GECKO

• GECKO is:
  • A supporting infrastructure for genetics education that facilitates translation of research
  • Enabling the development, collection, dissemination and evaluation of genetics educational materials
  • A Research & Development Knowledge Translation Cycle

• Mission:
  • To increase genetics literacy in healthcare professionals

• Founded in 2011 with support from the Children’s Hospital of Eastern Ontario Department of Genetics
  • Additional support from Mount Sinai Hospital, Department of Family & Community Medicine, University of Toronto
• Canadian setting
  • Regional genetics centres provide genetic counselling and some education
  • A single comprehensive genetics institute or knowledge management centre does not exist in Canada
  • Genetic testing is covered by provincial insurance plans to variable degrees across the provinces if eligibility criteria are met
  • Health care providers can order some genetic tests if they feel competent to provide pre-test counselling and discussion of results
  • Direct to consumer genetic testing just beginning to reach Canadian consumers
The GEC-KO team

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Professor of Pediatrics at the University of Ottawa and retired Clinical Geneticist at Children’s Hospital of Eastern Ontario

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Manager of GEC-KO
Board certified genetic counsellor at the Children’s Hospital of Eastern Ontario (CHEO) in Ottawa

Advisory Board
Canadian Experts
Aim 1: Genetics Education for Primary Care Providers

• Program Development & Implementation
  – Informed by:
    • needs assessment
    • literature search
    • evidence
    • existing quality, evidenced based resources
  – Reflect Canadian guidelines where possible
  – Primary care relevant
Genomic medicine in primary care

• GenetiKit study
  – Responsive timely knowledge support service called Gene Messenger
  – Results:
    • Significant increase in appropriate genetics referral decisions and confidence in core primary care genetic medicine competencies
    • Wanted web site
      – Relevant
      – Evidence-based, reliable
      – Up to date

Carroll et al Family Practice 2011
Point of Care Tools

• Tools on a variety of genomic topics ready to use at the point of care

• Intended to:
  – Facilitate integration of genomic medicine into practice
  – Help identify and appropriately refer patients who may benefit from genetic services and reassure those at population risk
### Point of Care: Lynch syndrome

#### Red Flags

<table>
<thead>
<tr>
<th>Hereditary Cancers</th>
<th>Hemochromatosis</th>
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<tbody>
<tr>
<td>Hypertrophic Cardiomyopathy</td>
<td>Ethnicity-based screening in Canada</td>
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<tr>
<td>Factor V Leiden</td>
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</table>

#### Personal History LS Red Flags

- Colorectal cancer (CRC) diagnosis at an early age (<50 years). Higher suspicion of LS if diagnosed <35 years.
- Endometrial cancer diagnosis at an early age (<50 years)
- Multiple primary LS-related cancer diagnoses, regardless of age
- A CRC diagnosis and one or more 1st degree relatives with a LS-related cancer, with one of the cancers diagnosed <50 years
- A CRC diagnosis and two or more 1st or 2nd degree relatives with LS-related cancers regardless of age
- A CRC diagnosis <60 years and histological features suspicious for LS (excess infiltrating lymphocytes, mucinous/signet cell features, Crohn’s-like reaction), particularly when primary tumour is right sided

#### Family History LS Red Flags

- Consider referring your patient if he/she:
  - Has a known LS causing mutation in the family
  - Meets the revised Amsterdam criteria, meaning he/she has at least three relatives with a cancer associated with LS (Box 1).
  - The following criteria should also be present:
    - One must be a first degree relative of the other two;
    - At least two successive generations must be affected (autosomal dominant inheritance);
    - At least one relative with LS-related cancer should be diagnosed before age 50;
    - Tumour pathology should be verified when possible and other CRC syndromes should be ruled out

#### Box 1: Lynch Syndrome-related Cancers

- Colorectal
- Small bowel
- Endometrial
- Hepato-biliary
- Kidney
- Pancreatic
- Gastric
- Brain
- Ovarian
- Ureter
- Sebaceous (adenoma or carcinoma)

