

University of Minnesota Lab Medicine and Pathology

Molecular Genetics Rotation

<u>Location:</u>	Mayo D210 (Molecular Diagnostics Laboratory)
<u>Duration:</u>	One month
<u>Rotation Directors:</u>	Sophia Yohe, MD – phone: 612-273-3098 (pager 899-9175)
<u>Other Faculty:</u>	Andrew Nelson, MD, PhD, Pawel Mroz, MD, PhD, Bharat Thyagarajan, MD, PhD, MPH, Michelle Dolan, MD & Genetic Counselors: Matt Bower, Whiwon Lee & Katie Wiens

General Description:

The rotation in the Molecular Diagnostics Laboratory (MDL) is designed to provide the trainee with an introduction to molecular diagnostics, including basic concepts in molecular genetics and molecular pathology, methods and techniques, laboratory logistics (i.e., specimen procurement, processing, and a general knowledge of laboratory work-flow), and indications for /appropriate utilization of molecular testing.

The first week:

- Get to know the layout of the lab and learn how to sign onto Lab Director (the MDL LIS) using the resident login
- Read protocols for and learn how to interpret basic tests (Factor V Leiden, prothrombin gene mutation, engraftments, hemochromatosis, MTHFR, GNR)
- Calculate %D and %R on a single donor engraftment that has mixed chimerism
- Get or watch the basic introductory methods lecture
- Spend 1-1 ½ days rotating through various benches in the laboratory to obtain a basic understanding of the various techniques used in molecular diagnostics
- Read articles related to the basic testing
- Learn triage rules for GNR, collect patient information and triage all GNRs with the fellow or staff (if the fellow is absent)
- For those patients referred to the laboratory for testing for hematological malignancies and solid tumors, obtain clinical histories and relevant results from other laboratories (Special Hematology, Flow Cytometry/Immunophenotyping, Surgical Pathology, Cytogenetics). This information should be obtained prior to reviewing cases with staff person on service.
- Review test results as they become available with the Molecular Diagnostics Fellow PRIOR to case sign out with the staff person on service. The trainee should be prepared to answer questions regarding any particular case.
- During the rotation, trainees may be asked to perform literature searches with regard to difficult/unusual cases. The findings of the literature search are discussed with the MDL staff and fellows.
- Review tumor slides with staff/fellow and estimate tumor percentage as assessment of sample adequacy for tumor testing.
- Start required reading.
- Attend case sign out with staff person on service.

The remaining weeks:

- Continue all on-going responsibilities from week 1
- Preview all basic tests (as listed above)
- Read protocols for other testing
- Start to preview other testing as you become exposed and comfortable with that test
- Triage GNR then run past fellow or staff
- Read articles related to other testing
- Finish required reading
- Attend case sign out with staff person on service.

- Optional: help triage NGS oncology cases, read positive signed out inherited NGS cases and look at data in lab director, calculate sensitivity on maternal cell contamination cases

Goals and Objectives:

Upon completion of this rotation, the resident will be able to:

Goal #1: Discuss how sample type, sample handling and processing, and testing method affect test results and be able to choose the best test for a given scenario

Goal #2: Interpret molecular genomic tests, including being familiar in the use of databases and literature that may assist interpretation

Goal #3: Evaluate quality control of molecular genomic testing and evaluate for appropriateness of testing

Goal #4: Correlate molecular genomic test results with patient history and other ancillary testing for a patient-centered interpretation

- Understand basic principles of molecular biology and human genetics (MK)
- Know specimen requirements for molecular diagnostic testing (MK)
- Understand how DNA and RNA are extracted (MK)
- Understand PCR and it's variants (reverse-transcriptase, RFLP, allele-specific, multiplex, nested, quantitative) (MK)
- Understand the basic principles of DNA sequencing (Sanger and NGS) (MK)
- Understand the basic molecular pathology for diseases commonly tested in the clinical molecular diagnostic laboratory (MK)
- Recognize the importance of QA in laboratory testing and interpretation (PC)
- Incorporate pertinent history and ancillary studies into the interpretation of molecular testing (PC)
- Understand the use of molecular testing in the diagnosis and management of disease (PC)
- Present cases and use the discussion to update one's own knowledge base and care of patients (PBLI)
- Incorporate new knowledge to improving patient care (PBLI)
- Understand the relationship/overlap between molecular testing and other laboratory tests (e.g., flow cytometry, cytogenetics) (SBP)
- Understand laboratory practice issues including proficiency testing, certification, QA/QC, and Medicare compliance (SBP)
- Apply the indications for testing T and B cell GNRs to ensure correct testing is being done (SBP)
- Demonstrate ability to interact with all members of laboratory (ICS)
- Demonstrate ability to verbalize a concise and relevant history that is pertinent to the testing being performed (ICS)
- Maintain professional relationships with all members of the laboratory and clinicians (Prof)
- Demonstrate honesty, integrity, dependability (Prof)
- Provide constructive feedback about the rotation and receive feedback (Prof)

