

# Division of Pathology & Laboratory Medicine

| DIVISION PROFILE                         |           |
|--|-----------|
| Number of Faculty                        | 14        |
| Number of Fellows                        |           |
| Clinical Fellows                         | 2         |
| Number of Support Personnel              | 14        |
| Annual Total Grant Support (direct)      | \$149,560 |
| Annual Total Industry Contracts (direct) | \$6,091   |
| Number of Peer Reviewed Publications     | 26        |
| Patient Encounters                       |           |
| Outpatient                               | 1,038,030 |
| Inpatient                                | 983,290   |

## FACULTY LISTING

David P. Witte, MD, Professor, Division Director, Division of Pathology & Laboratory Medicine  
Edgar T. Ballard, MD, Associate Professor  
Kevin E. Bove, MD, Professor  
Margaret Collins, MD, Associate Professor, Director, Pathology Training Program  
Gail H. Deutsch, MD, Assistant Professor  
Lili Miles, MD, Assistant Professor  
Michael Miles, PharmD, Professor  
Jun Q. Mo, MD, Assistant Professor  
Joel Mortensen, PhD, Associate Professor, Director, Diagnostic Infectious Disease Testing Laboratory  
Marina Nikiforova, MD, Assistant Professor, Director, Molecular Pathology  
Kenneth Setchell, PhD, Professor, Director, Mass Spectrometry  
Paul E. Steele, MD, Associate Professor, Medical Director, Clinical Laboratory  
Keith F. Stringer, MD, Assistant Professor  
Peter Tang, PhD, Assistant Professor

## OVERVIEW

The Division of Pathology & Laboratory Medicine provides full anatomic pathology and clinical lab diagnostic service to CCHMC patients as well as regional and national diagnostic consultation service. The anatomic path clinical service utilizes traditional tools of anatomic pathology including light microscopy, histochemistry, immunohistochemistry and electron microscopy (EM) as well as providing molecular technology including in situ hybridization and PCR analysis. The clinical lab utilizes state-of-the-art facilities, technology and technical expertise to provide a diagnostic testing service including microbiology, virology, serology, chemistry, special chemistry and hematology as well as a full service blood transfusion program in cooperation with the Hoxworth Regional Blood Center. In addition to the base lab, which performs more than 2,000,000 diagnostic tests each year, the recently established clinical lab operation at the Bethesda Oak facility provides core support for the lab services at the Cincinnati Center for Clinical Research. This lab was established to perform lab studies in support of human clinical trials in accordance with FDA and GLP quality standards. The division has an accredited fellowship training program in pediatric pathology as well as being an integral component of the UC Pathology Department residency training program by providing pediatric pathology learning experience for the pathology residents who rotate through CCHMC. The division has an active research program both at the clinical and basic science level. Ongoing clinical collaborative studies involve most clinical subdivisions at CCHMC including a wide range of clinical disorders such as eosinophilic GI disorders, motility disorders, metabolic liver diseases, inflammatory bowel disease, interstitial lung disease, and muscle disorders. The basic research in the molecular path lab focuses on a better understanding of the molecular and biologic mechanisms that contribute to the pathogenesis of developmental anomalies in childhood diseases through a morphologic understanding of the processes that regulate and promote normal development during embryogenesis as well as morphologic characterization of a number of animal models for pediatric diseases. The division provides core morphology lab support for numerous NIH funded projects

throughout CCHMC as well as investigators at UC. The mass spectroscopy core facility has been upgraded with state of the art instrumentation including a magnetic sector mass spec capable of performing fast atom bombardment and GC-MS electron ionization studies, GC-MS, and LC tandem MS. This facility provides support for basic research studies, clinical trials, and routine clinical diagnostic lab testing.



*Left to Right: (1<sup>st</sup> row) D. Witte, J. Mortensen, M. Nikiforova, L. Miles, J. Mo, K. Bove (2<sup>nd</sup> row) E. Ballard, P. Steele, G. Deutsch, M. Collins, P. Tang, K. Stringer*

