CCMG Genetic and Genomic Diagnostics Training Guidelines and Specialty Requirements

Preamble

The aim of the Genetic and Genomic Diagnostics (GGD) Training Program is to produce scientific specialists with the competence to apply genomic testing effectively in genetic disorders. Competence implies the individual has the knowledge, skills and attitudes to:

1. Identify and interpret abnormalities from the single nucleotide to the whole chromosome level
2. Provide consultation to healthcare practitioners regarding laboratory testing particularly as it relates to the management of patients and their families with genetic disorders
3. Assume the day-to-day responsibilities for the operation and standards of a genomic diagnostic laboratory.

The Genetic and Genomic Diagnostics Geneticist will have a thorough grounding in the theory, methodology and techniques of DNA and chromosome analysis, and will be familiar with a broad spectrum of disorders representing all modes of inheritance and indications typically encountered in the diagnostic laboratory setting.

Trainees are expected to participate fully in all aspects of laboratory medicine in this field; multi-disciplinary case discussion, rounds, seminars and meetings related to testing of nucleic acids. There is increasing responsibility over the 2-year training period to include more independence in result interpretation, test development, laboratory management, quality assurance and other competencies as outlined here in the Training Guidelines.

The CCMG training guidelines are modeled after the CanMEDS 2015 framework[1] and were largely inspired by the Competence by Design approach of the Royal College of Physicians and Surgeons of Canada[2]. The CanMEDS framework includes the competencies required of specialists and the role of the specialist beyond that of the specialty medical expert. The other roles of the specialist are that of communicator, collaborator, leader, health advocate, scholar and professional.

Required Background

Trainees must have a PhD and/or an MD degree.

A candidate's PhD must have a strong genetics content. The required educational experience would approximate that required for an MSc in genetics and molecular biology. If this experience is lacking, the trainee must gain this knowledge through suitable courses and/or private study. PhD trainees must have successfully defended and submitted the final version of their PhD thesis before beginning CCMG training. The start date for training cannot be before submission of the

final version, with all revisions (if any) approved by the relevant university officer(s). Each training centre has its own process for evaluation of doctoral degrees earned outside Canada

Individuals with an MD degree should have a Genetics or Laboratory Medicine background (such as Pathology or Clinical Biochemistry). They must have completed at least 3 years of residency training in a program accredited by the Royal College of Physicians and Surgeons of Canada (RCPSC) and/or Collège des Médecins du Québec (CMQ) and/or, for international medical graduates, in a RCPSC-approved training program (refer to RCPSC website). MD candidate must demonstrate previous suitable exposure to Genomic Medicine, either through courses undertaken during their curriculum or clinical rotations.

I. Administrative Aspects

1. Supervisory committee:

a. Each trainee's program will be supervised by a committee headed by a Fellow of the CCMG in Cytogenetics, Molecular Genetics or GGD who takes primary responsibility for the training (a.k.a. supervisor).
b. The committee will consist of the supervisor (head) and a minimum of two additional members. Other members might consist of clinical geneticists, molecular geneticists, cytogeneticists or GGD geneticists. The structure of the committee will vary depending on the background of the trainee, but must contain individuals trained and certified to sign out cytogenetic and molecular genetic results.
c. The program director or supervisor on behalf of the committee ensures the trainee is registered with the CCMG Credentials Committee by submitting a registration form to the CCMG Office within the first three months of commencing training.
d. The committee takes responsibility for ensuring the training program is meeting the needs of the trainee and is in keeping with CCMG guidelines, including graduation of responsibility in the laboratory and clinical setting. The committee must submit an outline of planned and completed training in the CCMG GGD program logbook.
e. The committee meets at least every six months with the candidate, reviews logbook progress and ensures that in-training evaluation reports (ITER) are completed and discussed with the trainee. The ITERs are specific to each of the GGD training units and include assessment of the learning objectives associated with the unit as well as longitudinal competencies that apply throughout the training program. The Clinical Genetics and Electives rotations are assessed with the general ITER for the GGD program. A minimum of one ITER (specific to the unit) must be completed per training unit. If the trainee needs remedial work, the committee must ensure that this is provided.
f. The committee completes the Final In-Training Evaluation Report (FITER) for submission to the CCMG office upon completion of training or as directed in the credentials letter. Please note that the FITER is additional to the ITER covering the last training unit(s).

2. Location of training

a. The GGD training program must take place in a CCMG-accredited centre. A trainee will be allowed up to 15 weeks or 25% of the duration of the seven core units training (refer to Table 1) in a non CCMG-accredited centre.
b. Elective training may be done at non-accredited centres at the discretion of the supervisory committee.
c. In the event that accreditation of a centre is terminated during the candidate's training, it is the joint responsibility of the trainee and the training centre to find a suitable alternate CCMG training centre. The Credentials Committee must be informed by letter of the alternative plan.

3. Training in foreign centres

a. Training in American centres accredited by the American Board of Medical Genetics and Genomics (ABMGG) is recognized by the CCMG as long as this training fulfills CCMG training prerequisites and credentialing requirements. It is the responsibility of the trainee to ensure compliance with and completion of all requirements of the CCMG.

4. Part-time training

a. Part-time training is recognized by the CCMG, provided it conforms to all requirements in this document and the trainee spends a minimum of 50% of time in the program.
b. The total amount of time must equal two complete years of full-time training [104 weeks full-time equivalent (FTE)].
c. Part-time trainees must fill out the FTE conversion column in the training program outline section of the CCMG GGD program logbook.

5. Second specialty training

a. Individual clinical cytogenetics and molecular genetics training programs with a discipline-specific examination will be allowed until the 2026 examination cycle. After that time, it will be possible to train in a single specialty but only the GGD training program examination will be available. Please note that previous provisions for examination deferral or repeat attempts within 5 years as indicated on the CCMG website, may not apply since the single specialty exam will no longer be available after June 2026.
b. The minimum training duration is one-year full-time equivalent (52 weeks).
c. Fellows already certified in Biochemical Laboratory Genetics, Biochemical Clinical Genetics or RCPSC Clinical Genetics or equivalent must have completed their second specialty training by June 30, 2024 in order to have two attempts at writing the single specialty examinations (examination cycles 2024 and 2026).
d. Fellows certified in Clinical Cytogenetics or Molecular Genetics can complete their training at any time but must be aware that the single specialty examination will no longer be available after June 2026.

e. Detailed information on the content of the second specialty training in either Clinical Cytogenetics or Molecular Genetics can be found in a separate document entitled "Second Specialty Training Guidelines and Requirements" available on the CCMG website.

6. Credentialing

a. Candidates are advised to review the Credentialing requirements on the website early in their training to facilitate Credentials submission and review.
b. Because of the density of the training program and the amount of knowledge expected to be acquired in a short time period, exemption to any part of the program will **not** be granted.

7. Leave of absence

a. Trainees who are withdrawing from the program or who are taking a leave of absence from their training program must submit a Withdrawal/Leave of Absence Trainee Form to the Credentials Committee. The form is available in the Credentialing section of the CCMG website. Submit the form to the CCMG Management office.

II. Content of Training

Minimum of two-year (104 weeks) full-time training program.

