Genetics Education Canada

Knowledge Organization

GEC KO

www.geneticseducation.ca

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ISCC
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GEC KO
Genetics Education Canada - Knowledge Organization
Centre d'éducation en génétique canadien - Connaissances organisées

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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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

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www.geneticseducation.ca

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

Hereditary Cancers

Hereditary Hemochromatosis

Hypertrophic Cardiomyopathy

Ethnicity-based screening in Canada

Factor V Leiden

GEC•KO Point of Care

Part II: Red Flags to identify patients **at high risk** of **Lynch Syndrome** most likely to benefit from referral to genetics

Personal History LS Red Flags	Family History LS Red Flags

Consider referring your patient if he/she has:
• Colorectal cancer (CRC) diagnosis at an early age (<50 years). Higher suspicion of LS if diagnosed <35years.
• 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
	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

LS is the abbreviation for Lynch syndrome

Box 1: Lynch Syndrome-related cancers

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

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

CHEO | Mount Sinai Hospital, Joseph and Wolf Lebovic Health Complex | Family & Community Medicine, University of Toronto | uOttawa

Updated Oct 2014

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Point of Care: Factor V Leiden

Point of Care Tools Educatio

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- Family History
  - General family history tool
  - Red Flags
- Hereditary Cancers
- Hereditary Hemochromatosis
- Hypertrophic Cardiomyopathy
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- Factor V Leiden

GEC-KO Point of Care

Management recommendations for asymptomatic FVL carriers

Education	Additional testing	During high risk situations
Carriers should be educated about: ✓ 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) ✓ The signs and symptoms of VTE that require immediate medical attention ✓ The potential need for prophylactic anticoagulation in high-risk circumstances (e.g. postpartum)[4]	FVL is often seen with other inherited and/or acquired disorders. An individual with FVL should be tested for other thrombophilia disorders to better assess the absolute risk of thrombosis[1,2]. Consider:[1] ✓ Genetic testing for prothrombin 20210G>A variant ✓ Serologic assays for anticardiolipin antibodies and antibeta2glycoprotein 1 antibodies ✓ Multiple phospholipid-dependent coagulation assays for a lupus inhibitor	During high-risk clinical situations (e.g. surgery, pregnancy) prophylactic anticoagulation may prevent some VTE episodes. However, there is no evidence confirming the benefit of primary prophylaxis for asymptomatic FVL heterozygotes. Decisions regarding prophylactic anticoagulation should be based on a risk/benefit assessment in each individual case. [1,3] Consultation with a specialist may be considered.

For more information on FVL see the GEC-KO *on the run* or the more comprehensive GEC-KO Messenger at www.geneticseducation.ca in Educational Resources.

[1] Kujovich JL. Factor V Leiden thrombophilia. *Genet Med* 2011; 13(1): 1-13

[2] Grody WW, Griffin JH, Taylor AK, Korf BR, Heit JA, ACMG Factor V. Leiden Working Group. American College of Medical Genetics consensus statement on factor V Leiden mutation testing. *Genet Med* 2001; 3(2):139-48

[3] Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, Colwell CW; American College of Chest Physicians. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest* 2008; 133(6 Suppl):381S-453S.

CHEO · Mount Sinai Hospital, Joseph and Wolf Lebovic Health Complex, Bright Minds. Big Hearts. The Best Medicine. · Family & Community Medicine, University of Toronto · uOttawa

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 GenetiKit project. Findings from this study were published and can be found in Carroll JC, Wilson BJ, Allanson J, Grimshaw J, Blaine SM, Meschino WS, Permaul JA, Graham ID. GenetiKit: 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)

