthritis Foundation. Dr. Glass was the keynote speaker at the annual scientific meeting of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) held in Denver CO, and was also an invited speaker at the European League Against Rheumatism (EULAR) annual meeting in Amsterdam, the Netherlands. Dr. Colbert was a co-organizer and speaker at an NIH conference to address the unmet needs in spondylitis research.

The beginning of FY 2007 will mark a significant change for the division. After 17 years as Director, David Glass, MD, has accepted a new position as Associate Director of the Cincinnati Children's Research Foundation (CCRF). Under Dr. Glass' leadership the division has grown tremendously, and is recognized internationally as one of the foremost centers for pediatric rheumatology research and patient care. Robert A. Colbert, MD, PhD, who joined the division in 1994 and became an Associate Director in 2002, will take on the responsibilities of division Director.

HIGHLIGHTS

Hermine Brunner, MD, MSc, Janalee Taylor, RN, MSN, CNS, Paula Melson, RPT, T. Brent Graham, MD, and Murray Passo, MD – Disparities in Outcome Among Children with Juvenile Rheumatoid Arthritis (JRA). JRA represents a group of chronic, autoimmune diseases with joint inflammation that can adversely affect quality of life that often persists into adulthood. Studies in adults with arthritis suggest that socioeconomic status impacts prognosis, but no information has been available as to whether this is also true in children. Investigators in the division together with Maria Britto, MD, and Uma Kotagal, MD, published a study in 'Arthritis Care & Research' examining the relationship between patient health insurance coverage, used as an indicator of socioeconomic status, and outcomes for children with JRA, and found that those on Medicaid had significantly lower health-related quality of life (HRQOL) and more disability than patients with private insurance. The disparities did not appear to be due to differences in health care utilization, and the authors hypothesized that poverty-related factors and medication adherence might be responsible. This study is the

first to document a clinically important association between insurance status and disease outcome in JRA, but more work will be needed to determine whether access to care and utilization of health care resources are truly equivalent between the two groups with different health insurance status. This study was made possible by ongoing quality Improvement and clinical effectiveness efforts.

David Glass, MD, Hermine Brunner, MD, MSc, and Susan Thompson, PhD – Impaired Reproductive Fitness in Mothers of Children with JRA. Predisposition to JRA is due to complex genetic and environmental factors. Although it is uncommon to find families where multiple children are affected with JRA, it is not uncommon to find other types of autoimmune disease. Dr. Glass and colleagues found that mothers of children with JRA were more likely to have pregnancy complications including miscarriages and preterm deliveries, than mothers of healthy children who were best friends of the JRA mothers. This work was published in the journal 'Rheumatology'. The authors hypothesized that these differences may be due to the intrauterine immunological environment, which is known to play a role in certain types of miscarriages, and further, that this early environment may even contribute to the development of JRA several years later. Additional studies are aimed at investigating these possibilities.

Thomas Griffin, MD, PhD, and Robert Colbert, MD, PhD – T Cell Proliferation is Influenced by Immunoproteasomes. T cells play an important role in the adaptive immune response, including abnormal processes such as autoimmunity. Proteasomes are key molecular machines involved in the degradation of proteins inside the cell. Protein degradation is instrumental for the regulation of many biological pathways, and also provides pieces of proteins (peptides) that are displayed to the immune system that help in the process of discriminating self from non-self. Immunoproteasomes are specialized proteasomes that function primarily in cells of the immune system or in other cells that have been exposed to certain cytokines. Dr. Griffin has been studying the function of immunoproteasomes and discovered that in addition to their well-recognized role in generating peptides, they also appear to be important for regulating T cell proliferation. Cells lacking immunoproteasome subunits tend to hyperproliferate, leading to a build up of T cells with a memory phenotype. These studies, published in the 'Journal of Immunology', may open up a new line of investigation into non-canonical proteasome functions, and have implications for the development of autoimmunity.

