GOALS & OBJECTIVES: Cytogenetics Laboratory

The overall goal of the Clinical Cytogenetics Training Program is to provide the trainee with the skills they will need to direct a cytogenetics diagnostic laboratory. This includes gaining expertise in test design and validation; interpretation, troubleshooting, reporting and communication of results to providers; proper quality control and assurance and to direct a fellowship program in the future. In addition, the trainee will perform research in cytogenetic testing.

The specific skills to master are outlined below:

Patient Care and Laboratory Skills:

1. Preanalytical Laboratory Skills
    - Determine whether the appropriate lab tests were selected based on diagnosis and/or clinical features
    - Assess whether appropriate specimen was collected
    - Be knowledgeable about specimen collection, storage, stability, acceptability, specimen accessioning, specimen tracking, and appropriate documentation of necessary records and use of the clinical database.
    - Understand the importance of specimen tracking from accessioning though reporting
2. Analytical Laboratory Skills
    - Processing of specimens to produce analyzable metaphases
        - Practice proper sterile culture techniques and understands importance of protective precautions to limit employee exposure to infectious agents
        - Understand the appropriate media selection and additives for different cultures including blood, bone marrow, chorionic villi, amniotic fluid and skin fibroblasts
        - Establish and monitor culture growth and troubleshoot problematic specimens (eg. bloody amniotic fluid)
        - Understand procedures for reporting growth failure
        - Knowledgeable about the use of mitogens, intercalating agents, and special agents for chromosome breakage studies
        - Harvest different specimen and culture types (eg. in situ, flask, blood culture)
        - Banding of chromosomes using different methods including trypsin and Giemsa, C-banding, Q-banding, R-banding and NOR staining and ability to distinguish which methods are appropriate.
        - Use of inverted microscope and stereomicroscope for analysis of specimens and cultures
        - Destaining and restaining of slides for multiple uses when appropriate
        - Understand the processes of documentation for culture set-up and conditions, reagents and lot numbers used and all quality control measures used
    - Perform chromosome analysis, interpret results and report findings
        - Understand brightfield microscopy and computerized imaging system
        - Analyze chromosomes under the microscope and select appropriate metaphases for capture and perform karyotyping
        - Document the analysis appropriately and understand the procedures for verbally reporting abnormal results to Director
        - Properly identify numerical and structural abnormalities and proper use of ISCN nomenclature

        - Assess banding resolution
        - Interpret the results and generate report using appropriate ISCN nomenclature and predict phenotype and impact on patient care
        - Communicate abnormal results and cases requiring follow-up or additional studies directly to health care professions
        - Troubleshooting technical difficulties
        - Understanding the limitations of the technology
    - Fluorescence in situ hybridization (FISH)
        - Preparation of slides for interphase and metaphase FISH analysis
        - Labeling of probes – direct and indirect labeling
        - Perform pretreatment, denaturation, hybridizations, washing and counterstaining for a variety of FISH probe types
        - Analyze FISH slides for interphase and metaphase analysis, capture appropriate images and document analysis
        - Understand probe validation and normal range/cut-off values for each probe used
        - Run appropriate controls with all experiments
        - Interpret and report FISH results using appropriate ISCN nomenclature and predict phenotype and impact on patient care
        - Communicate abnormal results and cases requiring follow-up or additional studies directly to health care professions
        - Troubleshooting technical difficulties
        - Understanding the limitations of the technology
    - Array Comparative Genomic Hybridization (aCGH)
        - DNA extraction and determination of quality using spectrophotometer and agarose gel electrophoresis
        - Fluorescent labeling of DNA, hybridization to microarray, and washing of array
        - Scanning and software analysis of array results
        - Appropriate use of databases (eg. Database of Genomic Variants, UCSC Browser, Decipher, etc.) to interpret the results
        - Appropriate confirmation of positive results by FISH or quantitative PCR and follow-up of parental specimens when necessary
        - Interpret and report aCGH results using appropriate ISCN nomenclature and predict phenotype and impact on patient care
        - Communicate abnormal results and cases requiring follow-up or additional studies directly to health care professions
        - Troubleshooting technical difficulties
        - Understanding the limitations of the technology
3. Postanalytical Laboratory Skills-through all lab rotations
    - Competent in practicing general lab quality management procedures
        - Perform reagent controls with all assays including tracking critical reagents lots, testing new critical reagents prior to use, appropriate labeling of all reagents
        - Perform quality control with all assays, compile QC record, track QC trend
        - Daily tracking of equipment performance
        - Perform regular calibration procedures
        - Demonstrate knowledge in setting up and implementing necessary quality measure to assure and improve testing quality
        - Get involved with preparation for lab inspections
    - Results interpretation and reporting
        - Competent in result interpretation. Can recognize numerical and structural chromosome abnormalities, abnormal FISH and array CGH results. Can predict the phenotypic outcome and/or convey reproductive risk for different abnormalities