The GGD training program is organized in a series of units covering related topics in genomic diagnostic that are meant to facilitate the acquisition of core competencies essential for a Laboratory Geneticist in the prescribed time. All trainees will begin with the Transition to Discipline (TTD) unit, then move on to the three Foundations units before transitioning to the Core units. The order of the core units is suggested, but not mandated. A training unit should be done all in one block with exclusion of topics that have to be covered at other centres. However, if the cases requirements for one unit are not satisfied within the allocated duration, it is acceptable to continue to log required cases throughout the entire training period. The Transition to Practice (TTP) unit is to be done towards the end of the training program. The training outline for a specific trainee must be recorded in the CCMG GGD program logbook in the specified section.

Table 1. Outline of the recommended GGD unit topics and timeline. Details of mandatory and elective training are below the Table. Detailed key features, assessment plan and general milestones for each unit are on the following pages.

Stage	Unit	General Topics	Suggested Duration
TTD	Transition to Discipline	Quality management system Specimen accessioning Education activities	2 weeks
Foundations	General Genetics Concepts – Part 1	Basic constitutional chromosome analysis	12 weeks

Foundations	General Genetics Concepts – Part 2	Nucleic acid extraction PCR Southern blot Repeat expansion disorders Linkage analysis concept	4 weeks
Foundations	Prenatal Genetics	Molecular and cytogenetic prenatal diagnosis Rapid Aneuploidy detection Concepts of mosaicism, maternal cell contamination, uniparental disomy, trisomy rescue	8 weeks
Core	Copy Number Variation	Chromosomal microarray Quantitative PCR Multiplex Ligation-dependent Probe Amplification	8 weeks
Core	Single Nucleotide Variation and Residual Risk Calculation	PCR and sequencing methods to detect sequence variants Variant interpretation Risk calculation	8 weeks
Core	Next Generation Sequencing	Next generation sequencing platforms and targeted panels Whole-exome/genome sequencing Data interpretation	10 weeks
Core	Non-Mendelian Genetics	Imprinting, uniparental disomy Incomplete penetrance, variable expressivity Germline mosaicism Mitochondrial genome diseases	4 weeks
Core	Structural Variation and Advanced Chromosome Analysis	Advanced clinical cytogenetics Structural chromosome rearrangements Chromosome breakage syndrome	10 weeks
Core	Cancer Genetics – Part 1	Cancer chromosome analysis	10 weeks
Core	Cancer Genetics – Part 2	Inherited and acquired molecular alterations in cancer	8 weeks
TTP	Transition to Practice	Assisted laboratory direction	4 weeks
	TOTAL		88 weeks

II.1. Minimum of 88 weeks in laboratories(y) that provide(s) clinical cytogenetics and molecular genetics diagnostic services as outlined in this document.
Note: Training sites must ensure compliance with their laboratory accreditation programs. This may require bench work performed by a trainee be performed using non-clinical samples or under

supervision of appropriately certified individuals at the discretion of the training center, and supervised result reporting (co-signed) or the use of archival cases.

Training must include:

a. **Technical skills**: Hands-on experience in genetic techniques with the CCMG GGD program logbook recording involvement in 200 cases in the appropriate section. Cases must demonstrate experience in a variety of techniques with specific case requirements listed in each unit (refer to Table 2). If a required technique is not performed at a Training Centre, it is acceptable to observe this technique during a rotation at another Centre instead of performing the assay, up to a maximum of 20 cases.

   It is the responsibility of the local fellowship committee to determine if the trainee requires more cases to achieve the required expertise with all technical aspects.

b. **Interpretative and consultative skills**: Experience in interpreting results and communication to others, with the CCMG GGD program logbook recording involvement in 400 cases in the appropriate section. The candidate is required to request ancillary testing as appropriate, review result data, write the correct karyotype or variant nomenclature and write the interpretation.

   Case distribution: The cases documented must demonstrate a variety of sample or tissue type, methodologies and indications. It is the responsibility of the Supervisory Committee to ensure there is sufficient variety. Credentialing may be withheld if these criteria are not met. Case requirements for each technology are specified in each unit and outlined in Table 2. The representation of sample types and indications for testing for all cases is as follows:

   - Sample types **(minimum 30 of each)**:
     - Prenatal- cultured or direct amniotic fluid and CVS
     - Tissue- product of conception, skin biopsy, buccal smear, saliva, tissue biopsy, FFPE tissue
     - Peripheral blood- pediatric and adult samples
     - Oncology- bone marrow, unstimulated blood, tumour
   - Methodologies **(as outlined in Table 2)**:
   - Indication **(minimum 10 of each)**:
     - Confirmation of diagnosis (chromosomal or molecular)
     - Prenatal
     - Presymptomatic
     - Carrier testing
     - Cancer diagnosis, prognosis or treatment monitoring
     - Identity testing and/or relationship testing or maternal cell contamination (MCC) testing or chimerism/post-transplant testing

Abnormal/illustrative cases: At least 200 in total or 50% of the cases must represent abnormal results (e.g. reportable karyotype findings, chromosomal microarray findings, reportable sequence, dosage or methylation findings, technical artefact) or illustrative scenarios (maternal cell contamination, contamination of cell cultures, handling of mislabelled specimens, level I mosaicism, acrocentric polymorphism, chimerism). In order to meet the abnormal/ illustrative minimums in each category, archival material (inactive cases illustrative of a rare abnormal result that is unlikely to be seen during the training period) may be used (to a maximum of 80 archival cases or 20% of the cases in each unit). Abnormal results observed during technical experience can also be logged. It is the sole responsibility of the local fellowship committee to determine the total number of cases, over and over the minimums specified here to be reviewed by the candidate to ensure a high level of competence.

c. Management skills: **Minimum of 4 weeks devoted to assisted-laboratory direction and oversight of laboratory services**. The cases reviewed are entered in the CCMG GGD program logbook in the appropriate section.

It is recognized that not all training centres will be able to provide a fully comprehensive training program. Those responsible for training at a given center must identify any 'gaps' and encourage trainees to obtain the appropriate training at other CCMG- or ABMGG- accredited centres to meet the overall training objectives of the program.

Table 2 Summary of technical and consultative assessment minimum case requirements for each training unit.