Daniel Lovell, MD, MPH, David Glass, MD, Murray Passo, MD, T. Brent Graham, MD, Edward Giannini, MSc, DrPH – Calcium Supplementation Increases Bone Mineral Density in Children with JRA. Children with JRA are more likely to develop osteoporosis for a number of reasons related to both the chronic inflammatory process and the medication used to treat the disease. Dr. Lovell and colleagues performed a randomized, double-blind, placebo-controlled trial of calcium supplementation in children with JRA and found a small but significant benefit of calcium in increasing total body bone mineral density. This work indicates that dietary calcium supplementation can be beneficial with little to no apparent risk.

TRAINING

Jennifer Huggins, MD	NA	University of Rochester School of Medicine and Dentistry
Lisa Petiniot, MD	PL-II	Cincinnati Children's Hospital Medical Center
Svetlana Lvovich	PL-II	Children's Hospital of NJ at Newark Beth Israel Medical Center
Natasha Ruth, MD	PL-III	University of South Carolina School of Medicine
Michael Shishov, MD	PL-III	New York University Medical Center
Judith A. Smith, MD, PhD	PL-IV	Cincinnati Children's Hospital Medical Center

GRANTS, CONTRACTS AND INDUSTRY AGREEMENTS

Grant and Contract Awards	Annual Direct/Project Period Direct
---------------------------	-------------------------------------

Brunner, H	
Prevention of Cardiovascular Pediatric Systemic Lupus Erythematosus	
National Institutes of Health (Duke University subcontract)	
N01 AR 002265	\$14,052/\$72,242
09/30/02 – 09/29/06	

Triptorelin for Ovary Protection in Childhood Lupus		
Food and Drug Administration		
FD-R-992369-02	09/30/03– 09/29/07	\$300,000/\$900,000
Development of Autoimmunity During Puberty in SLE		
National Institutes of Health (University of Oklahoma subcontract)		
R03 AR 052453	07/01/05 – 06/30/06	\$3,600
Towards Biomarkers for Lupus Renal Disease		
Alliance for Lupus Research		
	01/15/06 – 01/14/08	\$221,347/\$440,642
Meaningful Outcome Measures for Pediatric Lupus Trials		
National Institutes of Health		
R01 AR 051868	09/28/04 – 05/31/07	\$133,780/\$401,000
<hr/>		
Colbert, R		
Gene Expression in Pediatric Arthritis		
National Institutes of Health		
P01 AR 048929	08/22/03 – 07/31/08	\$1,110,953/\$5,234,051
Colbert, R	\$538,289	Administrative Core
Glass, D	\$103,672	Project 1
Colbert, R	\$87,021	Project 3
Grom, A	\$113,273	Project 4
Thompson, S	\$106,192	Core A
Pestian, J	\$162,507	Core B
Pediatric Rheumatology Training Grant		
National Institutes of Health		
T32 AR 007594	05/01/05 – 04/30/10	\$266,160/\$1,464,420
HLA-B27 Misfolding in Spondyloarthritis Pathogenesis		
National Institutes of Health		
R01 AR 048372	09/28/01 – 08/31/06	\$250,000/\$1,250,000
<hr/>		
Glass, D		
NIAMS Multidisciplinary Clinical Research Center		
National Institutes of Health		
P60 AR 047784	09/01/01 - 6/30/06	\$580,144/\$3,218,871
Glass, D	\$73,723	Administrative Core
Giannini, E	\$133,334	Methodology Core
Dardzinski, B	\$123,558	Project 3
Glass, D	\$249,529	Project 4
Research Registry for Juvenile Rheumatoid Arthritis		
National Institutes of Health		
N01 AR 042272	09/30/04 – 09/29/09	\$1,166,927/\$4,255,695
Arthritis Foundation Gene Expression		
Arthritis Foundation		
	08/22/03 – 07/31/08	\$250,000/\$1,290,000
HLA/KIR Region Genetics in Pediatric Arthritis		
National Institutes of Health		
U01 AI 067150	09/30/05 – 03/31/10	\$292,949/\$1,297,495
<hr/>		
Griffin, T		
Propeptide Mediation of Immuno Proteasome Assembly		
National Institutes of Health		
K08 AR 049733	04/15/03 – 03/31/07	\$110,750/\$443,000
<hr/>		
Ruth, N		
Rheumatology Fellowship Award Program		
Amgen, Inc.		
	07/01/05 – 06/30/06	\$25,000