For more information on Lynch Syndrome such as screening recommendations see the complete [GEC-KO Messenger](www.geneticseducation.ca) at www.geneticseducation.ca

Updated Oct 2014
### Management recommendations for asymptomatic FVL carriers

<table>
<thead>
<tr>
<th>Education</th>
<th>Additional testing</th>
<th>During high risk situations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carriers should be educated about:</strong>&lt;br&gt; - Circumstances that might increase the likelihood of VTE (obesity, age, surgery, reduced mobility due to injury or travel, use of oral contraceptives, HRT, or SERMs, and pregnancy)&lt;br&gt; - The signs and symptoms of VTE that require immediate medical attention&lt;br&gt; - The potential need for prophylactic anticoagulation in high-risk circumstances (e.g. postpartum)⁴</td>
<td><strong>FVL is often seen with other inherited and/or acquired disorders.</strong>&lt;br&gt; An individual with FVL should be tested for other thrombophilia disorders to better assess the absolute risk of thrombosis¹,².&lt;br&gt; Consider:¹&lt;br&gt; - Genetic testing for prothrombin 20210G-&gt;A variant&lt;br&gt; - Serologic assays for anticardiolipin antibodies and antithrombin2glycoprotein 1 antibodies&lt;br&gt; - Multiple phospholipid-dependent coagulation assays for a lupus inhibitor</td>
<td><strong>During high-risk clinical situations (e.g. surgery, pregnancy) prophylactic anticoagulation may prevent some VTE episodes.</strong>&lt;br&gt; However, there is no evidence confirming the benefit of primary prophylaxis for asymptomatic FVL heterozygotes.&lt;br&gt; Decisions regarding prophylactic anticoagulation should be based on a risk/benefit assessment in each individual case.¹³&lt;br&gt; Consultation with a specialist may be considered.</td>
</tr>
</tbody>
</table>

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For more information on FVL see the GEC-KO *on the run* or the more comprehensive GEC-KO Messenger at [www.geneticseducation.ca](http://www.geneticseducation.ca) in Educational Resources.

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Educational Resources

• A library of resources to help integrate relevant genomic information into practice
  – GECKO on the run
  – GECKO Messengers
  – Fact Sheets
  – Basic Genetic Principles
  – Glossary
  – Additional Resources
Educational Resources: GECKO on the run

GEC-KO on the run

Each GEC-KO on the run is a concise summary for healthcare providers on a genetic disorder, technology or topic. For access to a more comprehensive summary, view or download a GEC-KO Messenger found in the left-hand menu. Use CTRL + F function to search key words on this page.

GEC-KO Messengers and GEC-KO on the run are written by a team that includes genetic counsellors, geneticists and genetic researchers. All are reviewed by a family physician. They are evidence-based and referenced, and feature a ‘bottom line’ with recommendations. They were developed as a ‘spin-off’ of the successful Gene Messengers which were part of the GenetKit project.

Findings from this study were published and can be found in Carroll JC, Wilson BJ, Alanson J, Grimshaw J, Blaire SM, Meschino WS, Permaul JA, Graham ID. GenetKit: a randomized controlled trial to enhance delivery of genetics services by family physicians. Fam Pract 2011; 28(6): 615-23.

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z 1,2,3...

A

Alzheimer disease |  PDF | AD | Dementia | apolipoprotein E | APOE | presenilin | PSEN | amyloid | APP | LOAD | EOAD | GEC-KO on the run (2014)

C

Chromosomal microarray |  PDF | CMA | Technology | Autism Spectrum Disorder | Developmental Delay | GEC-KO on the run (2013)

Codeine and Breastfeeding |  PDF | Pharmacogenomics | SNPs | Metabolism | cytochrome P450 | CYP 2D6 | GEC-KO on the run (2013)