Unit	Technical Assessment	No.	Interpretative/Consultative Assessment	No.
Transition to Discipline	N/A		Request information from ordering physician	2 requests
General Genetics Concepts – Part 1	Constitutional chromosomes wet lab – Blood set up, harvest, slide preparation and banding	5 cases	G-banded karyotypes/metaphases review and interpretation	30 cases
	Wet lab – Metaphase FISH set-up and washes	5 cases		
	Constitutional chromosomes dry lab – Complete analysis of cases, including: selecting appropriate metaphases at microscope or from scanning results, image capture, analyzing and karyotyping required number of cells, recording on worksheet, determine analysis result	5 cases		
	Constitutional chromosomes dry lab –	15 cases	Metaphase FISH images review and	10 cases

	Karyotyping or metaphase analysis only		interpretation	
	Dry lab – Metaphase FISH slide assessment	5 cases		
General Genetics Concepts – Part 2	Nucleic acids extraction from any of 3 different sources (blood, blood spots, buccal, tissue culture, direct amniotic fluid, CVS, saliva or tissue)	5 cases	Repeat expansion disorders - Result review and interpretation	10 cases
			Identity or relationship testing – Result review and interpretation	2 cases
	Identity or relationship testing	2 cases	Linkage analysis - Review of current, archival or exemplary cases	2 cases
	Repeat-primed PCR for expansion repeat disorders	5 cases		
Prenatal Genetics	Wet lab – Prenatal specimen (amniocytes, CVS, fibroblasts) set up, maintenance, harvest, slide preparation and banding	3 cases	Prenatal G-banded karyotypes/metaphases review and interpretation	10 cases
	Dry lab – Prenatal specimens karyotyping only	5 cases		
	Wet lab - Rapid Aneuploidy detection assay [(FISH or QF-PCR) and/or NIPS]	3 cases	Rapid Aneuploidy detection assay review and interpretation	10 cases
Copy Number Variation	Wet lab - Dosage-based tests such as chromosomal microarray, qPCR, MLPA, etc. (must include minimum of 2 different methods)	10 cases	Dosage-based tests: data review and interpretation	30 cases
	Dry lab – Data analysis for dosage-based tests (must include minimum of 10 cases for each of chromosomal microarray, qPCR and MLPA)	30 cases		
Single Nucleotide Variation and Residual Risk	PCR-based assay for SNV detection such as qPCR, allele-specific PCR, mass array, bead array, restriction enzyme digest (must include minimum of 2 different methods)	5 cases	Single Nucleotide variant data review and interpretation	10 cases
			Residual Risk Calculation	5 cases
	Sanger sequencing for SNV detection/confirmation	3 cases		
Next Generation Sequencing	Observation of library preparation and NGS panel set-up	4 runs	NGS data review and variant interpretation	25 cases
	Observation of WES/WGS library preparation and set-up	1 run	WES/WGS data review and variant interpretation	5 cases
Non-Mendelian Genetics	Set-up and analysis of testing for imprinting disorders, uniparental disomy, mitochondrial genome disorders (must include minimum of 2 areas)	10 cases	Data review and interpretation for imprinting disorder, uniparental disomy, mitochondrial genome disorder, follow-up from suspected germline or somatic mosaicism of a Mendelian disorder (minimum 2, maximum 10 cases of each type)	20 cases

Structural Variation and Advanced Chromosome Analysis	Dry lab – Karyotyping only	20 cases	G-banded karyotypes/metaphases review and interpretation	30 cases
Cancer Genetics – Part 1	Wet lab – Oncology specimen set-up, harvest, slide preparation and banding	3 cases	G-banded karyotypes/metaphases review and interpretation	20 cases
	Dry lab – Complete analysis of cases, including: selecting appropriate metaphases at microscope or from scanning results, image capture, analyzing and karyotyping required number of cells, recording on worksheet, determine analysis result	5 cases	Chimerism (post-transplant) testing review and interpretation	3 cases
	Dry lab – Karyotyping only	20 cases	Interphase FISH images review and interpretation	10 cases
	Dry lab – Interphase FISH (including FFPE tissue FISH if possible) slide assessment	10 cases		
Cancer Genetics – Part 2	Nucleic acid extraction from FFPE tissue slide or curls	3 cases	Data review and interpretation of hereditary cancer gene(s) or gene panel – one case reported in the context of microsatellite instability and/or immunohistochemistry	10 cases
	PCR-based methods for cancer prognosis and follow-up (RT-PCR, RQ-PCR, clonality, …)	5 cases		
	Observation of library preparation and NGS panel set-up for somatic variant detection	2 runs	Data review and interpretation of familial or founder variant in a hereditary cancer gene	20 cases
			Data review and interpretation of PCR-based tests for cancer prognosis and follow-up	5 cases
			Data review and interpretation of actionable somatic variant from at least two cancer types	20 cases
Transition to Practice			Management of caseload and supervision of the laboratory	

II.2. Test development, verification, validation, update, documentation, and determination and recording of quality parameters: **Involvement in a minimum of two aspects of these test quality initiatives in the laboratory** to be recorded in the CCMG GGD program logbook in the appropriate section.

II.3. Clinical Genetics sessions: Participation in a **minimum of 25 patient encounters** (counselling

session) with a CCMG/ABMGG-certified clinical geneticist or CAGC/ABMG-certified genetic counselor, but not necessarily in a CCMG-accredited centre. This rotation may occur as a block or throughout the training program. The trainee should record participation in a minimum of 25 counselling sessions, representing at least 4 of the following clinical scenarios: prenatal, pediatric, adult, metabolic, cancer and neurogenetic in the CCMG GGD program logbook in the appropriate section. Participation must include developing an understanding of the issues through literature searches and discussions with clinical colleagues.

II.4. Courses/conferences

a. Participation in educational events and courses prescribed by the trainee's supervisory committee is to be documented in the CCMG GGD program logbook in the appropriate section.
b. **Documented attendance** at one local (e.g. departmental annual research day, Research Institute research day), national or international genetics/genomics meeting during the training period.

II.5. Logbooks: CCMG logbook templates available on the CCMG website **must be used**. Patient confidentiality must be guarded. Therefore, before submitting to the CCMG office, cases must have all identifiers removed (including sample ID numbers) so as not to be traceable.

II.6. Electives training: Provides additional training opportunities in related areas of interest to the trainee. Elective training must be approved by the supervisory committee.

a. Rotations in related fields, such as molecular pathology, biochemical genetics, pathology, embryopathology, developmental genetics, oncology, hematology and relevant aspects of obstetrics.
b. Visits to other genetic service laboratories or CCMG training centres.

A logbook should not only be viewed as a mechanism for tracking the number of cases/experiences accumulated but as a means for documenting learning, illustrative cases and approaches/ troubleshooting undertaken that may be reflected upon and recalled as the trainee prepares for the CCMG examination and begins their career as a laboratory geneticist. The logbook should be reviewed regularly and discussed by the supervisor and trainee to ensure they represent the breadth of testing required and acquisition of competencies.

The following pages provide a detailed presentation of the recommended GGD unit topics. They have been organized in a cohesive way and include similar features:

Title: The title includes the name of the training program followed by the stage of training and item number. Items in each stage of training begin at number one. The unit name appears immediately after the title.

Key features:	The key features section describes the scope of the GGD training unit and includes its area of focus, as well as learning and procedural requirements.
Assessment Plan:	The assessment plan describes the nature of the information that should be recorded in the trainee's logbook in order for the Supervisory Committee to have enough information to assess the trainee's progress, and for credentialing purposes. These requirements are meant to provide the trainee with the breadth of technical and interpretative knowledge necessary for their future career.
Learning objectives:	Each training units is comprised of several CanMEDS competencies. The learning objectives are linked to the corresponding key and enabling competency within the CanMEDS 2015 Physician Competency Framework by a series of letters and numbers. For example, if the code is ME 1.6. - ME refers to the CanMEDS Role, Medical Expert. Other possibilities are COM= Communicator, COL= Collaborator, L= Leader, HA= Health Advocate, S= Scholar and P= Professional. - 1.6 refers to the Key and enabling competencies within the aforementioned Role.

