



## Our Experts

Our experts provide testing, diagnosis and clinical services for a broad range of immunodeficiencies and related disorders, including autoimmune lymphoproliferative disease (ALPS) and familial hemophagocytic lymphohistiocytosis (FHL).

**Kejian Zhang, MD, MBA**  
Director,  
Molecular Genetics Laboratory

**Alexandra (Lisa) Filipovich, MD**  
Director,  
Immunodeficiency and Histiocytosis Program

**Judith Johnson, MS, CGC**  
Genetic Counselor/Program Coordinator

**Jack J. H. Bleasing, MD, PhD**  
Associate Director,  
Immunodeficiency and Histiocytosis Program

**Bradley Tinkle, MD, PhD**  
Assistant Director,  
Molecular Genetics Laboratory

### Ongoing Research Benefits Patients

Our experts are actively engaged in promising research to better understand and treat immunodeficiency disorders; patients benefit by having access to the latest and best opportunities research has to offer. Updated *GeneReviews*<sup>®</sup>, a quarterly newsletter, peer-reviewed publications and our recontact program keep you up-to-date about new developments.

### Contact us for:

- Guidance in test selection
- In-depth clinical interpretations and recommendations
- Recommendations for genetic counseling and coordination of studies for at-risk family members

**Molecular Genetics Lab**  
513-636-4474

**Diagnostic Immunology Lab**  
513-636-4685

**Clinical Services**  
513-636-6639

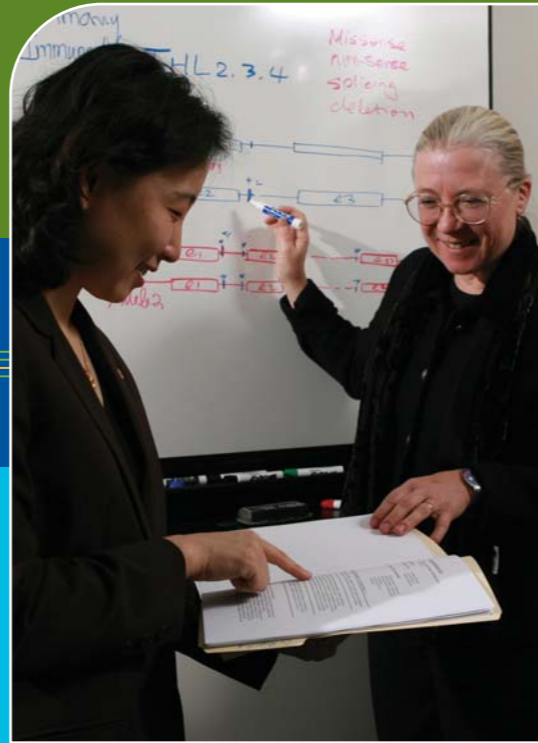
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A FOCIS Center of Excellence  
Cincinnati Children's was named a Federation of Clinical Immunology Societies (FOCIS) Center of Excellence in recognition of multidisciplinary immunology research, education and patient care. The Molecular Genetics and Diagnostic Immunology laboratories are certified by CAP and CLIA.

## Clinically Relevant Reports



*"At Cincinnati Children's they understand what we're doing, why we need the information and what's going on with my patients. Without exception, an expert has always been available to discuss interpretation of results when I needed consultation. Their test results are presented in a more useable, relevant form than other labs, and results are provided in a timely fashion."*

**J. Sande, MD**  
Pediatric Medical Director,  
Lowder Stem Cell Transplant Unit  
Children's Hospital of Alabama



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Diagnostic Center for Heritable Immunodeficiencies

**Molecular Genetics Lab**  
513-636-4474

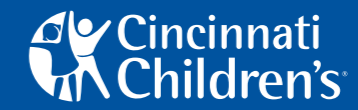
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## Diagnostic Center for Heritable Immunodeficiencies

A FOCIS Center of Excellence

- Molecular Genetics Laboratory
- Diagnostic Immunology Laboratory
- Clinical Immunodeficiency Services



*Offering a comprehensive approach to diagnosis and management featuring clinically relevant lab reports and expert consultation*



# Comprehensive Immunodeficiency Services

to meet the specific needs of your patients

At Cincinnati Children's, we provide a *comprehensive* approach to the diagnosis and management of common as well as life-threatening primary immunodeficiencies and hemophagocytic disorders. We offer:



## State-of-the-art genetic testing

PCR-based full gene sequence analysis and detailed interpretation of test results.

## Functional immunological testing

A complete battery of assays for immune function and rapid screening of life-threatening immunodeficiencies are used to direct the molecular genetic work-up, aid in the interpretation of novel genetic findings, and provide essential information relevant to treatment and clinical monitoring.

## Ease in accessing services

Genetic and immunologic tests may be ordered in tandem. Follow-up testing, coordination of family studies, genetic counseling and comprehensive clinical services can be easily arranged.

## Clinical services

Clinical expert consultations are available by phone or email. Rapid referrals also are accepted.

Our experts collaborate closely with referring physicians as you provide care for your patients with these rare disorders. We can provide all or some of these services, depending on your needs.

## Coordination of Lab Tests Enable Accurate Diagnosis

For rare primary immunodeficiencies, a laboratory's ability to interpret a genetic test result in the context of immunologic testing may be of paramount importance, as the following case demonstrates.