Colorectal Cancer |  PDF | Lynch syndrome | Colorectal | Hereditary non-polyposis colorectal cancer (HNPCC) syndrome | GEC-KO on the run (2014)
Educational Resources: GECKO on the run

DIRECT TO CONSUMER GENETIC TESTING

Bottom line: Direct-to-consumer genetic testing (DTC-GT) is over-the-counter genetic testing available online to consumers through private companies. Generally, results report an individual’s risk to develop a medical condition as being below average/low, average/general population, and above average/high based on genome wide association studies (GWAS). Results may provide medically useful information for consumers and potentially provide support and motivation for lifestyle changes (e.g., weight loss, smoking cessation) or even more vigilant surveillance (e.g., breast cancer screening), reveal carrier status of single gene conditions (e.g., cystic fibrosis), effectiveness and side-effect risk of certain pharmaceuticals, in addition to medically irrelevant information (e.g., curly hair). Currently, DTC-GT is not regulated or accountable to an appropriate governing body. Numerous professional societies express concern about how DTC-GT is marketed to consumers, what and how information is provided and the lack of genetic counseling. Family health history-based risk assessment is still the gold standard in initial assessment for heritable conditions.

WHAT IS DIRECT-TO-CONSUMER GENETIC TESTING?

Direct-to-consumer genetic testing (DTC-GT), also referred to as personal genome testing, refers to genetic testing available for over-the-counter purchase without the requirement of health care provider involvement. Generally, DTC-GT is marketed with the promise of providing predictive genetic risk assessment for a variety of health conditions (e.g., diabetes, cancer, obesity) and information regarding response to and/or side-effect risk of certain pharmaceuticals (e.g., clopidogrel, statins). Increasingly personal genome testing companies are requiring provider involvement.

DTC-GT uses data generated from genome-wide association studies (GWAS). GWAS are case-control studies which examine many common variations in our genetic code (single nucleotide polymorphisms [SNPs]). They compare large groups of individuals (unaffected controls versus individuals with symptoms of a specific disease or those experiencing a particular medication response) in an attempt to distinguish between non-harmful changes in the DNA code and pathogenic, disease causing/predisposing changes. SNPs (pronounced ‘snips’) are the most common type of genetic variation. Each SNP represents a difference in a single DNA building block, a nucleotide. SNPs occur normally in an individual’s genome about once in every 300 nucleotides, thus there are about 10 million SNPs in the human genome.

DTC-GT uses odds ratios and relative risks to categorize an individual as at increased risk (higher than average), average (general population risk), or at decreased risk (lower than average).

DTC-GT can also screen for single gene disorders (e.g., cystic fibrosis, HFE-associated hemochromatosis). Additionally, DTC-GT is advertised to assist in diet and exercise planning and can uncover medically irrelevant information such as bitter taste perception or curly hair.

Generally, DTC-GT is available online to anyone for a cost. Genetic testing for DTC-GT is usually performed on a saliva sample.
Non-Invasive Prenatal Testing (NPT) is a screening test to prenatally detect Down syndrome and other aneuploidies. NPT assesses fragments of cell-free DNA (cfDNA) that are circulating in maternal blood to determine if there is an increased chance that the fetus has aneuploidy. NPT should be considered in pregnancies at increased risk of aneuploidy. NPT has higher sensitivity and specificity for Down syndrome (trisomy 21) and trisomy 18 than current screening tests – First Trimester Screening (FTS)/Integrated Prenatal Screening (IPS)/ Maternal Serum Screening (MSS) - however it is not considered to be diagnostic. Positive results should be confirmed by diagnostic testing (amniocentesis or chorionic villus sampling) prior to any irrevocable action. Negative results may indicate additional follow-up testing and consultation. Women who do not meet criteria can pay for NIFT themselves. Price varies by company (795$-1,205$).

What is Non-Invasive Prenatal Testing?

