Medical Genetics and Genomics: The Emory Experience

Michael J. Gambello, MD, PhD
Professor
Department of Human Genetics
Emory University School of Medicine
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 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.
Division of Medical Genetics
A Diverse Group of Genetics Professionals
Mandate of the Division of Medical Genetics

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. Clinical Laboratory Programs
   Laboratory Genetics and Genomics
   Clinical Biochemical Genetics

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

4. ABGC Accredited Genetic Counseling Training Program

5. Human Genetics and Nutrition
Medical Genetics and Genomics

Liz McKenna
Program Coordinator

Michael J. Gambello, MD, PhD
Program Director

William Wilcox, MD, PhD
Program Director MBG

Hong Li, MD, PhD

Jaime Vengoechea, MD

Rossana Sanchez, MD

Stephanie Wechsler, MD

Juanita Neira, 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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>General Genetics &amp; Metabolism</td>
<td>General Genetics &amp; Metabolism</td>
<td>Molecular Genetics Laboratory at EGL</td>
<td>General Genetics &amp; Metabolism</td>
<td>General Genetics &amp; Metabolism</td>
<td>Biochem. Laboratory at EGL No Call/Clinic Dec. 1-12</td>
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<tr>
<td></td>
<td>One week Call Outpatient Clinic 4 days/week</td>
<td>One week Call Outpatient Clinic 4 days/week</td>
<td>No Call/Clinic 2 weeks</td>
<td>One week Call</td>
<td>NAMA Oct 12-18 (Option to take Year 2)</td>
<td>Vacation one week</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Cytogenetics Laboratory at EGL No Call/Clinic 2 weeks</td>
<td></td>
<td></td>
<td>General Genetics &amp; Metabolism</td>
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<td>Dec. 13-31</td>
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<thead>
<tr>
<th>Months</th>
<th>January</th>
<th>February</th>
<th>March</th>
<th>April</th>
<th>May</th>
<th>June</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prenatal Genetics at EUH Midtown</td>
<td>Vacation 2 weeks</td>
<td>General Genetics &amp; Metabolism</td>
<td>General Genetics &amp; Metabolism</td>
<td>Self-Directed Learning</td>
<td>Cancer Genetics Winship Cancer Institute</td>
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<tr>
<td></td>
<td>No Call</td>
<td>General Genetics/Metab Outpatient Clinic 4 days/week</td>
<td>One week Call Outpatient Clinic 4 days/week</td>
<td>One week Call Outpatient Clinic 4 days/week</td>
<td>No Call</td>
<td>No Call</td>
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# Sample Schedule – Year 2

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<tr>
<th>Months</th>
<th>July</th>
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<th>September</th>
<th>October</th>
<th>November</th>
<th>December</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Activity</td>
<td>General Genetics &amp; Metabolism</td>
<td>Self-Directed Learning</td>
<td>Self-Directed Learning</td>
<td>Lysosomal Storage Diseases</td>
<td>General Genetics &amp; Metabolism</td>
<td>General Genetics &amp; Metabolism</td>
</tr>
<tr>
<td></td>
<td>One week Call Outpatient Clinic 4 days/week</td>
<td>No Call/Clinic</td>
<td>No Call/Clinic</td>
<td>One Week Call Outpatient Clinic 4 days/week</td>
<td>One week Call Outpatient Clinic 4 days/week</td>
<td>One week Call &amp; Vacation One week</td>
</tr>
</tbody>
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<th>Months</th>
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<th>June</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Activity</td>
<td>Prenatal Genetics at EUH Midtown</td>
<td>Specialty Clinics</td>
<td>General Genetics &amp; Metabolism</td>
<td>General Genetics &amp; Metabolism</td>
<td>General Genetics &amp; Metabolism</td>
<td>General Genetics &amp; Metabolism</td>
</tr>
<tr>
<td></td>
<td>No Call</td>
<td>NF1, TSC, Neuromuscular 22q11.2 Huntington</td>
<td>One week Call</td>
<td>One week Call Outpatient Clinic 4 days/week</td>
<td>One week Call Outpatient Clinic 4 days/week</td>
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</tbody>
</table>
Outpatient Clinics

- 85% Pediatric 15% Adult
- 5000 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 Clinic
- NF1/TSC Clinic
- 22q11.2 Clinic
- Prenatal Clinic
- Cancer 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 Hospital

When on call, resident is the first person called

No outpatient duties when on call

Resident always reviews plan with attending
Laboratory Rotations

- Emory Genetics Labs/Eurofins
- 2 weeks molecular
- 2 weeks cytogenetics
- 2 weeks biochemical

Arun Ankala, MSc, PhD
Laboratory Program Director
Approximate Births by occurrence (ref. 2010 NCHS data)
135,411

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

- 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

Power Point Presentation 25-30 minutes each

Projected on web, so remote attendance possible

Laboratory director(s) and lab trainees involved.