- Understand the heterogeneity, variability, and natural history of chromosome disorders.
- Draft accurate and concise clinical reports summarizing findings and interpretations, sensitivity and limitations of the testing
- Communicate results clearly with healthcare professionals (physicians and genetic counselors

4. Rotations in Molecular Genetics and Biochemical Genetics non-specialty laboratories
    - Understand the indications for performing molecular and biochemical testing
    - Understand the technologies employed and the technical workflow
    - Understand the quality control measures implemented in the laboratory
    - Understand interpretation and reporting of results
    - Understand the limitations of the technologies employed

Medical Genetics Knowledge:

1. Understand the principles of biology and genetics related to cytogenetics covered by departmental and divisional seminars, journal clubs and case conferences and the departmental medical genetics course run annually
2. Understand the principles of chromosome structure and function
    a. Cell cycle, mitosis and meiosis
    b. DNA structure and genetic code
    c. Chromosome ultrastructure and specialized functions
3. Understand principles of clinical cytogenetics
    a. Etiology of chromosome disorders
        i. Aneuploidy: non-disjunction, anaphase lag
        ii. Polyploidy: dispermy and failure of polar body separation
        iii. Imprinting and uniparental disomy
        iv. Chromosome breakage syndromes and specific defects
        v. Structural rearrangements: non-allelic homologous recombination (NAHR) and non-homologous end joining (NHEJ)
        vi. Isochromosome formation: centromere misdivision and breakage fusion bridge cycles
        vii. Translocations: chromosome segregation in meiosis
        viii. Inversions: inversion loop formation and recombinant products
    b. Genetic counseling and risk recurrence for chromosomal disorders
    c. Cancer cytogenetics and hematopoiesis
    d. Clinical features of constitutional abnormalities (eg. aneuploidies, and microdeletion/duplication syndromes and acquired cytogenetic disorders (ie. hematologic malignancies and solid tumors)
4. Understand basic embryology and how it relates to the origin of specific tissues such as blood, chorionic villi, amniotic fluid and skin
5. Understand the basic principles of inheritance
6. Understand genetic toxicology as it relates to chromosome abnormalities
7. Understand how to interpret and use standard ISCN nomenclature to describe karyotypes, FISH and array CGH results

Practice-Based Learning

1. Review the literature to obtain information on cytogenetic techniques and their use in clinical medicine
2. Participate in presenting positive cases at weekly division case conference
3. Participate in the “Clinical Genetics” Journal club

4. Attend departmental graduate level Medical Genetics course equivalent to one semester
5. Attend and participate in laboratory meetings by presenting papers at the monthly "Special Topics in Cytogenetics" journal club
6. Attend weekly departmental seminars

Interpersonal & Communication Skills

1. Can obtain clinical information to assist the lab in appropriate test selection
2. Can explain clinical findings and their significance to laboratory staff
3. Can communicate laboratory results in a appropriate manner to referring physicians and genetic counselors
4. Can participate in genetic counseling sessions to appropriately communicate laboratory results to patients and their families

Professionalism

1. Demonstrates respect for patient confidentiality
2. Considers sensitivity to patients of diverse backgrounds when communicating lab results
3. Considers ethical issues in genetics, particularly those raised by cytogenetic testing

System-Based Practice

1. Work effectively with various members of the clinical and laboratory team to facilitate accurate and appropriate patient testing and reporting of results
2. Is aware of the cost and risks/benefits of obtaining samples and providing testing
3. Participate in lab quality management process including quality control, quality assurance and quality improvement
4. Be familiar with other lab management processes including laboratory information systems, billing and reimbursement issues and policy implications

Research-related activities

1. Learn IRB and HIPAA regulations, protocols, and consent process
2. Development of new laboratory tests and validation of assays for clinical use
3. Participate in ongoing translational research projects related to cytogenetics