The learning objectives above reference the corresponding ACGME core competencies: Patient Care (PC), Medical Knowledge (MK), Professionalism (Prof), Communication Skills (CS), Practice Based Learning and Improvement (PBLI), and Systems-Based Practice (SBP).

Assigned Reading:

Basic Genetics (required)

- Human Genetics: Vogel and Motulksy
 - Chapter 2: Human Genome Sequence and Variation

- Chapter 9: Epigenetics

Technical details (required)

- Current Protocols in Human Genetics (available online through the UMN library)
 - [APPENDIX 3B Isolation of Genomic DNA from Mammalian Cells](#)
 - [APPENDIX 3C Extraction and Precipitation of DNA](#)
 - [APPENDIX 3I Preparation of DNA from Fixed, Paraffin-Embedded Tissue](#)
 - [APPENDIX 3F Denaturing Polyacrylamide Gel Electrophoresis](#)
 - [UNIT 11.3 Profiling Human Gene Expression with cDNA Microarrays](#)
 - [UNIT 2.5 PCR Methods of Genotyping](#)
 - [UNIT 2.6 Genotyping by Ligation Assays](#)
 - [UNIT 2.7 Restriction Fragment Length Polymorphism Analysis](#) (includes agarose gel electrophoresis)
 - [UNIT 2.10 Genotyping Using the TaqMan Assay](#)
 - [UNIT 7.7 Mutation Detection by Cycle Sequencing](#)
 - [UNIT 7.9 Mutation Detection Using Automated Fluorescence-Based Sequencing](#)
 - [UNIT 7.15 Selection of a Platform for Mutation Detection](#)

Standard operating procedures (SOPs) for all tests performed in the MDL including background information, testing protocols, and result interpretation for each of the diseases tested.

Interpretation (required)

- Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Richards S, et al. Genet in Med. 2015 (on shared google drive ACMG AMP variant interpretation 2015, in inherited papers)
- Li MM, Datto M, Duncavage EJ et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. *J Mol Diagn.* 2017;19(1):4-23. (2016 AMP ASCO CAP guidelines, in general papers)

Optional Reading:

- Current Protocols in Human Genetics (available online through the UMN library)
 - [UNIT 7.11 Human Mutation Databases](#)
 - [UNIT 9.2 Quality Assurance and Quality Improvement in U.S. Clinical Molecular Genetic Laboratories](#)
 - [UNIT 10.6 Methylation-Specific PCR](#)

Optional learning materials:

- Videos on principles of genetics:
<http://www.youtube.com/user/DNALearningCenter/videos?sort=dd&view=0&page=2>

Call Duties: There is no call on this rotation.

During the rotation, the trainee is expected to join the following conferences:

- Clinical Pathology Conference: Tues 12:00-1:00 PM (weekly) – Mayo D175
- Resident Didactic Series: Wed 7:00-8:00 AM & 9:15-10:15 AM (weekly) – Mayo D175
- Lab Medicine/Pathology Grand Rounds: Wed 8:00-9:00 AM (weekly) – 450 MCRB
- Molecular Diagnostics Staff Meeting: discussion of issues in laboratory management, and interesting cases in the MDL. Mondays at noon.
- Hematologic Malignancy Conference- alternating Mondays at 4:15 PM

Other Requirements:

- CP case logs should be emailed to faculty throughout the rotation to meet program requirements. Please send the case to the faculty that signed out that case, who will review the case and email feedback to residents. The resident is responsible to upload to the case log repository (available through the resident intranet).

Assessment methods:

Resident performance on this rotation will be assessed by:

- Formative feedback provided by attending physician(s)
- Performance evaluation by faculty based upon review by faculty working with the resident during the rotation. Residents will be evaluated on performance of daily activities, on participation in required meetings and conferences, and on presentations.