Non-invasive prenatal testing (NPT) is a highly sensitive and specific way to screen for particular chromosome aneuploidies (an abnormal chromosome number (extra or missing)), in particular trisomies 13, 18 and 21/Down syndrome. NPT can also be used for sex chromosome identification for the purpose of fetal sex determination where there is increased risk for an X-linked disorder or a sex chromosome abnormality.

NPT assesses fragments of cell-free DNA (cfDNA) derived from the placenta that are circulating in maternal blood and represent the fetal genetic profile. CFDNA from the pregnancy comprises approximately 10% of DNA in maternal blood and the amount increases with gestational age. Companies offering NPT use various technologies to analyze cfDNA. Some detect higher relative amounts of DNA from an aneuploid fetus by comparing quantity to a reference chromosome, whereas if there is a normal, higher or lower than expected quantity of particular DNA sequences found on select chromosomes (13, 18, 21, X, Y). Others sequence and analyse single-nucleotide polymorphisms (SNPs) to differentiate between maternal and fetal genotypes. **NPT is a non-invasive test performed on a maternal blood sample that poses no risk to pregnancy.** Testing can be carried out as early as 9 weeks gestation. A dating ultrasound is recommended prior to drawing the blood sample to ensure viability, obtain an accurate gestational age, and to exclude multiple pregnancies.

NPT validation studies in high risk populations have demonstrated high pick-up rates/sensitivity for the detection of Down syndrome (sensitivity 99-100%), trisomy 18 (sensitivity 97-100%), trisomy 13 (sensitivity 79-92%) and sex chromosome differences. False-positive rates are reported to be less than 2% overall. Early studies suggest that the positive predictive value (PPV) of NPT in an unselected, general obstetrical population (low risk) is about 45% for Down syndrome (versus about 4% for standard screening) and about 40% for trisomy 18 (versus about 8% for standard screening). The PPV appears to be significantly higher in high risk populations. A number of women (<6%) have required a repeat blood draw due to initial test failure. Most studies have commercial affiliations.

At the present time, it is recommended that all women under age 40 at estimated date of birth (EDB) be offered prenatal screening, using FTS, IPS or MSS. If a woman is screen positive, NPT may be considered as a secondary screen of higher sensitivity. Women 40 years or older at EDB can be offered NPT as a first screen for aneuploidy. NPT is not a replacement for diagnostic prenatal testing. A positive NPT result should be confirmed by diagnostic testing (amniocentesis or chorionic villus sampling) prior to any irrevocable action. The expected benefit of NPT will be fewer women undergoing secondary invasive diagnostic tests associated with a risk of
Lynch Syndrome

Lynch Syndrome: Hereditary Non-Polyposis Colorectal Cancer Predisposition Syndrome

Bottom line:

Lynch syndrome (LS), also known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC), is the most common hereditary colorectal cancer predisposition syndrome. It is an autosomal dominant condition that results in an increased lifetime risk of colorectal cancer (CRC) in addition to other cancers. Individuals at high or intermediate risk of LS should be referred for a genetic consultation for consideration of genetic testing. Surveillance and management of CRC and other cancers should be guided by genetic test results and/or family/personal history. Studies show that conversations between patients and their healthcare providers are the strongest driver of screening participation.

- WHAT IS LYNCH SYNDROME?
- WHO SHOULD BE OFFERED GENETIC TESTING?
- WHAT DO THE GENETIC TEST RESULTS MEAN?

If your patient has been found to carry a mutation in a Lynch syndrome gene, he/she has an increased lifetime risk to develop certain cancers (Table 1). This also means that family members are at risk of carrying the same mutation and of having similar cancer risks. Evidence is emerging from population-based studies that these cancer risks are gene specific.

Table 1. Lifetime cancer risks for individuals who have inherited a mutation in a Lynch syndrome gene as compared to the general population.