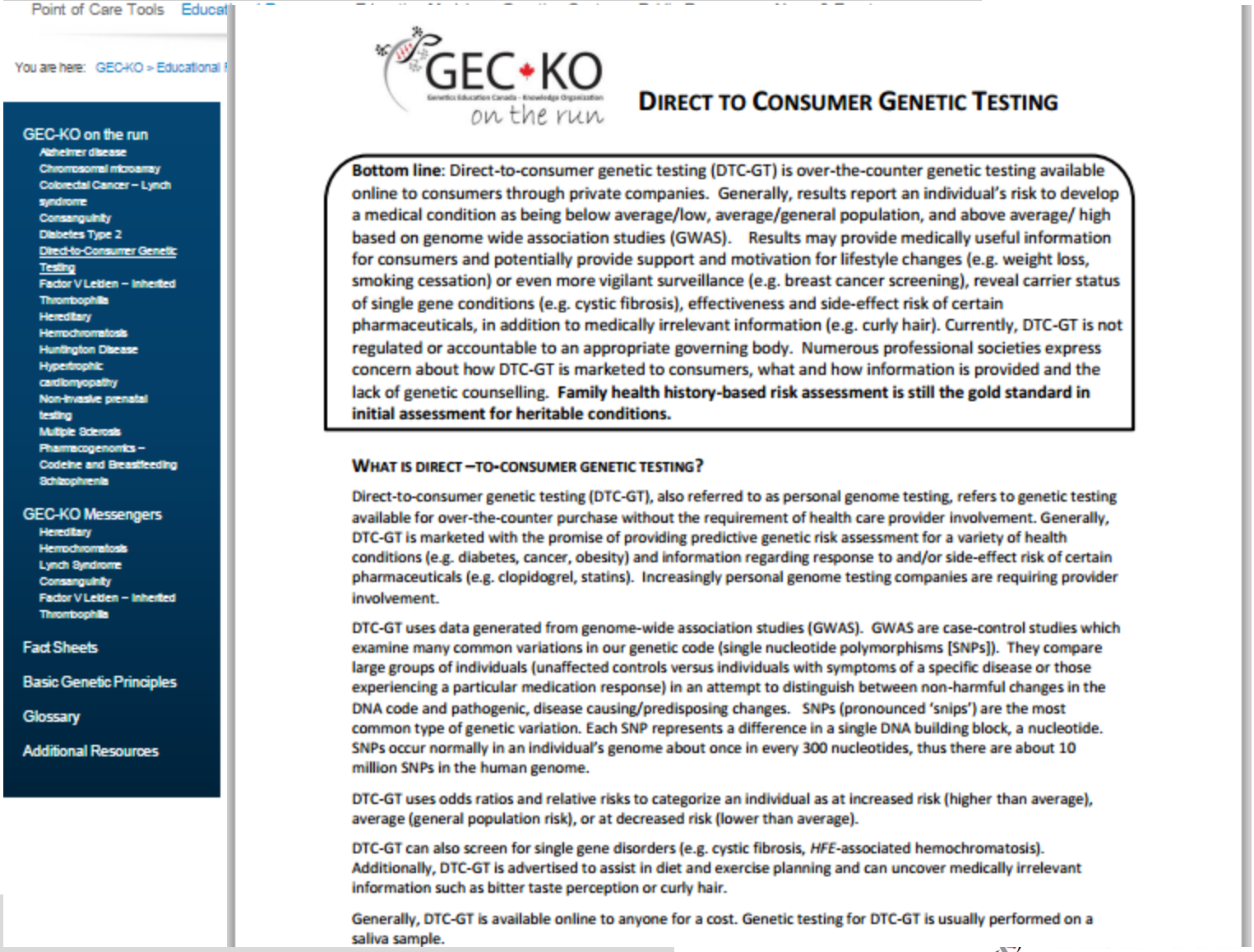
C

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 rur* (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*



Point of Care Tools Educat

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GEC-KO on the run
- Alzheimer disease
- Chromosomal microarray
- Colorectal Cancer – Lynch syndrome
- Consanguinity
- Diabetes Type 2
- Direct-to-Consumer Genetic Testing
- Factor V Leiden – Inherited Thrombophilia
- Hereditary Hemochromatosis
- Huntington Disease
- Hypertrophic cardiomyopathy
- Non-invasive prenatal testing
- Multiple Sclerosis
- Pharmacogenomics – Codeine and Breastfeeding
- Schizophrenia

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Basic Genetic Principles

Glossary

Additional Resources

GEC•KO Genetics Education Canada - Knowledge Organization 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 counselling. **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.

Educational Resources: GECKO *on the run*

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

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NON-INVASIVE PRENATAL TESTING

Non-Invasive Prenatal Testing (NIPT) is a screening test to prenatally detect Down syndrome and other aneuploidies. NIPT 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. NIPT should be considered in pregnancies at increased risk of aneuploidy. NIPT 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 NIPT themselves. Price varies by company (795$-1,200$).

WHAT IS NON-INVASIVE PRENATAL TESTING?

Non-invasive prenatal testing (NIPT) 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. NIPT 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.

NIPT 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 NIPT use various technologies to analyze cfDNA. Some detect higher relative amounts of DNA from an aneuploid fetus by comparing quantity to a reference chromosome, determining 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. **NIPT 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.

NIPT 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 NIPT 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, NIPT may be considered as a secondary screen of higher sensitivity. Women 40 years or older at EDB can be offered NIPT as a first screen for aneuploidy. **NIPT is not a replacement for diagnostic prenatal testing.** A positive NIPT result should be confirmed by diagnostic testing (amniocentesis or chorionic villus sampling [CVS]) prior to any irrevocable action. The expected benefit of NIPT will be fewer women undergoing secondary invasive diagnostic tests associated with a risk of

Educational Resources: GECKO Messenger

Lynch Syndrome

Last updated April 2014

Lynch Syndrome: Hereditary Non-Polyposis Colorectal Cancer Predisposition Syndrome

Download the comprehensive GEC-KO Messenger, the quick reference GEC-KO *on the run*, and/or the point of care triage tool.

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?

v 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)[3]. 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[8,9].

