Medical Genetics and Genomics: The Emory Experience

Michael J. Gambello, MD, PhD
Professor and Program Director
Department of Human Genetics
Emory University School of Medicine
Welcome to the Department of Human Genetics (DOHG). It is an exciting time for human genetics with the ongoing revolution in genetics and genomics. Our unique combination of a full-fledged basic research faculty along with the comprehensive clinical genetics division places us at the forefront of contemporary translational research and predictive, precision health.

Peng Jin, PhD
Chair, Department of Human Genetics
History of the Division of Medical Genetics in the Department of Human Genetics

1970 Founded by Louis “Skip” Elsas II, M.D. in the Department of Pediatrics

2001-2020 Former Chair, Stephen T. Warren, Ph.D. founded The Department of Human Genetics

2002 The Division becomes affiliated with The Department of Human Genetics emphasizing the important relationship between medical genetics and human genetics research.

https://med.emory.edu/departments/human-genetics/patient-care/physicians-counselors.html
Division of Medical Genetics
A Diverse Group of Genetics Professionals
Our Missions

Clinical Care

Clinical and Basic Science Research

Education
Educational Programs in Genetics at Emory

1. ACGME Accredited Clinical Programs -
   Medical Genetics and Genomics (MGG)
   Medical Biochemical Genetics
   Pediatrics – MGG

2. Graduate Program
   (GMB – Genetics and Molecular Biology)

4. ABGC Accredited Genetic Counseling Training Program

5. Human Genetics and Nutrition
Core Physician Faculty

Hong Li, MD, PhD  
Director Metabolic Clinic

Michael J. Gambello, MD, PhD  
Program Director

William Wilcoxon, MD, PhD  
Program Director MBG

Stephanie Wechsler, MD

Jaime Vengoechea, MD

Rossana Sanchez, MD

Juanita Neira, MD

Emily Black, MD
### Sample Schedule – Year 1

<table>
<thead>
<tr>
<th>Months</th>
<th>July</th>
<th>August</th>
<th>September</th>
<th>October</th>
<th>November</th>
<th>December</th>
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<tbody>
<tr>
<td><strong>Clinical Activity</strong></td>
<td>General Genetics &amp; Metabolism Clinics 4 days/week</td>
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<td><strong>NAMA October (Option to take Year 2)</strong></td>
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<tr>
<td><strong>Vacation one week</strong></td>
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<tr>
<th>Months</th>
<th>January</th>
<th>February</th>
<th>March</th>
<th>April</th>
<th>May</th>
<th>June</th>
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<tbody>
<tr>
<td><strong>Clinical Activity</strong></td>
<td>Self Directed Study</td>
<td>Cancer Genetics Winship Cancer Institute</td>
<td>General Genetics &amp; Metabolism Clinics 4 days/week</td>
<td>General Genetics &amp; Metabolism</td>
<td>Molecular Genetics Laboratory No Call/Clinic 2 weeks</td>
<td>Biochem. Laboratory No Call/Clinic 2weeks</td>
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<td>Call Optional</td>
<td>No Call</td>
<td>One admin day/wk</td>
<td>One week Call Outpatient Clinic 4 days/week</td>
<td>Cytogenetics Laboratory No Call/Clinic 2 weeks</td>
<td>Vacation one week</td>
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<td></td>
<td>One week vacation</td>
<td></td>
<td>One week Call</td>
<td></td>
<td>No Call</td>
<td>Seld-Directed study one week</td>
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Outpatient Clinics

- 85% Pediatric 15% Adult
- 7000 visits/year
- Diverse patient population
- Large catchment area
- Referrals from
  - Pediatricians
  - Internists
  - Other Specialists
  - Hospital Follow-up
- Wait list 1-2 months
- Exploring Telemedicine

Georgia 10 million
Metro Atlanta 5 million
Outpatient Clinics

- General Genetics Clinics – Every Day
  - Intellectual disability, speech delay, dysmorphic features
  - Birth defects, failure to thrive, autism spectrum disorders
  - Family history of cancer, aortic dissection etc.

- Metabolism Clinics – Mondays, Tuesdays, Wednesdays
  - Abnormal newborn screens
  - Continuing Care
  - Lysosomal storage disease clinic
    - MPS, Gaucher, Fabry, Pompe etc.
Specialty Clinics

- Skeletal Disorders Clinic
- Craniofacial Clinic
- Fragile X and Down Syndrome Clinics
- Disorders of Sexual Development
- NF1/TSC Clinic
- 22q11.2 Clinic
- Prenatal Clinic
- Cancer Genetics Clinic
Inpatient Consultations

Majority at Children’s Healthcare of Atlanta –
Egleston Campus 278 beds
Scottish Rite Campus 273 beds
Some adult consultations at Emory University/Tower Hospitals

When on call, resident is the first person called
No outpatient duties when on call
 Resident always reviews plan with attending
Approximate Births in 2016
130,042

Major Racial/Ethnic Groups
White: 59%
American Indian: <1%
African American: 37%
Asian/Pacific islander: 4%
Hispanic Ethnicity: 16% (may also be included in race categories above)
Newborn Screening Follow-up

- Division has NBS follow-up contract with GA.