REFERENCE

1. Frank JR, Snell L, Sherbino J, editors. CanMEDS 2015 Physician Competency Framework. Ottawa: Royal College of Physicians and Surgeons of Canada; 2015.

2. Royal College of Physicians and Surgeons of Canada 2020, *Competence by Design*. [online] Ottawa, viewed 18 February 2020. http://www.royalcollege.ca/rcsite/cbd/competence-by-design-cbd-e

Genetic and Genomic Diagnosis Training Program: Transition to Discipline Quality Management System, Specimen Accessioning and Learning Plan

Suggested Duration: 2 weeks

Key Features:

- This unit focuses on acquiring a basic knowledge of the quality processes in a genomic diagnostic laboratory and on the accessioning of clinical specimens.
- This unit includes starting an education logbook to be updated and maintained through all stages of training.
- The specifics of the education activities will be determined by the individual trainee and the training program, and the logbook will be reviewed by the program director, primary supervisor and supervisory committee.

Assessment Plan:

Assessment is performed through logbook entries:

- Interpretative/Consultative cases logbook:
    - Two documented instances of follow-up/clarification on a test request with the ordering physician or health care provider

- Education Activities recorded in the CCMG GGD program logbook and to be maintained throughout the training

Learning Objectives:

1 **ME 1.3** Apply knowledge of an established Quality Management System in day-to-day activities [e.g. QMS01 from Clinical and Laboratory Standard Institute (CLSI)]
2 **ME 2.2** Identify basic principles of specimen adequacy
3 **ME 3.2** Describe sample accessioning in the laboratory including appropriate reasons for referral (e.g. carrier, diagnosis, pre-symptomatic)
4 **ME 3.3** Recognize and discuss the importance of the triaging and timing of specimen collection
5 **ME 5.1** Access and adhere to standard operating procedures (SOP) and document control processes
6 **L 1.1** Apply knowledge of the principles of quality assurance pertinent to laboratory medicine
7 **L 1.4** Describe the data available from health information systems to optimize patient care

8 **S 1.1** Create a learning plan in collaboration with a designated supervisor identifying learning needs related to laboratory genetics

9 **P 3.1** Demonstrate awareness of the relevant codes, policies, standards and laws (both local and provincial) governing laboratory practice including accreditation standards, and CLSI

Genetic and Genomic Diagnosis Training Program: Foundations #1

General Genetics – Part 1

Suggested Duration: 12 weeks

Key Features:

- This unit focuses on general chromosome analysis and its role in diagnosis, prediction of natural history and estimation of recurrence risk for congenital and reproductive disorders.
- This unit will expose the trainee to the major techniques used for chromosome analysis.
- This unit includes achieving a basic level of chromosome pattern recognition using various banding methods and fluorescence *in situ* hybridization (FISH), and their description using the current International System for Human Cytogenomic Nomenclature (ISCN)

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases logbook:
    - Constitutional chromosomes wet lab (set-up, harvest, slide preparation, slide banding): minimum 5 cases
    - Metaphase FISH wet lab (slide pre-treatment and probe application, FISH post-treatment): minimum 5 cases
    - Constitutional chromosomes dry lab – complete analysis (includes selecting appropriate metaphases at microscope or from scanning results, image capture, analyzing and karyotyping required number of cells, recording on worksheet, determine analysis result): minimum 5 cases
    - Constitutional chromosomes dry lab – karyotyping only: minimum 15 cases
    - Metaphase FISH dry lab (slide assessment): minimum 5 cases

- Interpretative/Consultative cases logbook:
    - Karyotype and metaphase review and interpretation (including request for ancillary testing such as special stains, FISH, as appropriate) with ISCN nomenclature and report writing: minimum 30 cases
    - Metaphase FISH image review and interpretation with ISCN nomenclature designation and report writing: minimum 10 cases

Learning Objectives:

1. **ME 1.3** Apply knowledge of the relevance of cytogenetics in the context of germline or constitutional diagnosis and recurrence risk
2. **ME 1.3** Apply in-depth knowledge of the biology, structure, function, and mitotic/meiotic segregation of chromosomes, including the sex chromosomes, to explain the mechanisms and consequences of chromosome anomalies and mosaicism
3. **ME 1.3** Apply knowledge of the origins and clinical consequences of common chromosome anomalies to the estimation of recurrence risk in offspring
4. **ME 1.3** Apply knowledge of population cytogenetics to the relative frequency of chromosome anomalies in conceptions, newborns and adults
5. **ME 1.3** Apply knowledge of the most recent guidelines or recommendations from the Canadian College of Medical Geneticists while reviewing and interpreting chromosome and FISH analyses
6. **ME 2.2** Achieve a basic level of chromosome recognition from normal blood lymphocytes on a print or at the microscope, of whole chromosome, whole arm, or G-band size anomalies
7. **ME 2.2** Demonstrate the ability to distinguish chromosome heteromorphisms, population variants and fragile sites from other anomalies and reports them when appropriate
8. **ME 3.1** Understand the benefits and limitations of different staining methods and FISH probe types to identify and characterize constitutional chromosome abnormalities
9. **ME 3.4** Perform all laboratory and analytical steps of the procedure to obtain banded chromosomes from constitutional specimens, from culture to metaphase analysis
10. **ME 3.4** Apply knowledge of chromosome and FISH staining techniques in selection of the most useful approach for an abnormal finding and of the parameters influencing the results of chromosome and FISH analyses for effective troubleshooting
11. **ME 3.4** Perform all laboratory and analytical steps of the FISH procedure on metaphase and interphase cells
12. **COM 2.3** Apply proper use of current ISCN guidelines to describe all results
13. **L 1.1** Apply standardized methods for FISH probe selection, validation, and interpretation of signal patterns including use of controls, in the detection of an anomaly

Genetic and Genomic Diagnosis Training Program: Foundations #2
General Genetics Part 2

Suggested Duration: 4 weeks

Key Features:

- This unit focuses on basic concepts related to general nucleic acid analysis.
- This unit includes understanding and performing:
    - Nucleic acid extraction
    - Polymerase Chain Reaction (PCR)
    - Identity testing
    - Repeat Expansion testing
- It also includes familiarization with the pathophysiology of genetic disorders and general linkage concepts

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases logbook:
    - Nucleic acid extractions from any 3 of the following specimen types: blood, blood spots, bone marrow, buccal, tissue culture (e.g. amniocytes, CVS, fibroblast), direct amniotic fluid, direct CVS, saliva or tissue (e.g. muscle, thymus): minimum 5 specimens
    - Identity and/or relationship testing: minimum 2 cases
    - Repeat-primed PCR for expansion repeat disorders: minimum 5 cases

- Interpretative/Consultative cases logbook:
    - Repeat expansion disorders - Result review and interpretation: minimum 10 cases
    - Identity and/or relationship testing – Result review and interpretation: minimum 2 cases
    - Linkage analysis - Review of current, archival or exemplary cases: minimum 2 cases

Learning Objectives:

1. **ME 1.3** Recognize and explain the role of gonadal and somatic mosaicism, variable penetrance, variable expressivity, *de novo* inheritance
2. **ME 1.3** Apply general linkage concepts to assess carrier/disease risk in an individual
3. **ME 2.2** Appropriately interpret data from PCR, repeat-primed PCR and Southern blot testing for repeat expansions including methylation and size mosaicism

4 **ME 2.2** Appropriately interpret microsatellite fragment size/pattern from an identity test
5 **ME 3.1** Describe different methods for DNA and RNA extraction, their advantages, limitations and clinical applications
6 **ME 3.1** Describe different nucleic acid quantification methods, their advantages, limitations, applications, and quality metrics
7 **ME 3.1** Demonstrate knowledge of the variables that affect PCR by being able to troubleshoot a reaction
8 **ME 3.4** Perform all laboratory and analytical steps of the procedure to obtain DNA or RNA of suitable quality
9 **ME 3.4** Perform all laboratory and analytical steps of the procedure for determining identity or relationship between specimens
10 **ME 3.4** Perform all laboratory and analytical steps of the procedure for repeat expansion testing

Genetic and Genomic Diagnosis Training Program: Foundations #3
Prenatal Genetics

Suggested Duration: 8 weeks

Key Features:

- This unit focuses on genetic testing in the prenatal context.
- This includes recognizing common chromosome anomalies using proper ISCN and understanding common concepts encountered such as mosaicism and maternal cell contamination.
- This unit also includes performing:
    - Cell culture
    - Rapid aneuploidy detection (RAD) assays: FISH or QF-PCR and/or Non-Invasive Prenatal Screening (NIPS)
    - Reporting and prioritization of tests.

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases logbook:
    - Prenatal chromosomes wet lab [*in situ* and/or flask set-up (can be observed if not achievable at a centre), culture maintenance, harvest, slide preparation, slide banding from prenatal specimen such as amniocytes, CVS, fibroblasts]: minimum 3 cases
    - Prenatal chromosomes dry lab – karyotyping only: minimum 5 cases
    - RAD assay wet lab (Interphase FISH or QF-PCR and/or NIPS): minimum 3 cases

- Interpretative/Consultative cases logbook:
    - Karyotype and metaphase review and interpretation (including request for ancillary testing such as special stains, FISH, as appropriate) with ISCN nomenclature and report writing: minimum 10 cases
    - RAD assay review and interpretation including maternal cell contamination (MCC) or zygosity studies, if applicable, with ISCN nomenclature designation and report writing: minimum 10 cases

Learning Objectives:

1. **ME 1.3** Apply knowledge of the most appropriate available testing techniques in prenatal diagnosis based on clinical indication, gestational age and specimen type
2. **ME 1.3** Describe the role of advanced maternal age on reproductive success in humans
3. **ME 1.3** Provide appropriate recommendations for follow-up of uniparental disomy (UPD) in the context of a familial rearrangement or marker involving an imprinted chromosome
4. **ME 1.3** Understand the statistical concepts associated with prenatal screening and testing and differentiate prenatal screening from prenatal testing
5. **ME 1.3** Apply knowledge of basic human embryology (including development of the placenta vs embryo proper), the sources of cells studied in prenatal genetic tests, the types of twinning and their impacts on cell source in prenatal genetic testing and the timing of organ system development
6. **ME 1.4** Analyze chromosomes from amniotic fluid, chorionic villus sampling and fibroblast tissue culture preparations and demonstrate ability to detect chromosome aneuploidy, Robertsonian translocations, large chromosome translocations, whole G-band size deletions and duplications in metaphase images
7. **ME 3.1** Describe the benefits and limitations of non-invasive prenatal screening in comparison to a biochemical screening program and its effect on a prenatal diagnosis program
8. **ME 3.2** Describe the methodology, benefits and limitations of the FISH and QF-PCR RAD testing kits available, including probe choice (location, size), possible artefacts, appropriate use of controls, cut-off determination and approaches to MCC detection
9. **ME 3.4** Perform all laboratory and analytical steps of the procedure to obtain chromosomes from prenatal specimens: set-up (or observation), culture maintenance, harvest and slide-making
10. **ME 3.4** Understand the parameters that influence cell growth (including cell types present in direct versus short and long term chorionic villi cultures), nucleic acid yield, and chromosome preparation including roles of gaseous atmosphere, humidity, temperature, and components of tissue culture media
11. **ME 4.1** Design and implement a plan to investigate prenatal mosaicism in chromosome studies and understand the concept and the definitions of mosaicism levels in flask vs in situ cultures of prenatal specimens
12. **ME 4.1** Design and implement a troubleshooting plan to investigate situations such as bacterial/fungal contamination in cultures or incubators, unexplained growth failure of tissue culture, or maternal cell contamination as a possible confounder of result interpretation
13. **ME 4.1** Implement a plan to investigate, report and follow up abnormal RAD or karyotype results
14. **COM 2.3** Apply proper use of the most recent ISCN to describe simple prenatal testing results

15 **COM 4.2** Report appropriately mosaic findings in a prenatal result and provide consultation to the ordering clinician as necessary

16 **COL 1.3** Understand the role of ultrasound examination in prenatal care and the common occurrences in this type of examination [hydrops, cystic hygroma, Congenital Cystic Adenomatoid Malformation (CCAM), gastroschisis, omphalocoele, brain abnormalities, etc.] through attendance at prenatal rounds or clinics

Genetic and Genomic Diagnosis Training Program: Core #1
Copy number variation analysis

Suggested Duration: 8 weeks

Key Features:

- This unit focuses on the use of chromosomal microarray (CMA), quantitative PCR (qPCR) and Multiplex Ligation-dependent Probe Amplification (MLPA) to investigate copy number variation (CNV).
- This unit also includes developing an understanding of methodology, data analysis, interpretation and proper clinical utility of these technologies.

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases logbook:
    - Dosage-based tests wet lab – processing of specimens for CMA, qPCR or MLPA: minimum 10 cases involving at least two different methods
    - Dosage-based tests dry lab – Data analysis for CNV testing such as CMA, qPCR, MLPA: minimum 10 cases for each method for a total of 30 cases.

- Interpretative/Consultative logbook:
    - Dosage-based tests – data review and interpretation: minimum 30 cases

Learning Objectives:

1. **ME 1.3** Understand the mechanisms whereby recurrent structural abnormalities arise (e.g. aberrant pairing, recombination at repetitive elements, etc.)
2. **ME 2.2** Understand and evaluate common referral reasons for CMA including common genetic deletion and duplication syndromes, referrals in the postnatal versus prenatal settings, etc.
3. **ME 2.2** Demonstrate the ability to interpret CMA data consistent with aneuploidy and common genetic deletion and duplication syndromes, and recognize and interpret material of unknown origin identified by chromosome analysis
4. **ME 2.2** Demonstrate the ability to design appropriate primers for qPCR and interpret data consistent with deletions and duplications

