



BWH Genetic Medicine Residency and Genetics Track Clinic, Course and Research Listings (rev. 12/04)



Brigham & Women's Hospital

Pulmonary Genetics Clinic

Clinic Preceptor: Edwin Silverman, MD, PhD

Clinic Time: Mondays 9 am – 12 noon

In addition to patients with conventional pulmonary disorders (COPD, asthma), and some requiring pulmonary transplant, this clinic sees 2 to 4 patients per session with adult CF (Cystic Fibrosis), α -1 antitrypsin deficiency, primary pulmonary hypertension, and precocious COPD. The latter refers to patients with early onset COPD who are negative for α -1 antitrypsin deficiency, have a positive family history and are non-smokers. Some patients and their families are being investigated with methacholine challenge. Several families with early onset COPD exist in which linkage analyses and efforts at gene identification are underway. Diagnostic and therapeutic considerations are discussed.

Renal Genetics Clinic

Clinic Preceptor: Martin Pollak, MD

Clinic Time: 1 pm – 5 pm

This clinic involves patients with PKD (polycystic kidney disease), Alport's Syndrome, cystinosis with a small contribution of patients with various heritable nephropathies such as focal segmental glomerulosclerosis. The preceptor also maintains an active research program in the genetics of heritable nephropathies.

Cardiovascular Genetics Clinic

Clinic Preceptors: Christine Seidman, MD and Carolyn Ho, MD

Clinic Time: Once per month on the first Thursday of the month from 10 am – 12 noon (Dr. Seidman) and twice per month every other Thursday 8 am – 12 noon (Dr. Ho)

These clinics deal with patients with familial hypertrophic cardiomyopathy (HCM), Long QT Syndrome or other arrhythmias who are being evaluated for potential genetic etiologies of cardiac sudden death. Patient and family phenotyping and molecular diagnosis are involved.

Cancer Genetics I

Clinic Preceptors: Judy Garber, MD and Sapna Syngal, MD

Clinic Time: Fridays 1 pm – 5 pm with a Patient Review Conference on Wednesdays 1 pm – 2:30 pm

This clinic represents intensive exposure to breast and colon cancer with an emphasis on familial predisposition and relative risk to unaffected family members. Molecular testing and implications for diagnosis and prognosis are emphasized. This clinic builds a foundation for continuation in PGY3. This Clinic involves interaction with Residents in the HMS Genetics Training Program and the BWH Internal Medicine Residency Program.

Rheumatology Clinic

Clinic Preceptors: Robert Plenge, MD, PhD and Jonathan Coblyn, MD, and colleagues

Clinic Time: Mondays 9 am – 12 noon

This clinic emphasizes exposure to patients with rheumatoid arthritis and SLE, the two predominant rheumatologic entities for which genetic parameters are currently best defined. Residents will see RA and SLE patients in whom genetic factors are likely to play a role (eg. on the basis of family history). In addition, residents will participate in the enrollment of patients in BRASS (Biomarkers in Rheumatoid Arthritis Study) which will provide a DNA registry for future genetic association studies. Although the number of patients with a clear genetic basis for

RA or SLE may be limited, rheumatology represents an important future area for the analysis of complex polygenic disease.

Hematology Genetics Clinic

Clinic Preceptors: Ellis Neufeld, M.D., Ph.D.

Clinic Time: Wednesdays 1 – 5 pm

Patients are seen with three types of inherited disorders: thrombotic states, bleeding disorders, and red cell defects. These diseases include deficiencies of protein C and S, hemophilia, sickle cell anemia, thalassemia, and hereditary spherocytosis. Molecular diagnosis, factor replacement and other therapeutic interventions are components of this Clinic.

Cancer Genetics II

Clinic Preceptors: Judy Garber, MD and Sapna Syngal, MD

Clinic Time: Fridays 1 pm – 5 pm

Prerequisite: Cancer Genetics I Clinic

This clinic in PGY3 consists of intensive exposure to patients with colon and breast cancer to whom genetic considerations apply. There is also an optional Patient Review Conference on Wednesdays from 1 – 2 pm. Residents in Cancer Genetics II will enjoy increased responsibility during this rotation and will also have the option of seeing patients with other gene-based oncological malignancies, including medullary carcinoma of thyroid.

