Molecular Genetic Pathology Fellowship Program
Overview of Program
Goals and Objectives

General organization

The practice of molecular genetic pathology is diverse and continually evolving. As such, a broad and also in-depth background of both basic and clinical molecular diagnostics is required for the successful practitioner. In addition, familiarity with the administrative and management aspects, including regulatory issues and cost analysis of a molecular diagnostic laboratory is important to understand. As part of laboratory and clinical rotations at each of the three core sites, University of Washington (UWMC), Fred Hutch Cancer Center (FHCC) and Seattle Children's Hospital (SCH), the fellow is expected to master these general goals and objectives pertaining to the location-specific context. In addition, the general duties and responsibilities of the fellow are described in conjunction with an overview of the ACGME core competencies to be assessed.

Goals and objectives

1. Apply understanding of basic molecular biology, including the structural and functional basics of DNA, RNA, mechanisms of inheritance, etc. to each laboratory and clinical rotation for patient care.
2. Master the relevant nomenclature and language molecular genetic pathology with an emphasis on accurate description of molecular variation/abnormalities at the DNA, RNA, and protein level for written reports, publications and clinical correspondence
3. Apply insight and knowledge of technical aspects of molecular techniques with an emphasis on appreciating the appropriate use for and utility of different diagnostic approaches. These techniques may include PCR, real-time RT-PCR, fragment analysis, allele-refractory mutation amplification, melting-curve analysis, *Invader* technologies, branched DNA techniques, MLPA, SSCP, DGGE, karyotype, FISH/CISH, and other more complex methods (including array CGH, optical genome mapping, and next generation sequencing, including targeted panels, whole exome, cell-free DNA, FusionPlex)
4. Command an understanding and demonstrate proficiency in navigating bioinformatics resources such as genome browsers (for example, http://genome.ucsc.edu/ or http://uswest.ensembl.org/index.html), gene databases (http://www.ncbi.nlm.nih.gov/sites/GeneTests/), disease-specific molecular databases (OMIM, NCBI, COSMIC, gnomAD, ClinVar,

mycancergenome.org, cBioPortal) for acquisition of pertinent patient-specific molecular data, commonly used genetic

software (Mutalyzer, Mutation Surveyor by SoftGenetics, LLC) GeneMapper and Sequence Analysis by Applied Biosystems), and use of websites (such as http://frodo.wi.mit.edu/primer3/) for assay development

5. Participate daily in patient-care activities, observing and/or actively participating in all aspects of the molecular pathology laboratory, including sample preparation, assay performance, data analysis, and report generation in all molecular tests performed by the laboratory
6. Develop understanding of strategies behind all molecular assays used in each laboratory, including advantages and disadvantages of methods and instruments
7. Understand appropriate management and triage of clinical samples (recognizing for example what an appropriate sample-type is) with an appreciation for cost-effective and evidence-based test utilization
8. Integrate knowledge from medical literature and available resources with patient-specific results to generate informative diagnostic reports
9. Participate with supervising faculty in the editing of written reports prior to finalization and report
10. Communicate to patient care providers to inform and/or discuss results as necessary, and/or present such information in multi-disciplinary conferences where applicable
11. Contribute to faculty, staff, resident, fellow education through scholarly activities, journal club presentation, case report, poster and manuscript preparation
12. Consider the intersection of issues affecting both molecular genetic pathology and diversity, equity, and inclusion in treatment of patients.
13. Understand the legal and regulatory framework of molecular genetic diagnostic assays in the United States and impact of such on test development, validation and insurance reimbursement.

Duties and responsibilities

1. Daily participation in the functioning of clinical molecular cytogenetic and cytogenomic laboratories
2. Communicate with laboratory staff or faculty and correspond with clinicians as necessary to effectively review and sign-out all molecular and cytogenetic/cytogenomic cases
3. Review all pertinent medical literature to develop broad, but in-depth background knowledge
4. Participate in laboratory management meetings, including those for quality assurance and personnel management when applicable
5. Attend all relevant pathology and clinical conferences and present or be available for consultation regarding molecular data when appropriate; in addition, attend as

many relevant molecular seminars as appropriate

6. Review quality assurance issues as applicable, including performance of yearly review of SOPs, review CAP proficiency testing of molecular results and CAP checklist for laboratory inspection
7. Review, observe and/or perform most if not all techniques and molecular assays performed in each laboratory to develop hands-on experience
8. Contribute to the development and validation of at least one novel, molecular diagnostic assay
9. Supervise junior residents in conjunction with non-MGP fellows, to residents, commensurate with experience regarding topics of molecular genetic pathology
10. Serve as "junior attending", commensurate with experience. This opportunity represents an increase in responsibility and will enable the fellow to gain experience in making decisions in preparation for future independent practice. This does not imply or require institutional credentialing.
11. Participate in the education of resident/fellow colleagues, faculty, and technical staff through journal club presentations, preparation of manuscripts and posters, if applicable
12. Research and present a seminar talk on intersections of molecular genetic pathology with diversity, equity and inclusion.