## HIGHLIGHTS

The clinical lab has relied on Cerner Classic as its laboratory information system (LIS) for the past 20 years. For the past two years, Pathology & Laboratory Medicine has embarked on a plan to replace the LIS 2008. This effort has led to the decision to move forward with replacing the current LIS with the new Cerner Millennium system, which will affect anatomic pathology, clinical lab medicine, clinical genetics, and all ancillary lab services at CCHMC. There are a number of new functions available with this new LIS which are expected to improve the overall efficiency of the clinical lab operation. This includes real-time monitoring of turn-around-times in the lab. This function will service the technical staff to keep them better informed of their work flow and identify potential delays in the system which would impact patient care. New capabilities such as new bar coding technology for more rapid processing of samples as well as automated verification of testing results are expected to enhance patient care, particularly in areas of high patient volumes and flow such as the ED and clinics, and should improve patient care efficiency and reduce hassles to healthcare givers. The system is also expected to improve customer service by providing more readily accessible lab results and tracking of samples within the lab. The system will also include the new Helix program, a new molecular diagnostic module, which will provide a unique clinical research tool as a result of its more standardized formatting of molecular data and improved searching capabilities. In addition to the LIS project, the lab has also during the past year replaced its main chemistry analyzer with the Vitros fusion machine, which will provide much more rapid general chemistry studies due to its advanced automated functions including capabilities of performing autodilutions of samples which currently require manual intervention by the technical staff, which increases turn-around-time of abnormally high values. During the past few years, the neonatology service at CCHMC has expanded its coverage to provide all neonatal clinical services within the region, in addition to staffing the neonatal intensive care unit at CCHMC. The division of pathology is now also playing a more significant regional role in perinatal and neonatal medical care in providing most of the autopsy support for all of the perinatal and neonatal clinical services within the region, which includes

University, Christ, Bethesda, Good Samaritan and the Mercy hospital systems. This now creates an even more comprehensive neonatal and perinatal care program throughout the region involving multiple divisions such as neonatology, surgery, radiology, cardiology, genetics, and now pathology. The mass spectrometry facility, under the direction of Dr. Setchell, is involved in studies investigating the role of phytoestrogens in disease prevention and treatment. Mass spec has developed methodologies for analysis of phytoestrogens and is playing a prominent role in collaboration with many international research groups that are studying the health benefit of these natural bioactive compounds. Other studies that are ongoing in mass spec include the anticancer effects of disulfate conjugate of ursodeoxycholate (SUDCA). As a result of these studies, Axcan Pharma is currently pursuing phase 2 and phase 3 clinical trials of SUDCA to determine its potential role in colon cancer prevention. Two NIH funded core labs exist within the division of pathology. One is a program under the direction of Mitch Cohen, MD. (Gastroenterology/Nutrition), which established the Cincinnati Center for Growth and Development. Under this support, the lab provides extensive morphology and pathologic support for a number of investigators, mostly at CCHMC, with research focuses on various aspects of pediatric digestive disease and intestinal development. A second core lab has been established in collaboration with the Division of Immunobiology and the Division of Allergy and Immunology. This grant, under the direction of Dr. Marsha Wills-Karp, will involve a multidisciplinary approach to study the role of interleukin-13 in experimental asthma. Dr. Gail Deutsch has a research program focused on embryonic foregut endoderm development. Dr. Deutsch also has a strong collaboration effort with the Divisions of Pulmonary Medicine, Pulmonary Biology and Radiology, involving pediatric interstitial lung diseases and has been involved with a multicenter effort to redefine these complex disorders. Dr. Margaret Collins is actively collaborating with Drs. Marc Rothenberg and Phil Putnam to provide support for their eosinophilic research program here at CCHMC. Pathology also has strong clinical collaborations related to muscle disorders between the Division of Neurology and Drs. Kevin Bove and Lili Miles, to the Hem/Onc division with Dr. Jun Mo, and the inflammatory bowel disease program interacts with Dr. Edgar Ballard.

## TRAINING

|                         |        |                           |
|-------------------------|--------|---------------------------|
| M. Cristina Pacheco, MD | PGY-VI | University of Cincinnati  |
| Yan Wang, MD            | PGY-VI | Fujian Medical University |

## GRANTS, CONTRACTS AND INDUSTRY AGREEMENTS

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

Miles, M

Evaluation of Coenzyme Q10 Efficacy in Pediatric Patients with Down Syndrome  
The Jerome LeJeune Foundation