General Genetics Clinic and Longitudinal Genetics Continuity Clinic

Instructors: Peter Tishler, MD; Michael Murray, MD; and HMS Genetics fellows

Clinic Time: Thursday 1 – 5 pm

This clinic serves three functions. First, it serves as clinic for patients with a wide variety of general genetic disorders including homocystinuria, hemochromatosis, enzyme deficiency disorders (Gaucher and Fabry's disease) and Connective Tissue Disorders. Second, trainees present interesting or challenging cases seen within the current week in the various specialty clinics to Combined Residency Program Faculty who are Board Certified in Medical Genetics and Internal Medicine (e.g. Dr. Michael Murray), which are then approved for inclusion in their logbook. Lastly, this clinic also serves as a vehicle for interaction with Medical Genetics fellows in the HMS Genetics Training Program who maintain their genetics longitudinal clinics at the same time. This Clinic offers Combined Program residents exposure to a large number of patients with general genetic disorders.

Antenatal Diagnostic Center

(Center for Fetal Medicine and Prenatal Genetics)

Instructor: Louise Wilkins-Haug, M.D., Ph.D. and colleagues

Clinic Time: Tuesday, 1 – 5 pm

A working knowledge should be achieved in the following areas of prenatal diagnosis: (1) risk of chromosomal abnormalities with increasing maternal age, indications, risks, and benefits to various options for prenatal diagnostic testing (CVS, early amnio, routine amnio, PUBS, FISH); (2) understanding of the evaluation of an elevated MSAFP;

differential diagnosis, mechanics of serum screening, indications for amniocentesis and ultrasound; (3) interpretation of serum screens and genetic ultrasound for risk of aneuploidy, the effects of specific variables on the risk estimate, use of serum screen results in women over 35 years of age, concept of likelihood ratios; (4) identification of persons at risk for population specific disorders, testing availability and limitations recognition of potential teratogens, resources for further information; (5) construction of a family history targeted to recognition of disorders impacting prenatal diagnostic testing

The expectation is for independent patient assessment and counseling after the first two weeks of observation. All patients are seen in conjunction with a genetic counselor or perinatologist. At a minimum we expect each resident in conjunction with a genetic counselor to independently complete a counseling session covering each of the following: (1) advanced maternal age; (2) positive serum screen for increased risk of NTD; (3) positive serum screen for increased risk of trisomy 21.

Laboratory for Molecular Medicine (LMM)

Laboratory Faculty: Drs. Cynthia Morton and Christine Seidman

This lab medicine elective is located at the 65 Lansdowne Street Building (Cambridge, MA) and is supported by the HPCGG. Current efforts are dedicated to design of re-sequencing chips for the ~20 genes known to cause hereditary deafness, and familial hypertrophic cardiomyopathy (HCM).

Clinical Cytogenetics

Laboratory faculty: Drs. Cynthia Morton, Mary Sandstrom, Patricia Miron, Stana Weremowicz, Frederick Bieber, Jonathan Fletcher, Bruce Korf, Bai-Lin Wu, and Leonard Atkins.

The BWH cytogenetics laboratory serves BWH, CH, and MGH. The laboratory processes a full range of cytogenetic specimens, including peripheral blood, skin fibroblasts, chorionic villus biopsy, amniotic fluid, bone marrow aspirates and solid tumors. Residents spend one month in the laboratory during the second year of training. Hands-on experience involves culturing peripheral blood specimens and gaining experience in karyotyping and FISH. An additional rotation of up to one year is available to interested residents

Resident Research Report

Instructor: Thomas Michel, M.D., Ph.D. and colleagues.

Time: Friday, 8:30 am -10:00 am

This activity includes presentations on a rotating basis by residents engaged in the BWH Research Residency. The meeting is attended by 6 to 8 research residents with 2 faculty preceptors. Genetic based investigations have traditionally represented a component of Resident Research Report and the plan is to increase the number of such presentations and to include increased participation by genetics based research faculty as preceptors.

Morning Report

Time: Monday to Thursday 9 am – 10 am; Friday 10 am – 12 noon

Instructors: BWH Internal Medicine Faculty and Chief Residents

Morning Report is an intellectual focal point for the existing BWH Internal Medicine Residency Program. Typically two illustrative cases selected from the wards, General Medical Service or Clinics are presented by the housestaff to a faculty attending who then creates a differential diagnosis and engages the housestaff in a discussion of pathophysiology and diagnostic and therapeutic options. Residents will attend Morning Report while at the BWH as much as possible. Residents rotating at nearby Children's Hospital will also have the option of attending. The inclusion of Combined Program residents in Internal Medicine Morning Report will create a favorable environment for

interaction between categorical and Combined Program residents and for the emphasis of genetic factors pertinent to the diseases of interest.

BWH Medical Grand Rounds

Time: 12 – 1 pm

Medical Grand Rounds once a week involves presentation of a variety of areas of contemporary internal medicine interest. This will include discussions of genetic disorders (past speakers have included Francis Collins, David Ginsburg and Rick Lifton) as well as issues in genetic epidemiology and pharmacogenetics (eg. Jeff Drazen). Increasing efforts will be directed towards increasing the number of speakers examining disease from a genetic perspective.