5 **ME 2.2** Demonstrate the ability to interpret MLPA data, including requests for appropriate confirmatory testing, and describe its use for confirmation of CNVs detected by Next-Generation Sequencing
6 **ME 2.2** Demonstrate knowledge and use of literature and guidelines relevant to CMA, MLPA and qPCR
7 **ME 3.1** Apply knowledge of the different CMA platforms used in clinical laboratories and describe their limitations and benefits in the context of clinical testing
8 **ME 3.2** Describe the best approach for the follow-up of CMA findings in relation to the clinical scenario
9 **ME 3.2** Describe the benefits and limitations of karyotype and CMA in both the pre- and post-natal contexts
10 **ME 3.2** Describe different types of qPCR and MLPA, their advantages, limitations and clinical utility
11 **ME 3.4** Apply knowledge of the steps involved and methodological basis of sample preparation, hybridization, washes and data analysis for different types of CMA used for clinical testing
12 **ME 3.4** Describe the methodological basis of qPCR including the use of reference genes and control samples in the context of clinical testing
13 **ME 3.4** Describe the methodological basis of MLPA and methylation-sensitive MLPA in the context of clinical testing
14 **COM 2.3** Use correct ISCN and Human Genome Variation Society (HGVS) nomenclature to describe CNVs
15 **L 1.1** Apply knowledge of validation/verification approaches for the establishment of CMA, qPCR and MLPA assays and their respective analysis software if applicable (e.g. original installation versus versioning upgrade)
16 **S 3.3** Apply knowledge and understand the inherent biases of the bioinformatics tools for the interpretation of CNVs, including control population and patient databases (e.g. DGV, DECIPHER, ClinVar/ClinGen, OMIM, Genome Browsers)

Genetic and Genomic Diagnosis Training Program: Core #2
Single Nucleotide Variation and Residual Risk Calculation

Suggested Duration: 8 weeks

Key Features:

- This unit ensures the learner establishes the skills and knowledge pertaining to single nucleotide variation (SNV) in individuals and populations.
- This unit focuses on molecular testing for the investigation of SNV and performing residual risk calculation.

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases logbook:
  - PCR-based assay wet lab – processing of specimens using methods such as qPCR, allele-specific PCR, mass array, bead array, restriction enzyme digest: minimum 5 cases involving at least two different methods
  - Sanger sequencing wet lab – processing of specimens using Sanger sequencing for SNV detection or confirmation: minimum 3 cases

- Interpretative/Consultative cases logbook:
  - SNV data review and interpretation with appropriate HGVS nomenclature and report writing: minimum 10 cases
  - Residual risk calculation: minimum 5 cases

Learning Objectives:

1 **ME 1.3** Apply knowledge of the pathophysiology of inherited genetic disorders and the concept of human variation in the context of genetic diseases with recurrent variants
2 **ME 1.3** Apply knowledge of the concept of founder variants in the context of variant interpretation
3 **ME 1.3** Apply knowledge of residual risk to germline or constitutional diagnosis, and of recurrence risk
4 **ME 1.3** Understand the statistical concepts of positive and negative predictive values, detection rate, specificity, sensitivity in the context of newborn and population-based screening and differentiate between DNA-based screening and diagnostic assays

5 **ME 1.4** Apply knowledge of various methods for the detection of sequence variation (including qPCR, allele-specific PCR, mass array, bead array, Sanger Sequencing, restriction enzyme digestion) and assess their benefits-limitations/ advantages-disadvantages
6 **ME 3.2** Understand the methodological basis of former single nucleotide variant scanning techniques (e.g. high resolution melting, pyrosequencing) and describe their advantages and limitations
7 **ME 3.2** Perform Bayesian analysis and residual risk calculation
8 **ME 3.4** Analyse Sanger sequencing traces to identify variants, recognize sequencing artifacts, flag unusual results and interpret complex sequences
9 **ME 3.4** Select appropriate reference sequences for sequence analysis
10 **ME 5.1** Link specific, inherited sequence variation with a patient's response to a pharmacological agent
11 **COM 2.3** Assign the correct HGVS nomenclature
12 **COM 2.3** Interpret and classify variants according to current guidelines in use [e.g. CCMG guidelines, ACMGG guidelines, disease-specific guidelines (ClinGen, etc.)]
13 **S 3.2** Utilize disease-specific databases, general population datasets and in silico algorithms to support variant interpretation

Genetic and Genomic Diagnosis Training Program: Core #3
Next Generation Sequencing

Suggested Duration: 10 weeks

Key Features:

- This unit focuses on the Next Generation Sequencing (NGS) technologies and their implementation in a clinical setting for diagnostic and disease management purposes.
- This unit will educate the trainee on the different approaches, platforms, data analysis parameters and performance of NGS-based assays.
- This unit includes analyzing data generated by NGS-based tests and interpreting test results with consideration of the clinical information provided.

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases logbook:
    - Observation of library preparation of NGS based tests: minimum 5 library preparations including at least one involving whole exome (WES) or whole genome sequencing (WGS) (in a research or non-accredited laboratory acceptable)

- Interpretative/Consultative cases logbook:
    - NGS data review and interpretation: minimum 25 cases
    - WES/WGS data review and interpretation (cases performed in a research or non-accredited laboratory are acceptable): minimum 5 cases

Learning Objectives:

1. **ME 1.3** Apply knowledge of the different analysis parameter settings to interpret a NGS-based assay
2. **ME 1.6** Judge the performance of a NGS test run and/or troubleshoot a false result or a failed NGS test run by applying knowledge of how different parameters (e.g. library preparation, sequencing chemistries, bioinformatics tools, genomic content, specimen type, etc.) influence the sensitivity/specificity and QC metrics of a NGS-based test
3. **ME 1.6** Assess the relevance (or absence of relevance) of a gene to a disease using current guidelines/criteria
4. **ME 2.2** Recognize the complementarity of NGS-based assays with results obtained using other testing methods (i.e. FISH, MLPA)

5 **ME 2.2** Appreciate the utility of NGS-based testing to detect copy-number variations (CNVs) including aneuploidy and chromosome rearrangements
6 **ME 2.2** Integrate data from WES/WGS trio analysis when appropriate
7 **ME 3.1** Understand the advantages and limitations of different NGS platforms
8 **ME 3.4** Analyze NGS-based test results by proper use of analysis software/bioinformatics tools
9 **ME 3.4** Interpret and classify the variants identified by applying knowledge of the pathophysiology of the disorder and human variation, current guidelines and interpretation criteria in use, including proper use of disease-specific databases, general population datasets and in silico algorithms
10 **ME 3.4** Compose validation plans for NGS-based tests, including validation in both wet-lab and dry-lab (bioinformatics) steps as well as in both constitutional (germline) and cancer (somatic) setting
11 **L 2.2** Select the most efficient approach for a diagnosis from NGS panel, whole-exome sequencing or whole-genome sequencing, based on clinical scenario, cost, sensitivity, material available, etc.

Genetic and Genomic Diagnosis Training Program: Core #4
Non-Mendelian Genetics

Suggested duration: 4 weeks

Key Features:

- This unit focuses on disorders that are inherited in a non-Mendelian manner, the biological basis and mechanisms of disease, and different methods for their detection.
- This unit also includes applying genetic concepts that may mimic non-Mendelian inheritance.