Smith, J		
HLA-B27 Misfolding and Cytokine Regulation Arthritis Foundation	07/01/04 – 06/30/07	\$35,500/\$106,500
Thompson, S		
Prevention of Cardiovascular Pediatric Systemic Lupus Erythematosus National Institutes of Health (Duke University subcontract) N01 AR 022265	08/01/02 – 07/31/07	\$30,997/\$149,392
Genomic Landscape in Large Scale Integrated JRA Studies National Institutes of Health R01 AR 050688	09/15/03 – 08/31/07	\$194,000/\$752,000
Nitric Oxide in Pediatric Statin-Treated SLE National Institutes of Health (Duke University subcontract) R01 AR 051307	07/01/03 – 06/30/07	\$6,417/\$25,394
Thornton, S		
The Role of Fibrinogen/Angiopoietin-Related Protein in Autoimmune Arthritis Arthritis Foundation	07/01/02 – 06/30/06	\$75,000/\$297,000
Current Year Direct		\$5,067,576
Industry Contracts		
Giannini, E		
Immunex Corporation		\$444,671
Lovell, D		
Bristol Meyer Squibb		\$108,561
Current Year Direct Receipts		\$553,232
TOTAL		\$5,620,808

PUBLICATIONS

1. Brunner HI, Bishnoi A, Barron AC, Houk LJ, Ware A, Farhey Y, Mongey AB, Strife CF, Graham TB, Passo MH. Disease outcomes and ovarian function of childhood-onset systemic lupus erythematosus. *Lupus* 2006;15(4):198-206.
2. Carey B, DeLay M, Strasser JE, Chalk C, Dudley-McClain K, Milligan GN, Brunner HI, Thornton S, Hirsch R. A soluble divalent class I MHC/IgG1 fusion protein activates CD8+ T cells in vivo. *Clin Immunol* 2005;116(1):65-76.
3. Caudill CM, Jayarapu K, Elenich L, Monaco JJ, Colbert RA, Griffin TA. T cells lacking immunoproteasome subunits MECL-1 and LMP7 hyperproliferate in response to polyclonal mitogens. *J Immunol* 2006;176(7):4075-82.
4. Colbert RA. Pediatric and heritable disorders. *Curr Opin Rheumatol* 2005;17(5):566-7.
5. Smith JA, Marker-Hermann E, Colbert RA. Pathogenesis of ankylosing spondylitis: current concepts. *Best Pract Res Clin Rheumatol* 2006;20(3):571-91.
6. Turner MJ, Sowders DP, DeLay ML, Mohapatra R, Bai S, Smith JA, Brandewie JR, Taurog JD, Colbert RA. HLA-B27 misfolding in transgenic rats is associated with activation of the unfolded protein response. *J Immunol* 2005;175(4):2438-48.
7. Ward MM, Bruckel J, Colbert R, Doedhar A, Emerson C, Genant H, Gladman DD, Inman R, Reveille JD, Sandborg C, Weisman MH, Davis JC, Jr. Summary of the 2005 annual research and education

meeting of the Spondyloarthritis Research and Therapy Network (SPARTAN). *J Rheumatol* 2006;33(5):978-82.