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Lynch syndrome lifetime cancer risk (carrier of a MLH1 or MSH2 gene mutation)</th>
<th>General Population Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>52-62%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Endometrial</td>
<td>25-60%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Stomach</td>
<td>6-13%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Ovarian</td>
<td>4-12%</td>
<td>1%</td>
</tr>
<tr>
<td>Hepatobiliary tract</td>
<td>1-4%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Urinary tract (uterus and renal pelvis)</td>
<td>1-4%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Small bowel</td>
<td>3-6%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Brain/central nervous system</td>
<td>1-3%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Sebaceous neoplasm</td>
<td>1-9%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
Genetics Centres

Point of Care Tools Educational Resources Education Modules Genetics Centres Public Resources News & Events

You are here: GEC > Genetics Centres > Canada > Clinic

Alberta

Calgary

Dr. R. Brian Lowry Clinical Genetics Unit
Alberta Children’s Hospital
2205 Shaganappi Trail NW
Calgary, AB T3B 5A2
Phone: 403-266-2113
Fax: 403-266-2217
Services: Adult, Cancer, Pediatric and General Genetics: outreach clinics (over 30 years) in Lethbridge, Red Deer, and Medicine Hat; telephone consultation

Cancer Genetics Research Clinic
Tom Baker Cancer Centre room 2C1107
1331-22nd Street NW
Calgary, AB T2N 4Z9
Phone: 403-264-5419
Fax: 403-264-5423

Early Prenatal Risk Assessment Program
Prenatal Genetics Clinic
Suite 701, St. Joseph’s Hospital NW
Calgary, AB T2N 4Z5
Phone: 403-264-5419
Fax: 403-264-5423

Edmonton

Medical Genetics Clinic (Formerly Genetic Metabolic Clinic, Medical Genetic Services, Lions公积金 Medical Genetics Clinic)
Shawnessy Children’s Hospital
2-50 Medical Sciences Building
University of Alberta Hospital
Edmonton, AB T6G 2H7
Phone: 780-407-7200
Fax: 780-407-6990
Services: Adult, Cancer, Pediatric, Biochemical, Cardiac, Neuropediatrics, Genetic and Prenatal Genetics

Referral information here
Hereditary cancer referral information here
Referral form here

Northern and Central Alberta Maternal – Fetal Medicine Centre
Lake Louise Hospital for Women, Ground level
10240 87 Avenue
Edmonton, AB T6H 3V5
Phone: 780-412-4613
Fax: 780-412-4616
Services: Prenatal
Additional Resources

Genetics Education

Sites with resources for both educators and learners.

The Genetics Education Program
This website gives primary healthcare providers practical, current information regarding screening and prevention of hereditary disorders. It contains information about specific genetic disorders as well as links to other sites where you can find more information.

http://www.mountsinai.on.ca/care/family-medicine-genetics-program

Genetics/Genomics Competency Centre for Education (G2C2)
A referatory funded by the NIH whose mission is to provide high-quality educational resources for group instruction or self-directed learning in genetics/genomics by healthcare educators and practitioners. The G2C2 solicits, reviews and organizes resources through an interdisciplinary collaborative exchange.

http://www.g-2-c-2.org/index.php

The NHS National Genetics and Genomics Education Centre
The NHS National Genetics and Genomics Education Centre was established in 2005 and funded by the Department of Health as one of the major initiatives of the 2003 Genetics White Paper ‘Our Inheritance, Our Future – Realising the potential of genetics in the NHS’. One of the main aims of the Centre was to improve the understanding of genetics among healthcare professionals and its role in modern healthcare.

Supporting the ongoing education of health professionals in genetics and, more recently, genomics has been a
General Resources

Family History
Disease-Specific Resources
Genetics Education
Professional Societies
Patient Support

Family History

| Family Medical History and Tools Resources Online | www.genome.gov/11510372 |
| American Medical Association (AMA) | www.ama-assn.org/ama/pub/physician-resources/medical-science/genetics-molecular-medicine/family-history.page |

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http://www.g-2-c-2.org/index.php
GECKO

• Next steps:
  – Evaluation
    • Usability of website
    • Effectiveness of tools
  – Dissemination
  – More topics
Questions?

www.geneticseducation.ca