- Angela Wittenauer, nurse coordinator, 6 nurses.

- NBS database

- Superb opportunity to learn about the management of positive screens for over 30 inborn errors of metabolism.

- NICHD Pilot projects led by Dr. Wilcox on NBS for MPS1 Pompe disease, XALD, SMA, Homocystinurica

- Forming a Long-term Follow-up Program
Didactic Learning

- **HGC 715 – Human Genetics Fall 3 credits**
  Kate Garber, PhD
  Course Director
  Multiple Lecturers

- **HGC 745 – Medical Genetics Fall/Spring 3 credits**
  Stephanie Wechsler, MD
  Course Director
  Multiple Lecturers
Clinical Conference

Drs. Li/Vengoechea coordinators.

CME credits for Faculty.

Weekly one hour presentation of two cases.

Presentations by GCs, GC students, residents, medical students.

Faculty Mentor assigned. Reviews presentations and ensures content for CME.

Power Point Presentation 25-30 minutes.

Resident gives a CC once a semester

ALL VIRTUAL 2020-2021
<table>
<thead>
<tr>
<th>Date</th>
<th>Presenter</th>
<th>Topic</th>
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<tbody>
<tr>
<td>09/18/18</td>
<td>Janette diMonda</td>
<td>From VUS to Diagnosis: A Case of Singleton-Merten Syndrome</td>
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<td>Morgan Simmons</td>
<td>Fabry Disease: Fact or Faux?</td>
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<td>10/02/18</td>
<td>Rachel Linnemann</td>
<td>Diagnostic Challenges in Cystic Fibrosis</td>
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<td>Rhea Behlmann</td>
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<td>10/09/18</td>
<td>Emily Davis Black</td>
<td>Review the management of PLA2G6-associated neurodegeneration and explore potential therapeutic options that are in clinical trials</td>
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<td>Matthew Walsh</td>
<td>X-linked Conelida de Lange Syndrome</td>
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<td>10/23/18</td>
<td>Chelsea Leonard</td>
<td>NAA10-Related Syndrome</td>
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<td>Georgia Loucopoulos</td>
<td>Patient decision-making for prenatal testing when faced with a VUS</td>
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<tr>
<td>11/06/18</td>
<td>Abdulrazak K.Alali</td>
<td>Holocarboxylase Synthetase Deficiency: A Case Presentation and Review Of The Literature</td>
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<td>Merlene Peter</td>
<td>The Tale of Two Translocations</td>
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<tr>
<td>11/13/18</td>
<td>Aixa Gonzalez Garcia</td>
<td>Inherited Systemic Hyalnosis (ANTXR2 related disorder)</td>
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<td>Ellie Westfall</td>
<td>Challenges of DICER1 Diagnosis</td>
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<tr>
<td>11/20/18</td>
<td>Christine Tallo</td>
<td>MLH1 Epimutations: An Overlooked Cause of Lynch Syndrome</td>
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<td>Virginia Casola</td>
<td>A Look Into Li-Fraumeni Syndrome</td>
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<tr>
<td>12/04/18</td>
<td>Allison Foley</td>
<td>A Review of Achondroplasia and Current Investigational Treatment Options</td>
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<td>Tina Kushary</td>
<td>Clinical and Molecular Diagnosis, Screening and Management of Beckwith-Wiedemann Syndrome: A Newly Published International Consensus Statement</td>
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Clinical Conference

**Speaker**
Emily Black, MD, Medical Genetics Resident PGY5

**Mentor**
Rossana Sánchez, MD

**Title of Presentation**
An Update on a Recurrent Microdeletion Syndrome

**Learning Objectives:**
1. Review an adult case of Smith Magenis syndrome, the clinical presentation, management and surveillance
2. Review the common deleted region in Smith Magenis syndrome
3. Discuss Birt Hogg Dube syndrome, the molecular etiology, clinical presentation and surveillance recommendations

**Presenter Financial Relationships:** NONE
**Company/Role:** Emory University
Medical Genetics Resident PGY5
**Financial Relationships of RSS Director, Planning Committee Members and Others:** NONE