Resident gives a CC once a semester
<table>
<thead>
<tr>
<th>Date</th>
<th>Presenter</th>
<th>Topic</th>
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</thead>
<tbody>
<tr>
<td>09/18/18</td>
<td>Janette diMonda</td>
<td>From VUS to Diagnosis: A Case of Singleton-Merten Syndrome</td>
</tr>
<tr>
<td></td>
<td>Morgan Simmons</td>
<td>Fabry Disease: Fact or Faux?</td>
</tr>
<tr>
<td>10/02/18</td>
<td>Rachel Linnemann</td>
<td>Diagnostic Challenges in Cystic Fibrosis</td>
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<tr>
<td></td>
<td>Rhea Behlmann</td>
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</tr>
<tr>
<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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<tr>
<td></td>
<td>Matthew Walsh</td>
<td>X-linked Conelida de Lange Syndrome</td>
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<tr>
<td>10/23/18</td>
<td>Chelsea Leonard</td>
<td>NAA10-Related Syndrome</td>
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<tr>
<td></td>
<td>Georgia Loucopoulos</td>
<td>Patient decision-making for prenatal testing when faced with a VUS</td>
</tr>
<tr>
<td>11/06/18</td>
<td>Abdurazak K.Alali</td>
<td>Holocarboxylase Synthetase Deficiency: A Case Presentation and Review Of The Literature</td>
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<tr>
<td></td>
<td>Merlene Peter</td>
<td>The Tale of Two Translocations</td>
</tr>
<tr>
<td>11/13/18</td>
<td>Aixa Gonzalez Garcia</td>
<td>Inherited Systemic Hyalinosis (ANTXR2 related disorder)</td>
</tr>
<tr>
<td></td>
<td>Ellie Westfall</td>
<td>Challenges of DICER1 Diagnosis</td>
</tr>
<tr>
<td>11/20/18</td>
<td>Christine Tallo</td>
<td>MLH1 Epimutations: An Overlooked Cause of Lynch Syndrome</td>
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<tr>
<td></td>
<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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<tr>
<td></td>
<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 Weekly Notice

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Emily Black, MD, Medical Genetics Resident PGY5</th>
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<tbody>
<tr>
<td>Mentor</td>
<td>Rossana Sánchez, MD</td>
</tr>
<tr>
<td>Title of Presentation</td>
<td>An Update on a Recurrent Microdeletion Syndrome</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Rachel Logan, MSSc, Genetic Counselor II</th>
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<tr>
<td>Mentor</td>
<td>Rossana Sánchez, MD</td>
</tr>
<tr>
<td>Title of Presentation</td>
<td>Parental Mosaicism and Monogenic Epilepsies: Case of CACNA1A – Associated Ataxia and Epileptic Encephalopathy</td>
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</table>

**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

<table>
<thead>
<tr>
<th>Commercial support for RSS/Session</th>
<th>NONE</th>
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</thead>
<tbody>
<tr>
<td>Financial Relationships of RSS Director, Planning Committee Members and Others</td>
<td>NONE</td>
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</tbody>
</table>
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

• 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.
Sign-Out Lab Rounds

- Thursday 12:30-1:30 PM
- Run by Emory Genetics Laboratory Training Program
- Three cases/session
  - Molecular
  - Biochemical
  - Cytogenetic
- Resident required to go during laboratory rotations
- EGL will project these on web so remote attendance possible
Self-Directed Learning

- 18 months clinical
- 1.5 months
- 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
Research Projects

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

• Comparing genotype-phenotype correlations between US and China cohorts identified on NBS. Could include 2-4 week trip to Hangzhou, China
  – Peng Jin, PhD
Research Projects

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

• 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: Stephanie
  - 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
We are a Fun Group!
Christmas at Dr. G’s
GRADUATION TIME
Atlanta is a GREAT City!!!