Table 1. Lifetime cancer risks for individuals who have inherited a mutation in a Lynch syndrome gene as compared to the general population.[3]

Cancer type	Lynch syndrome lifetime cancer risk (carrier of a *MLH1* or *MSH2* gene mutation)		General Pop old
	Risk	Mean age of diagnosis	Risk
Colon	52-82%	44-61 years	5.5%
Endometrial	25-60%	48-62 years	2.7%
Stomach	6-13%	56 years	<1%
Ovarian	4-12%	42.5 years	1%
Hepatobiliary tract	1-4%	Not yet reported	<1%
Urinary tract (ureter and renal pelvis)	1-4%	55 years	<1%
Small bowel	3-6%	49 years	<1%
Brain/ central nervous system	1-3%	50 years	<1%
Sebaceous neoplasm	1-9%	Not yet reported	<1%

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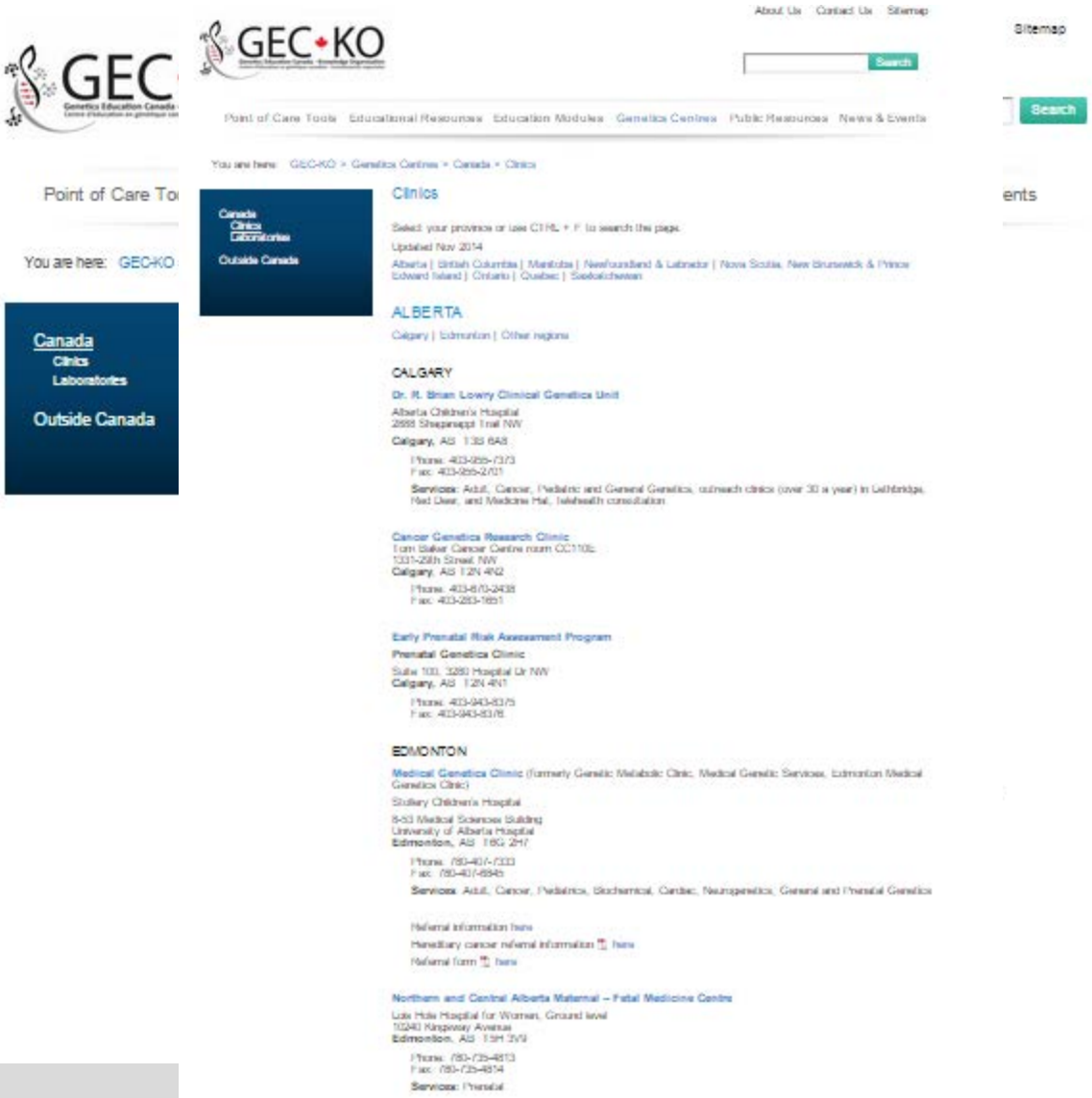
Genetics Centres



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GEC-KO Messengers
- Hereditary Hemochromatosis
- Lynch Syndrome

Additional Resources

Genetics Education

Sites with resources for both educators and learners.

The Genetics Education Program

This website gives primary health care 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 health care 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

Prenatal and Preconception Genetics

Newborn Genetics

Adult Genetics

General Resources

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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GECKO

- Next steps:
  - Evaluation
    - Usability of website
    - Effectiveness of tools
  - Dissemination
  - More topics

Questions?

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Genetics Education Canada - Knowledge Organization
Centre d'éducation en génétique canadien - Connaissances organisées