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**Speaker**
Rachel Logan, MSSc, Genetic Counselor II
Children’s Hospital of Atlanta

**Mentor**
Rossana Sánchez, MD

**Title of Presentation**
Parental Mosaicism and Monogenic Epilepsies: Case of CACNA1A – Associated Ataxia and Epileptic Encephalopathy

**Learning Objectives:**
1. Review the pathogenesis of CACNA1A – associated disorders
2. Describe the clinical features of CACNA1A – associated disorders
3. Discuss reports of parental mosaicism in monogenic epilepsies

**Presenter Financial Relationships:** NONE
**Company/Role:** Children’s Hospital of Atlanta, Genetic Counselor II
**Commercial support for RSS/Session:** NONE
**Financial Relationships of RSS Director, Planning Committee Members and Others:** NONE
Grand Rounds/ Research Seminars

- **Grand Rounds**
  - Every other week
  - Mondays 8-9 AM
  - Schedule posted on Dept. Website
  - Local and invited speakers
  - Resident will give one grand rounds each year
  - ALL VIRTUAL 2020-2021

- **Research Seminar**
  - Alternates with GR
  - Mondays 12-1 PM
  - Schedule on Dept. Website
  - Local and invited speakers
  - Residents should try to go. Discuss with Dr. Gambello.
  - ALL VIRTUAL 2020-2021
Self-Directed Learning

- 18 months clinical
- 1.5 months laboratory rotations
- 3 weeks vacation each year
- Leaves 3 months for dedicated self-directed learning
- Involvement in one clinical trial
- Opportunities for other projects/Poster and Manuscript Preparation
Research Opportunities

• Clinical Behavioral and molecular characterization of 3q29 deletion syndrome patients
  – Dr. Jennifer Mulle

• Elucidating inheritance patterns of dystonias
• Next-generation sequencing panels for dystonias
  – Dr. Hyder Jinnah

• Newborn screening performance improvement
  – Arthur Hagar, PhD
Research Projects

• Identifying novel ciliopathy mutations using cilia proteome and EGL databases.
  – Tamara Caspary, PhD

• Mining a longitudinal data set for patterns in outcomes of patients with classic galactosemia.
  – Judy Fridovich-Keil, PhD

• Screen for familial hyperlipidemia in EMR using LDL levels
  – Jaime Vengoechea, MD
Research Projects

• Development of a cell-free DNA-based biomarker for methylation status to be used for disease diagnosis and treatment.
  – Peng Jin, PhD

• Clinical definition and gene discovery for skeletal disorder
  – William Wilcox, MD, PhD

• Exploring methylation abnormalities in tuberous sclerosis complex
  – Michael Gambello, MD, PhD
Genetic Clinical Trials Group

- One of the most capable and experienced clinical trial centers for genetic disorders.
- 30 Sponsored clinical trials
- 10 Registries for genetic diseases
- 3 NIH contracts for newborn screening pilot studies
  - Pompe
  - MPS1, X-Linked ALD
  - SMA
- **ALL** trainees take part in at least one clinical trial
Examples

- Biomarin ACHON 111-301
  - Disease: Achondroplasia
  - PI: Wilcox
  - SC: Allison Foley
  - Actual/Proj Enrollment: 9

A Phase 3 Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of BMN 111 in Children with Achondroplasia

Neuronext FX-Learn
- PI: Amy Talboy;
- SC: Jean Luan McColl
- Actual/Proj Enrollment: 7

NIH sponsored, Phase 2, Double-blind, Placebo-controlled, Multicenter study for children with fragile X syndrome (FXS) (ages 32 months to 6 years of age - inclusive) extension
Teaching Opportunities

- Pediatric residents
- Pediatric neurology residents
- Pediatric liver residents
- Obstetric-gynecology residents
- Medical Students
- Genetic counseling students

Educating Primary Care Providers

- Grand Rounds
- Invited Lectures
- Workshops
- Community Outreach
- Core Resident Lectures
Meetings

• All trainees go to NAMA first or second year.

• One meeting a year, usually ACMG, SIMD, ASHG.

• Ideal to have an abstract for the meeting.

• Can sometimes get travel award for other meetings e.g. SERGG
Department Retreat

Residents and Fellows are encouraged to attend
Other Aspects of Program

- $1500 moving expense
- One administrative day/week with no scheduled clinics
- $600 book allowance
- 3 weeks vacation a year
Email us with QUESTIONS??

Liz McKenna
Program Coordinator
Elizabeth.mckenna@emory.edu

Michael J. Gambello, MD, PhD
Program Director
Mgambel@emory.edu
We are a Fun Group!
Christmas at Dr. G’s
GRADUATION TIME
Atlanta is a GREAT City!!!