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases logbook:
    - Non-Mendelian genetics wet lab – set-up and analysis of testing for imprinting disorders, uniparental disomy, mitochondrial genome disorders: minimum 10 cases involving at least two different subject areas

- Interpretative/Consultative cases logbook:
    - Data review and interpretation for imprinting disorder, uniparental disomy, mitochondrial genome disorder, follow-up from suspected germline or somatic mosaicism of a Mendelian disorder: minimum 20 cases– 2 to 10 cases of each type

Learning Objectives:

1. **ME 1.3** Apply knowledge of loss of gene expression from one parental chromosome through multiple mechanisms in the reporting of imprinting disorders
2. **ME 1.3** Apply knowledge of the concept of trisomy and monosomy rescue and its relationship to uniparental disomy/imprinting
3. **ME 1.3** Recognize tissue-specific sources of error for imprinting disorders in recommending the most appropriate tissue sample to test, (e.g. 11p15 imprinting disorders, prenatal tissues, etc.)
4. **ME 1.3** Recognize and explain the role of digenic inheritance, multifactorial inheritance, and polygenic risk scores in the interpretation of genetic test result findings
5. **ME 1.3** Apply knowledge of clinical presentation of well-characterized recurrent mitochondrial genome variants and the common methods used in their detection
6. **ME 1.3** Apply knowledge of homoplasmy and heteroplasmy in the interpretation and reporting of mitochondrial genome variants and recommend appropriate follow-up

7 **ME 2.4** Incorporate knowledge of mitochondrial disease presentation and inheritance pattern to recommend mitochondrial genome testing versus testing of nuclear encoded mitochondrial genes
8 **ME 3.1** Recommend the most appropriate tissue to test for mitochondrial genome testing or subsequent familial testing
9 **ME 3.4** Perform all laboratory and analytical steps of the procedure to detect an imprinting disorder
10 **ME 4.1** Select or recommend appropriate follow-up laboratory testing based on the specific imprinting disorder finding identified

Genetic and Genomic Diagnosis Training Program: Core #5
Structural Variation and Advanced Chromosome Analysis

Suggested duration: 10 weeks

Key Features:

- This unit focuses on advanced concepts in chromosome analysis and the recognition of structural rearrangements such as translocations, inversions, insertions, duplications, deletions, markers, rings, etc.
- The trainee should demonstrate increased self-confidence in chromosome recognition skills and in constitutional chromosome anomaly interpretation and reporting.

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases logbook:
    - Structural variation and advanced chromosome dry lab – karyotyping only: minimum 20 cases

- Interpretative/Consultative cases logbook:
    - Karyotypes and metaphases review and interpretation (including request for ancillary testing such as special stains, FISH, as appropriate) with ISCN nomenclature and report writing: minimum 30 cases

Learning Objectives:

1 **ME 1.3** Apply knowledge of the clinical implications and reproductive and recurrence risks for a carrier of a structural chromosome anomaly
2 **ME 1.3** Apply knowledge of the implications of chromosome mosaicism in performing a thorough investigation and reporting appropriately
3 **ME 1.3** Apply knowledge of recurrent microdeletion and microduplication syndromes, their underlying genomic architecture and the mechanism contributing to their recurrence in the context of report writing and recommendation for parental studies
4 **ME 1.3** Apply knowledge of the origins and clinical effects of X and Y chromosome aneuploidy and structural anomalies, including the effect of X-inactivation

5 **ME 1.3** Apply knowledge of the genetic mechanisms of DNA repair to the disorders resulting from their defects as well as the principles of chromothripsis and chromoanasynthesis in the context of clinical cytogenetics
6 **ME 1.4** Recognize structurally abnormal chromosomes in metaphases, karyotypes and inferences from chromosomal microarray results with appropriate follow-up test
7 **ME 1.4** Recognize well characterized cytogenetically visible unbalanced structural anomalies and describe their associated clinical features
8 **ME 2.2** Demonstrate the ability to distinguish between recombinant and derivative chromosomes and understand their different clinical significance
9 **ME 2.2** Demonstrate the ability to use chromosomal microarray SNP genotype (allele difference or B allele frequencies) to identify regions of homozygosity and describe their clinical significance (e.g. UPD, parental relationship), and to interpret complex rearrangements, mosaicism, chimerism, sample contamination, etc.
10 **ME 3.1** Describe the diagnostic testing methods for chromosome breakage syndromes, the associated recurrent chromosome findings, and their major clinical features
11 **ME 4.1** Coordinate the use of multiple diagnostic investigations to define a chromosome abnormality or heteromorphism, including appropriate use of different staining or molecular cytogenetic methods so as to ensure complementarity and efficiency
12 **COM 2.3** Apply proper use of the most recent ISCN to describe a chromosome anomaly

Genetic and Genomic Diagnosis Training Program: Core #6

Cancer Genetics – Part 1

Suggested Duration: 10 weeks

Key Features:

- This unit focuses on oncology chromosome analysis, how rearrangements contribute to cancer cell survival and the role of this analysis in diagnosis, prognosis, stratification and monitoring of hematological cancers and solid tumours.
- This unit also includes processing oncology specimens for chromosome analysis and FISH and using appropriate criteria for cell selection, clone establishment and discriminating constitutional versus acquired anomalies during analysis. An understanding of the method, advantages and disadvantages of interphase FISH on formalin fixed paraffin embedded (FFPE) tissues and on isolated nuclei is desirable.
- This unit also includes identifying recurrent and non-recurrent chromosome anomalies and significant interphase FISH signal patterns, and using the appropriate ISCN nomenclature to describe them.

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases logbook:
    - Cancer chromosomes wet lab (set-up, harvest, slide preparation, slide banding): minimum 3 cases
    - Cancer chromosomes dry lab – complete analysis (includes selecting appropriate metaphases at microscope or from scanning results, image capture, analyzing and karyotyping required number of cells, recording on worksheet, determine analysis result): minimum 5 cases
    - Cancer chromosomes dry lab – karyotyping only: minimum 20 cases
    - Interphase FISH (including FFPE tissue FISH if possible) dry lab (slide assessment): minimum 10 cases

- Interpretative/Consultative cases logbook:
    - Karyotypes and metaphases review and interpretation (including request for ancillary testing such as special stains, FISH, as appropriate) with ISCN nomenclature and report writing: minimum 20 cases
    - Chimerism/Post-transplant testing review and interpretation: minimum 3 cases

- Interphase FISH images review and interpretation with ISCN nomenclature designation and report writing: minimum 10 cases

Learning Objectives:

