GOALS AND OBJECTIVES
MOLECULAR PATHOLOGY AT TOH

MEDICAL EXPERT
Residents acquire expertise in the area of molecular pathology through a series of rotations as described below.

Introductory session on Molecular Oncology:

The learning objectives include:

- Review and update molecular mechanisms of cancer to understand cancer as: a) group of disorders influenced by environmental, infectious and hereditary factors, b) a multistep process (insult-genetic change-clonal expansion; and c) pre-neoplastic lesions.

- To become familiar with Cancer predisposition genes: a) +ve mediators of neoplastic development, b) proto-oncogenes, c) growth factors and receptors, d) metastasis, e) promoting genes, f) cell cycle control genes, g) genes that promote cellular homeostasis, h) negative mediators of neoplastic development, i) tumor suppressor genes, j) metastasis suppressor genes, k) cell cycle control genes, l) genes that promote differentiation, m) genes that promote cellular homeostasis.

- To understand molecular mechanisms of cancer predisposition: a) point mutations translocations, b) gene amplification, c) role of DNA repair genes, and d) role of telomerase.

- To have in depth reading material on: a) The nature and mechanisms of human gene mutation, b) Tumor genomic instability, c) Cell cycle control, d) Apoptosis and cancer, e) Oncogenes, and f) Tumor suppressor genes.

Inherited Cancers:

Learning objectives:

- The resident will become familiar with: a) The underlying molecular mechanisms, and diagnostic approaches for the following inherited cancers and associated genes:


- The resident will understand the ethical issues related to predisposition testing.
• Under the supervision of technologists, the residents will observe techniques of DNA sequencing, MLPA, protein truncation and PCR used to identify mutations responsible for inherited cancers.

• Hands on DNA sequencing. Residents will have an opportunity to sequence the PCR amplicon generated in a “Hematopathology” rotation to identify the common Factor V Mutation. This will familiarize them with sequencing technology and highlight an alternate approach to detecting the same mutation.

**Molecular pathology of solid tumors/hemachromatosis:**

• The residents will become familiar with the basic underlying mechanisms and diagnostic approaches for the following disorders and genes: a) Ewings sarcoma and EWS/FL1-1, b) synovial sarcoma and t(X:18) translocation, c) gastrointestinal stromal tumor and c-kit mutation, d) breast cancer and HER2/neu amplification, e) prostate cancer and TMPRSS2-ERG fusions, f) lung adenocarcinoma EGFR gene mutation and amplification, g) colorectal cancer and Microsatellite instability (MSI), h) oligodendroglioma and 1p and 19q deletion, and i) hemachromatosis and HEF gene mutations.

• Observation of molecular techniques. Under the supervision of technologists, the residents will observe the techniques of interphase FISH.

• Hands on real-time PCR and MSI analysis. Under the supervision of a technologist, the resident will have an opportunity to perform a real-time PCR analysis used to detect common hemachromatosis mutations, and PCR analysis of MSI of colorectal cancer. This will familiarize them with mutation analysis based on real-time PCR, and interpretation of MSI of colorectal cancer.

**COMMUNICATOR**

• Develop a basic framework of knowledge that will permit a pathologist to: 1) utilize results from molecular analysis in the preparation of anatomical pathology reports, 2) assist clinicians in understanding the relevance of these results with respect to patient care, and 3) guide clinicians in determining when molecular/cytogenetic diagnostics may be of benefit to their patients.

**COLLABORATOR**

• Appreciate that pathology is typically a team effort that benefits from technical, scientific and clinical expertise.

• Appreciate that the diagnosis of disease benefits from data from many disciplines, and that an anatomical pathologist may work together with the molecular laboratory director to serve as a bridge between clinical medicine and the molecular laboratory to promote the appropriate use of these methodologies.

**MANAGER**

• Gain an appreciation for the technical, intellectual, financial and personal challenges associated with maintaining a productive diagnostic laboratory.
• Learn to manage time effectively by multitasking in the laboratory.
• Learn about the expertise of the technologists and scientists working in the molecular laboratories, and their relationship with the Department in which they work.

HEALTH ADVOCATE
• Become familiar enough with the role of molecular diagnostics in Pathology that they will advocate the use of this technology in their practice
• Become familiar with the route by which a molecular test is introduced as a diagnostic tool, and how access to the testing is determined.

SCHOLAR
• Search, review and critically assess current scientific literature related to molecular diagnostics as it pertains to the discipline of pathology.
• Come to each session having read literature related to the topic of the day and being prepared to discuss the literature with a view to its relevance to the practice of pathology.

PROFESSIONAL
• Demonstrate respect for co-workers
• Appreciate ethical issues related to genetic testing, such as informed consent, confidentiality and autonomy.

The following texts are recommended:
- Leonard, DGB, Molecular Pathology in Clinical Practice 2007
- Provan D., and Gribben J. Molecular Hematology; Blackwell Publishing 2005.
- Coleman WB, and Tsongalis, Molecular Diagnostics for the Clinical Laboratorian. Humana Press 1997
- Killeen AA, Principals of Molecular Pathology, Humana Press 2004
- American Society of Hematology annual general meeting education books

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