Advanced Human Genetics Course

Instructors: Cynthia Morton, PhD; Gretchen Schneider, MS; and staff

Time: Wednesdays 8:30 am – 10 am

This course is required in PGY2 for all Combined Internal Medicine and Medical Genetics residents. It is divided into four blocks that typically consist of two lecture periods per course day. The goal of the course is to provide trainees with up-to-date information from leading physicians and scientists in particular classes of disorders of interest to genetics. The same course subserves a similar function for the existing Harvard-wide Medical Genetics Training Program. Credit for the course is given only upon satisfactory completion of a quarterly examinations. The course runs from September through June each academic year.

Children's Hospital Boston

Whereas Categorical Residents in the HMS Genetics Training Program spend six months at Children's Hospital during their first year in two three month blocks, residents in the Combined Internal Medicine Medical Genetics Residency Program will spend but three months, to allow more time for Internal Medicine based genetics. This three month block, taken in PGY2, involves coverage of the inpatient consultation service and participation in various outpatient genetics clinics, many of which involve exposure to adolescent patients.

Children's Hospital Inpatient Consultation Service

The inpatient consultation service sees patients for diagnosis, counseling, or management of genetic disease at the request of attending physicians and residents in the hospital. In addition, the resident on the inpatient service is responsible for rounding on patients followed by the genetics service who are hospitalized for acute illness. Approximately 30 new patients are seen per month; at any time a resident will follow 5-10 patients in the course of work-up or treatment. The consult service consists of a resident and an attending geneticist who round together at least once per day. Sources and types of consultations include: (1) **Newborns:** residents see patients in the newborn nurseries at Children's Hospital, and Brigham and Women's Hospital. Newborns are seen with congenital anomalies, single gene disorders, and inborn errors of metabolism. (2) **Medical Service:** patients are seen on the infant and toddler, school age, and adolescent services, as well as on neurology, oncology, transplantation, and cardiology. (3) **Intensive Care Unit:** there are two intensive care units, one for medical patients and one for surgical and cardiac patients. (4) **Surgical Services:** There are separate services for cardiac surgery, orthopedics, neurosurgery, and general surgery.

Residents on the inpatient service are responsible for all calls to the service Monday through Friday, including Monday through Thursday nights. Weekend call from Friday

night through Monday morning will be shared by Categorical first and second year residents and Combined Program residents, together with an attending physician on a rotating schedule.

Outpatient Clinics

Outpatient clinics are held every day. Residents participate in a general genetics clinic on Monday afternoon, Tuesday afternoon, Thursday afternoon, and Friday morning, and metabolism clinics Monday and Thursday mornings.

Genetics Clinic: Individuals evaluated in the Medical Genetics Clinic are primarily referred for diagnosis of genetic syndromes or diseases and assessment of recurrence risk and prenatal diagnostic options. Long-term management issues are generally addressed by other physicians or programs, in particular, the Coordinated Care Service, a service of the Division of General Pediatrics. However, some patients are intermittently followed in the Genetics clinics. These include patients with known diagnoses who are returning for yearly follow-up appointments to receive any updated information regarding their condition, or those patients who do not yet have a specific diagnosis who return yearly for re-consultation.

Metabolism Clinic: Metabolism Clinic is held on Tuesdays and on Thursday mornings. This is a multidisciplinary program that includes physicians, nutritionists, social workers, and psychologists. Patients with a wide range of metabolic disorders are seen, including amino and organic acid disorders, fatty acid oxidation defects, urea cycle disorders, peroxisomal disorders, lysosomal storage diseases, and disorders of energy metabolism. This clinic is the major referral site for newborns in eastern Massachusetts diagnosed by the New England Regional Newborn Screening Program. Residents are expected to see new patients and follow established patients, supervised by attending physicians. The metabolism service follows over 150 patients who have severe metabolic disorders prone to occasional metabolic crisis. First year residents assume responsibility for these patients, serving as the primary contact at Children's Hospital for these patients, their families, and their primary care providers.

Clinical Molecular Genetics

Drs. Bai-Lin Wu and Katherine Sims

Residents spend one month at either the Molecular Diagnosis Laboratory at Children's Hospital (Dr. Wu) or one month in the Molecular Neurogenetics Laboratory at MGH (Dr. Sims). Residents learn methods of DNA isolation, PCR, and Southern analysis, applied to diagnosis of fragile X, Duchenne/Becker dystrophy, cystic fibrosis, Prader-Willi/Angelman syndrome, mitochondrial disorders, and Y chromosome anomalies. Both direct mutation tests and linkage-based tests are performed, and residents are involved in both laboratory analysis and risk calculation. A variety of neurogenetic disorders are studied in this laboratory, including NF2, dystonia, and Norrie disease.