1. **ME 1.3** Apply knowledge of the relevance of cytogenetics to cancer diagnosis, prognosis, stratification for treatment and residual disease monitoring
2. **ME 1.3** Apply basic knowledge of normal hematopoiesis versus hematopathology of myeloproliferative neoplasia, myelodysplastic syndrome, and chronic and acute leukemia
3. **ME 1.3** Apply basic knowledge of the methodologies used by hematopathologists including, but not limited to, morphologic evaluation, cell counts, flow cytometry, and immunohistochemistry in refining necessary testing in oncology specimens
4. **ME 1.3** Apply knowledge of the most recent World Health Organization (WHO) classification systems of cancers to identify significant chromosomal and FISH anomalies
5. **ME 2.2** Demonstrate the ability to distinguish between constitutional and acquired chromosome abnormalities and recommend appropriate follow-up
6. **ME 2.2** Appropriately interpret data from chimerism studies in the context of hematopoietic stem cell transplant
7. **ME 3.1** Understand the benefits and limitations of chromosome techniques to identify and characterize cancer cells and compare and contrast to molecular techniques
8. **ME 3.1** Comprehend the design of the different FISH probe types and the criteria for probe selection
9. **ME 3.1** Understand the method, benefits and limitations of interphase FISH on formalin fixed paraffin embedded (FFPE) tissues and on isolated nuclei
10. **ME 3.4** Perform all laboratory and analytical steps of the procedure to obtain chromosomes from oncology specimens: culture, harvest, slide preparation, staining
11. **ME 3.4** Perform all laboratory and analytical steps of the procedure for chromosome analysis of oncology specimens: criteria for cell selection and clone establishment, chromosome identification, metaphase analysis, karyotyping, anomalies identification and characterization by additional tests
12. **ME 3.4** Perform all laboratory and analytical steps of the FISH procedure on interphase nuclei and FFPE tissue (if possible): set-up, probe application, washes, slide reading, nuclei selection, image capture
13. **ME 3.4** Understand the parameters that influence the quality of chromosome and FISH preparations and troubleshoot them
14. **ME 3.4** Recognize expected normal and abnormal as well as non-standard signal patterns of interphase FISH probes and report on their significance

15 **COM 2.3** Apply proper use of the most recent ISCN to describe a karyotype or FISH result, including clone definitions, modal number and relative position of FISH signals

16 **L 1.1** Review current standards and guidelines for clinical FISH probes

Genetic and Genomic Diagnosis Training Program: Core #7

Cancer Genetics – Part 2

Suggested Duration: 8 weeks

Key Features:

- This unit focuses on how inherited or acquired sequence alterations to the genome can be detected in the hereditary cancer or oncology setting, and used to inform diagnosis, prognosis, therapy or individual cancer risk.
- This unit includes an understanding of general tumour biology and development, particularly those factors that can influence molecular oncology testing including Knudson's two-hit hypothesis, tumour heterogeneity, tumour mutation burden and circulating tumour DNA.

Assessment Plan:

Assessment is performed through logbook entries:

- Technical cases Logbook
    - Nucleic acid extractions from FFPE tissue slides, curls or cell-free DNA: minimum 3 specimens
    - PCR-based methods for cancer prognosis and follow-up, such as Reverse Transcriptase PCR (RT-PCR) for fusion genes, Reverse Quantitative PCR for minimal residual disease, B- and T-cell clonality, targeted mutations assays: minimum 5 cases
    - Observation of library preparation and NGS panel set-up for somatic variant detection: minimum 2 library preps and sequencing runs

- Interpretative/Consultative cases logbook:
    - Data review and interpretation where testing occurred for one or more gene(s) in the context of a personal or family history of a suspected hereditary cancer: minimum 10 cases. At least one of these cases must be interpreted in the context of a reported microsatellite instability and/or immunohistochemistry.
    - Sequencing data review and interpretation where targeted analysis was undertaken to determine the hereditary cancer risk from a familial or founder population variant: minimum 20 cases.
    - Data review and interpretation of PCR-based tests for cancer prognosis and follow-up: 5 cases.

- NGS data review and interpretation where specific somatic variants were tested for prognosis or predictive/companion diagnostic testing from at least two different cancer types: minimum 20 cases.

Learning Objectives:

1 **ME 1.3** Apply knowledge of microsatellite instability and immunohistochemistry in Lynch syndrome testing algorithms and in the interpretation of identified germline and somatic variants
2 **ME 1.3** Apply knowledge of NGS characteristics of somatic variants versus germline variants and recommend appropriate clinical follow-up in the reporting of germline variants from somatic testing
3 **ME 1.3** Apply knowledge of basic tumour biology, analytical factors and tumour sampling, and their impact on somatic tumour variant detection in different tissues
4 **ME 1.3** Apply basic knowledge of the concepts of oncogenes, tumor suppressor genes, fusion genes to understand pathogenic variants associated with cancer
5 **ME 2.2** Select additional testing based on an appreciation of the diagnostic possibilities, clinical context, available specimens, and the relevance and capabilities of available technologies
6 **ME 2.2** Apply knowledge of clinical indications and criteria that warrant hereditary cancer testing, including the role of predictive testing in cancer predisposition and cancer risk assessment
7 **ME 3.1** Apply knowledge of minimal residual disease detection based on the variant type previously identified to select the most appropriate technology for testing
8 **ME 3.4** Apply knowledge to troubleshoot testing for recurrent somatic variants including SNV, amplification and fusion genes and correctly report the diagnostic and prognostic associations of these variants
9 **ME 4.1** Report appropriate recommendations for follow-up testing and/or family studies based on the specific variant identified
10 **COM 5.2** Recognize and appropriately report common molecular genetic variants for different cancer types that contribute prognostic, diagnostic, or therapeutic information
11 **S 3.3** Apply knowledge of existing databases and published interpretation criteria, including their inherent limitations, used to interpret germline versus somatic variants in the context of different cancers
12 **S 3.4** Understand the potential utility of circulating tumour DNA in the management of neoplasms

Genetic and Genomic Diagnosis Training Program: Transition to Practice #1
Assisted Laboratory Direction

Minimum Duration: 4 weeks

Key Features:

- This unit focuses on the role of a Laboratory Geneticist reviewing cases and providing oversight of quality laboratory services, including the review and sign-out of a full workload of cases.
- This unit includes considerations of laboratory utilization and resource stewardship as well as quality control and assurance, including process excellence (LEAN, six-sigma, etc.), external proficiency testing, and appropriate resource utilization and measurement.
- It also includes adherence to provincial, national, and international standards and guidelines as appropriate and applicable.

Assessment Plan:

Assessment is performed through logbook entries and feedback from/ discussion with training supervisor:

- Recording of cases reviewed in the Interpretative/Consultative logbook

Learning Objectives:

Part A: Managing the caseload

1. **ME 1.4** Perform timely, accurate diagnostic assessments
2. **ME 1.5** Set priorities, triage, and manage the workload within accepted turnaround times
3. **ME 1.5** Carry out professional duties in the face of multiple competing demands
4. **COM 4.1** Formulate comprehensive and clinically meaningful reports
5. **COL 1.2** Work effectively with other health professionals
6. **L 2.1** Allocate health care resources for optimal patient care
7. **L 3.1** Provide clinical direction of the laboratory including a primary role in troubleshooting
8. **L 4.2** Describe the principles of workload measurement within the laboratory
9. **S 3.1** Recognize uncertainty and knowledge gaps in clinical and other professional encounters relevant to Laboratory Genetics
10. **S 3.4** Integrate best evidence and clinical expertise into decision-making
11. **P 1.1** Exhibit appropriate professional behaviours

Part B: Supervising the laboratory

1. **ME 5.2** Adhere to quality management processes throughout the pre-analytic, analytic, and post-analytic phase
2. **COL 1.2** Discuss the role and responsibilities of a Laboratory Geneticist
3. **COL 1.2** Recognize and respect the scope of practice and expertise of other health professionals in the laboratory
4. **L 3.1** Provide guidance and support for questions arising in the laboratory