8. Brzezinski JL, Deka R, Menon AG, Glass DN, Choi E. Variability in TRBV haplotype frequency and composition in Caucasian, African American, Western African and Chinese populations. *Int J Immunogenet* 2005;32(6):413-20.
9. Graham TB. Imaging in juvenile arthritis. *Curr Opin Rheumatol* 2005;17(5):574-8.
10. Graham TB, Laor T, Dardzinski BJ. Quantitative magnetic resonance imaging of the hands and wrists of children with juvenile rheumatoid arthritis. *J Rheumatol* 2005;32(9):1811-20.
11. Kashikar-Zuck S, Swain NF, Jones BA, Graham TB. Efficacy of cognitive-behavioral intervention for juvenile primary fibromyalgia syndrome. *J Rheumatol* 2005;32(8):1594-602.
12. Fall N, Bove KE, Stringer K, Lovell DJ, Brunner HI, Weiss J, Higgins GC, Bowyer SL, Graham TB, Thornton S, Grom AA. Association between lack of angiogenic response in muscle tissue and high expression of angiostatic ELR-negative CXC chemokines in patients with juvenile dermatomyositis: possible link to vasculopathy. *Arthritis Rheum* 2005;52(10):3175-80.
13. Lovell DJ, Reiff A, Jones OY, Schneider R, Nocton J, Stein LD, Gedalia A, Ilowite NT, Wallace CA, Whitmore JB, White B, Giannini EH. Long-term safety and efficacy of etanercept in children with polyarticular-course juvenile rheumatoid arthritis. *Arthritis Rheum* 2006;54(6):1987-94.
14. Reiff A, Lovell DJ, Adelsberg JV, Kiss MH, Goodman S, Zavalier MF, Chen PY, Bolognese JA, Cavanaugh PF, 2nd, Reicin AS, Giannini EH. Evaluation of the comparative efficacy and tolerability of rofecoxib and naproxen in children and adolescents with juvenile rheumatoid arthritis: a 12-week randomized controlled clinical trial with a 52-week open-label extension. *J Rheumatol* 2006;33(5):985-95.
15. Ruperto N, Ravelli A, Cuttica R, Espada G, Ozen S, Porras O, Sztajn bok F, Falcini F, Kasapcopur O, Venning H, Bica B, Merino R, Coto C, Ros J, Susic G, Gamir ML, Minden K, See Y, Uziel Y, Mukamel M, Riley P, Zulian F, Olivieri AN, Cimaz R, Girschick H, Rumba I, Cavuto S, Pistorio A, Lovell DJ, Martini A. The Pediatric Rheumatology International Trials Organization criteria for the evaluation of response to therapy in juvenile systemic lupus erythematosus: prospective validation of the disease activity core set. *Arthritis Rheum* 2005;52(9):2854-64.
16. Stark LJ, Davis AM, Janicke DM, Mackner LM, Hommel KA, Bean JA, Lovell D, Heubi JE, Kalkwarf HJ. A randomized clinical trial of dietary calcium to improve bone accretion in children with juvenile rheumatoid arthritis. *J Pediatr* 2006;148(4):501-7.
17. Wargula JC, Lovell DJ, Passo MH, Bove KE, Santangelo JD, Levinson JE. What more can we learn from muscle histopathology in children with dermatomyositis/polymyositis? *Clin Exp Rheumatol* 2006;24(3):333-43.
18. Chung YL, Rider LG, Bell JD, Summers RM, Zemel LS, Rennebohm RM, Passo MH, Hicks J, Miller FW, Scott DL. Muscle metabolites, detected in urine by proton spectroscopy, correlate with disease damage in juvenile idiopathic inflammatory myopathies. *Arthritis Rheum* 2005;53(4):565-70.
19. Passo M. Emerging therapies in juvenile rheumatoid/idiopathic arthritis. *Curr Probl Pediatr Adolesc Health Care* 2006;36(3):97-103.
20. Barnes M, Freudenberg J, Thompson S, Aronow B, Pavlidis P. Experimental comparison and cross-validation of the Affymetrix and Illumina gene expression analysis platforms. *Nucleic Acids Res* 2005;33(18):5914-23.
21. Phelan JD, Thompson SD, Glass DN. Susceptibility to JRA/JIA: complementing general autoimmune and arthritis traits. *Genes Immun* 2006;7(1):1-10.
22. Thornton S. Contribution of angiogenic genes to the complex genetic trait underlying Kawasaki disease. *Arthritis Rheum* 2006;54(5):1361-5.

1.