An asymptomatic female with a family history of X-linked lymphoproliferative disease presented for carrier testing. To everyone's surprise, two previously reported mutations in SH2D1A were identified, one on each chromosome. A report provided by other laboratories would likely end there.

In our Molecular Genetics Laboratory we obtained samples from multiple family members for molecular genetic testing. Concurrently, in our Diagnostic Immunology Laboratory we performed immunologic studies of SAP expression, the protein deficient in XLP secondary to SH2D1A mutations. This allowed us to correlate deficient SAP expression with the maternal allele and normal SAP expression with the paternal allele. We concluded that the paternal allele was a benign polymorphism (in contrast to its previously published pathogenicity) and posed no risk to the patient or paternally-related family members.

# Laboratory Reports

offer superior interpretation & recommendations

"There is a difference." This is what we often hear from referring physicians when comparing test reports from Cincinnati Children's to other labs.

Our reports include detailed interpretations of test results by board-certified geneticists and specific *clinical* recommendations from our pediatric immunodeficiency experts.

See the difference for yourself by viewing the sample test report found at [www.cincinnatichildrens.org/dchi](http://www.cincinnatichildrens.org/dchi).



visit

[www.cincinnatichildrens.org/dchi](http://www.cincinnatichildrens.org/dchi)

Find information regarding disorders, indications for testing, methodology, test requisition and shipping instructions.

## Diagnostic Immunology Laboratory

Immunologic screening tests for specific disorders (available depending on the clinical indications and results of initial immunologic tests):

- X-linked hyper IgM syndrome (HIGM1)
  - CD40 ligand upregulation by flow cytometry
- X-linked lymphoproliferative disease (XLP)
  - SAP detection by flow cytometry
- X-linked severe combined immunodeficiency (XSCID)
  - CD132 detection by flow cytometry
- IL7R-alpha defective severe combined immunodeficiency
  - CD127 detection by flow cytometry
- HLH screening
  - NK-cell function
  - Perforin expression detection by flow cytometry
  - Granzyme B detection by flow cytometry
  - CD107 detection by flow cytometry (future assay)
- X-linked immune dysregulation, polyendocrinopathy, enteropathy syndrome (IPEX)
  - FOXP3 detection by flow cytometry
- Wiskott-Aldrich syndrome (WAS)
  - WAS protein detection by flow cytometry
- Autoimmune lymphoproliferative syndrome (ALPS)
  - ALPS panel by flow cytometry
  - FAS apoptosis assay
- Common variable immunodeficiency (autosomal recessive hyper IgM syndrome)
  - B-cell panel by flow cytometry
  - ICOS upregulation by flow cytometry
  - BAFF system panel

Diagnostic cellular immune functions tests standardized for pediatric populations:

- Lymphocyte phenotyping
  - Lymphocyte subpopulations
  - TCR alpha beta/gamma delta
  - TCR V beta clonogram
  - Activation markers
  - CD45 RA/RO (CCR7 upon request)
  - CD40 ligand/ICOS
  - CD132/127
  - ALPS panel
  - B-cell panel
- Neutrophil/monocyte functional assays
  - Phagocytosis and killing
  - Chemotaxis
  - Oxidative burst
  - Adhesion markers
  - Leuko64 assay
  - CD163 monocyte activation marker
- Intracellular assays
  - Perforin
  - Granzyme B
  - WAS protein
  - SAP
  - Cytokines
- Lymphocyte functional assays
  - Mitogen stimulation
  - Antigen stimulation
  - NK-cell function
  - Cytotoxic lymphocyte function

## Molecular Genetics Laboratory

Full gene sequence analysis and comprehensive clinical interpretation for symptomatic individuals and their family members:

- Autoimmune lymphoproliferative syndrome (ALPS)
  - FAS (TNFRSF6)
  - Fas ligand\* (FASL)
  - Caspase 10\* (CASP10)
  - FAS/FASL/CASP10 in sorted lymphocytes\* (somatic mutation detection)
- Familial hemophagocytic lymphohistiocytosis (FHL)
  - Perforin 1 (PRF1)
  - MUNC13-4 (UNC13D)
  - Syntaxin 11 (STX11)
- X-linked immune dysregulation, polyendocrinopathy, enteropathy syndrome (IPEX)
  - FOXP3
- Wiskott-Aldrich syndrome (WAS), X-linked thrombocytopenia (XLT) and X-linked neutropenia (XLN)
  - WAS
- X-linked lymphoproliferative disease (XLP)
  - SH2D1A
  - BIRC4
- X-linked hyper IgM syndrome (HIGM1)
  - CD40 ligand
- X-linked severe combined immunodeficiency (XSCID)
  - IL2RG
- Congenital neutropenia
  - HAX1\*

\* Research testing only. Please email us at [dcbi@ccbmc.org](mailto:dcbi@ccbmc.org) for more information.

## Clinical Services Offered

- Initial diagnostic evaluations
- Expert consultations for diagnoses and management of (suspected) immunodeficiency disorders
- Ongoing management
- Genetic counseling
- Home-based therapies
- Participation in national trials
- Hematopoietic stem cell transplantation for children using related and unrelated donors (marrow, cord blood, peripheral stem cells)
- Comprehensive evaluation of chronic/recurrent immune cytopenias, in collaboration with the Blood Disease Center