The MGP Fellow should meet with the supervising faculty/staff or laboratory director at the start of each site rotation (lab and clinic) to delineate and clarify expectations for each rotation. The MGP Fellow should assume full responsibility and ownership of all molecular cases that pass through the laboratory, as per the supervising faculty/staff and look to develop his/her professional experience according to the ACGME Milestones goals.

Supervision and evaluation

For each clinical and laboratory rotation, the fellow should inquire with the supervising faculty regarding rotation-specific goals and objectives, and duties at the beginning of the rotation and as outlined at the MGP internal webpage. The fellow will work directly with the staff diagnostician and/or designee, including technical laboratory staff, to fulfill daily patient care duties. The fellows will be required to keep a Logbook of all cases (both clinical and laboratory) with which the fellow is involved to document their experience. This case log must be reviewed by the site/clinic supervisor or supervising clinicians/physicians/staff and submitted to the fellowship director for incorporation into the fellow's portfolio at the mid-year and end-of-year reviews, and is a non-negotiable requirement for successful completion of the program. During and at the end of each rotation, a specific evaluation will be completed by each the supervising faculty member.

Teaching staff

Appropriate supervising faculty will be indicated as per each specific laboratory and

clinical rotation. One or more molecular pathology attending staff members will be on service and available to help answer questions and/or deal with difficult situations. A laboratory technical manager, technical specialist and/or a lead technologist may also be available to help with laboratory administrative and technical issues. The program is designed in such a way that the MGP fellow can assume increasing responsibility over the course of the training program according to their level of prior experience, education, ability, and knowledge.

ACGME Core Competencies

The program will integrate the following ACGME Competencies into the curriculum:

Professionalism

Fellows will demonstrate a commitment to professionalism and an adherence to ethical principles.

Patient Care and Procedural Skills

Fellows will be able to provide patient care that is patient- and family-centered, compassionate, equitable, appropriate, and effective for the treatment of health problems and the promotion of health.

Fellows will demonstrate competence:

- as consultants in clinical decision-making in collaboration with professionals from related disciplines and in the cost-effective use of molecular genetic and genomic testing
- in developing an approach for genetic and genomic testing to categorize conditions in a manner that facilitates clinical management
- This experience will include participation in clinical conferences and exposure to patient care.
- in providing appropriate and effective patient care consultations to physicians and other health professionals, both intra- and inter-departmentally.

Fellows will be able to perform all medical, diagnostic, and surgical procedures considered essential for the area of practice.

- Fellows should participate in performing the patient and laboratory procedures for which they will be expected to supervise ancillary staff members.

Medical Knowledge

Fellows will demonstrate knowledge of established and evolving biomedical, clinical, epidemiological, and social- behavioral sciences, including scientific inquiry, as well as the application of this knowledge to patient care.

Fellows will demonstrate

- their knowledge of molecular biology and biochemistry of nucleic acids and proteins, including:
    - structure; function; replication mechanisms; in vitro synthesis; and, the roles of DNA and various RNA classes and proteins in cellular biology.

- their knowledge of the mechanism of regulation of gene expression in prokaryotes and eukaryotes;
- their knowledge of the biochemical mechanisms of pathogenic variants;
- their detailed knowledge of disease processes at the molecular level and the methods used for their detection;
    - These diseases and conditions include solid tumors, leukemia-lymphomas, infectious diseases, inherited Mendelian diseases, somatic overgrowth disorders, biochemical genetics, and non-Mendelian and acquired genetic diseases (e.g., mitochondrial disorders, triplet repeats, expansion disorders, cytogenetic aberrations, and imprinting disorders).
- their knowledge of HLA typing/identity testing and the principles of linkage analysis;
- their knowledge of statistics as applied to diagnosis and management, test performance and applications, limitations of genetic and genomic test methodologies, and calculation of primary and residual risk;
- their knowledge and understanding of the principles of molecular diagnostic, prognostic, and therapeutic testing for patients with infectious diseases and cancer, and tests to monitor affected patients;
- their knowledge of autopsy and surgical pathology procedures, infectious diseases, hematopathology, and other relevant pathology activities;
    - Fellows will demonstrate knowledge of how to select and appropriately sample fresh and fixed tissue for molecular testing
- their knowledge of laboratory regulatory and accreditation requirements; and,
- their knowledge of the requirements for establishing and operating a molecular genetic pathology laboratory, laboratory management, and supervising and training laboratory personnel in advanced techniques.
- their knowledge and insight as to the impact and importance of considering diversity, equity and inclusion in the practice of molecular genetic pathology

Fellows will be able to incorporate clinical and other laboratory information into the interpretation and the reporting of genetic and genomic results.

Practice-based Learning and Improvement
Fellows will demonstrate the ability to investigate and evaluate their care of patients, to appraise and assimilate clinical and scientific evidence, and to continuously improve patient care based on constant self-evaluation and lifelong learning.

Interpersonal and Communication Skills
Fellows will demonstrate interpersonal and communication skills that result in the effective exchange of information and collaboration with patients, their families, and health professionals.

Systems-based Practice
Fellows will demonstrate an awareness of and responsiveness to the larger context and system of health care, including the structural and social determinants of health, as well as the ability to call effectively on other resources to provide optimal health care.