12/01/05 – 11/30/06

\$22,620

Witte, D

Interleukin-13 in Experimental Asthma

National Institutes of Health

P01 HL 076383

07/01/04 – 06/30/09

\$126,940/\$751,280

Current Year Direct

\$149,560

### Industry Contracts

Witte, D

Microbiology Research

\$6,091

Current Year Direct Receipts

\$6,091

**TOTAL**

**\$155,651**

## PUBLICATIONS

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2. Ryckman F, Alfonso M, Tiao G, Bove KE. Transplantation for hepatic malignancy in children. In: Busuttill RW, Klintmalm GB, editors. *Transplantation of the liver*; 2nd ed. Philadelphia: Elsevier Saunders; 2005. p. 367-378.
3. Hinton RB, Jr., Deutsch GH, Pearl JM, Hobart HH, Morris CA, Benson DW. Bilateral semilunar valve disease in a child with partial deletion of the Williams-Beuren syndrome region is associated with elastin haploinsufficiency. *J Heart Valve Dis* 2006;15(3):352-5.
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5. Langston C, Patterson K, Dishop MK, Askin F, Baker P, Chou P, Cool C, Coventry S, Cutz E, Davis M, Deutsch G, Galambos C, Pugh J, Wert S, White F. A protocol for the handling of tissue obtained by operative lung biopsy: recommendations of the chILD pathology co-operative group. *Pediatr Dev Pathol* 2006;9(3):173-80.
6. Bravo M, White D, Miles L, Cotton R. Adenomatoid odontogenic tumor mimicking a dentigerous cyst. *Int J Pediatr Otorhinolaryngol* 2005;69(12):1685-8.
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10. Miles L, Wong BL, Dinopoulos A, Morehart PJ, Hofmann IA, Bove KE. Investigation of children for mitochondrialopathy confirms need for strict patient selection, improved morphological criteria, and better laboratory methods. *Hum Pathol* 2006;37(2):173-84.
11. Qian Y, Zhou X, Hu Y, Tong Y, Li R, Lu F, Yang H, Mo JQ, Qu J, Guan MX. Clinical evaluation and mitochondrial DNA sequence analysis in three Chinese families with Leber's hereditary optic neuropathy. *Biochem Biophys Res Commun* 2005;332(2):614-21.
12. Qu J, Li R, Zhou X, Tong Y, Lu F, Qian Y, Hu Y, Mo JQ, West CE, Guan MX. The novel A4435G mutation in the mitochondrial tRNAMet may modulate the phenotypic expression of the LHON-associated ND4 G11778A mutation. *Invest Ophthalmol Vis Sci* 2006;47(2):475-83.
13. Yuan H, Qian Y, Xu Y, Cao J, Bai L, Shen W, Ji F, Zhang X, Kang D, Mo JQ, Greinwald JH, Han D, Zhai S, Young WY, Guan MX. Cosegregation of the G7444A mutation in the mitochondrial COI/tRNA(Ser(UCN)) genes with the 12S rRNA A1555G mutation in a Chinese family with aminoglycoside-induced and nonsyndromic hearing loss. *Am J Med Genet A* 2005;138(2):133-40.
14. Yoon SS, Coakley R, Lau GW, Lyman SV, Gaston B, Karabulut AC, Hennigan RF, Hwang SH, Buettner G, Schurr MJ, Mortensen JE, Burns JL, Speert D, Boucher RC, Hassett DJ. Anaerobic killing of mucoid *Pseudomonas aeruginosa* by acidified nitrite derivatives under cystic fibrosis airway conditions. *J Clin Invest* 2006;116(2):436-46.
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16. Bu L, Setchell KD, Lephart ED. Influences of dietary soy isoflavones on metabolism but not nociception and stress hormone responses in ovariectomized female rats. *Reprod Biol Endocrinol* 2005;3:58-67.
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23. Waters PJ, Khashu M, Lillquist Y, Senger C, Mattman A, Demos M, Setchell KD, Rupar A, Scott P, Blau N, Vallance HD. Neonatal hyperphenylalaninemia, perinatal hemochromatosis, and renal tubulopathy: a unique patient or a novel metabolic disorder? *Mol Genet Metab* 2005;86 Suppl 1:S148-52.
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25. Pysher TJ, Bach PR, Geaghan SM, Hamilton MS, Laposata M, Lockitch G, Brugnara C, Coffin CM, Pasquali M, Rinaldo P, Roberts WL, Rutledge JC, Ashwood ER, Blaylock RC, Campos JM, Goldsmith B, Jones PM, Lim M, Meikle AW, Perkins SL, Perry DA, Petti CA, Rogers BB, Steele PE, Weiss RL, Woods G. Teaching pediatric laboratory medicine to pathology residents. *Arch Pathol Lab Med* 2006;130(7):1031-8.
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