Specialty Clinics: Outpatient clinics are held in genetics and metabolism and there are specialty clinics for neurofibromatosis, Smith-Lemli-Opitz syndrome, and skeletal dysplasias.

Massachusetts General Hospital

Cancer Genetics Clinics

Daniel Haber, MD, PhD; Kristen Shannon, MS, CGC; and colleagues

A number of Cancer Genetics Clinics are available at the MGH under the auspices of the MGH Cancer Center. These include:

Breast/Ovarian Cancer Genetics Clinic

Paula D. Ryan, MD, PhD – Director

Location: Cox 1 - Gillette Center for Women's Cancers

Times: Mondays 9am-12pm; 1pm-5pm

Gastrointestinal Cancer Genetics Clinic

Daniel C. Chung, MD – Director

Location: Blake 4 – GI Associates

Times: 2nd Tuesday of month, 12pm-5pm

3rd Tuesday of month, 9am-12pm

Eunice Kwak, MD, PhD

Location: Cox 2 – Outpatient Clinic

Times: 1st Wednesday of month, 1pm-5pm

VHL/Hereditary Renal Cell Cancer Clinic

Othon Iliopoulos, MD

Location: 10 Emerson Place – 1st floor

Times: 2nd & 4th Tuesday of month, 1pm-5pm

Melanoma Genetics Program

Hensin Tsao, MD

Location: Zero Emerson Place – Suite 104

Times: 1st and 3rd Wednesday of month, 9am-12pm

Lipid Disorders Clinic: Dr. Mason Freeman sees patients each week on Wednesdays with a variety of inherited hyperlipidemias. This Clinic involves phenotype analysis, genetic diagnosis and therapeutic intervention.

Reproductive Genetics Clinic: Dr. William Crowley and colleagues see patients once per week with a variety of genetically based reproductive syndromes. Patient evaluation is coupled with efforts at genetic diagnosis.

Neurogenetics/Neurofibromatosis: These clinics meet on alternate Wednesdays. Residents are supervised by Dr. Katherine Sims in Neurogenetics Clinic and by Dr. Mia MacCollin in Neurofibromatosis Clinic. The Huntington's Disease Clinic meets every other Wednesday afternoon; the residents are supervised by Drs. Jang-Ho Cha and Stephen Hersch. Both children and adults are seen in all of these clinics.

Neuromuscular Disease Clinic: Directed by Dr. Robert Brown, a clinical neurologist who is actively involved in molecular genetics, the genetics resident will see primarily adult patients with any type of muscle disease.

General Genetics Clinic: Patients are seen on Tuesday afternoons and Friday mornings in the MGH Genetics Clinic at 50 Staniford Street by Drs. Joan Stoler and Carol Hoffman (Genetic Counselor and Clinical Coordinator). This Clinic involves a large number of patients with Connective Tissue (EDS, Marfan's and OI), Endocrine (Premature Ovarian Failure), and Mucopolysaccharide (Sanfilippo Syndrome)Disorders.

Genetics, Teratology and Metabolism Clinic: This is a weekly clinic held on Thursday mornings. Patients are seen for diagnosis and counseling of single gene disorders, multifactorial disorders, and congenital anomaly syndromes. Approximately 20% of patients are adults. The clinic is staffed by Drs. Lewis Holmes and Vivian Shih.

Prenatal Diagnosis Clinic: Patients are seen daily as needed. Residents are supervised by Dr. Lewis Holmes, Dr. Joan Stoler, and work along with Ms. Gwen Norwood-Reeve and Carrie Haverty, certified genetic counselors.

Biochemical Genetics:

Drs. Vivian Shih and Marvin Natowicz

Residents spend one month at either the MGH (Dr. Shih) or at the Shriver Center in Waltham, MA (Dr. Natowicz). At MGH they will become familiar with amino acid analysis (ion exchange chromatography) and organic acid analysis (gas chromatography/mass spectrometry). At the Shriver Center, residents are exposed to a number of different metabolic technologies, including thin layer chromatography (for analysis of simple sugars, mucopolysaccharides and oligosaccharides); HPLC (urine sulfatide analysis); spectrophotometric, fluorometric and isotope-based enzyme assays; gas chromatography-mass spectrometry (e.g., very long chain fatty acid analysis); fast atom bombardment-mass spectrometry (analysis of urine bile acids); and tissue culture.

Inpatient Consultations: Patients are seen on both the Medicine and Pediatrics service and elsewhere in the hospital.