THE LANDSCAPE OF PERSONALIZED MEDICINE IN CANADA

Best Practices in Personalized Medicine – B2PM
Vancouver, March 8, 2011

Katherine Bonter
Director of Advocacy & Promotion
Centre of Excellence in Personalized Medicine
OVERVIEW

Cepmed and its Initiatives

Canadian Landscape of Personalized Medicine (PM)

• Investment in ‘omics infrastructure
• Regulation and oversight of medical testing
• Commercialization of and access to testing
• Genetic non-discrimination
ABOUT CEPMED

A federally funded Centre of Excellence in Research & Commercialization (CECR)

Founded in 2008 by the Montreal Heart Institute (MHI) & Genome Quebec with industry support

Promoting the science & practice of personalized medicine in Canada through

- **Public - Private Partnerships**
  - generate revenues & commercial rights

- **Commercializing Technologies**
  - leverage affiliated platforms

- **Knowledge Translation**
  - collaborate with & support stakeholders

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[Logos and affiliations]

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5/4/2011
ID biomarkers for personalizing treatment of CVD, a study carried-out in parallel with a Phase III clinical trial of Dalcetrapib.

ID biomarkers for predicting the efficacy and safety of Ivabradine, as part of large-scale phase III SIGNIFY clinical trial.

ID biomarkers with potential as a companion diagnostic Torceptrapib – as part of a Phase III Torceptrapib trial (currently halted).

ID genomic biomarkers of statin toxicity, ID patients at risk of side-effects.

Monitoring PTT variation and optimizing dose in warfarin therapy.
Commercialization of Technology Platforms

Montreal Health Innovations Coordinating Center (MHICC)
- Non-profit CRO (Phase II - IV trials)
- 130 employees (US and Canada)
- Gateway to pharmaceutical companies

Montreal Heart Institute Biobank
- one of the largest CVD biobanks in the world
- 11,000 high-quality samples with extensive phenotype info and consent

Pharmacogenomics Centre
- Expertise in custom SNP panel development, GWAS, deep sequencing

Impact of Cepmed initiatives
- Leveraged 3 platforms in public-private partnerships
- Added 5,000 samples to the MHI biobank
- Positioned MHICC as leader in clinical trials coupled with PGx studies
- Negotiated 5 licenses, supported filing and prosecution 15+ patent applications
- Jobs created/maintained: 15/180+
Canadian Physician Survey in Personalized Medicine

Design and objectives
Access physicians’ perceptions and experiences in genetic testing and PM
Openness to adoption, state of practice, benefits/impacts and barriers to adoption
Compare across specialties and provinces

Some of the findings....

Majority of respondents:

- Have positive perception of PM and report positive impact in practice
- Do not feel sufficiently informed or confident practicing in this area
- Cite a lack of guidelines and clinical evidence and limited provider knowledge as key barriers
- Report that genetic tests useful in their practice are not readily available
Objectives

– Describe optimal use and adoption of PM based on best available evidence
– Provide strategy for continuing medical education
– Promote efficient use of resources

Status

– Terms of reference & 2-yr contracts signed by 22 members
– Two meetings held for each panel
– Scope of mandate established
– Outreach to enabling stakeholders in progress

CARDIOLOGY PANEL
Chair: Dr. Jean-Claude Tardif
Members:
Dr. Andrew Krahn, Dr. Bob Roberts, Dr. Paul Khairy, Dr. Candace Lee, Dr. Gregor Andelfinger, Dr. Milan Gupta

ONCOLOGY PANEL
Chair: Dr. Charles Butts
Members:
Dr. Gerry Batist, Dr. Malcolm Moore, Dr. Charles Blanke, Dr. Suzanne Kamel-Reid, Dr. Michael Sawyer

STRATEGIC PANEL
Chair: Dr. Simon Sutcliffe
Members:
Dr. Sean Blaine, Dr. David Keast, Dr. Mark Elwood, Dr. Jeffery Hoch, Ms. Jill Davies, Dr. Serge Dulude
Canadian Personalized Medicine Landscape

Recognize Value

Build Infrastructure for Adoption

Translate into Practice

Implement Standardize

LEGAL PROTECTIONS, NON-DISCRIMINATION

TECHNOLOGY, TOOLS EXPERTISE

REGULATION, OVERSIGHT

LABORATORY INFRASTRUCTURE

Adapted from Case for Personalized Medicine, 2009, “Convergence of Forces”, Personalized Medicine Coalition
Canadian Investment in ‘Omics

Genome Canada Investments (2001-10)

$277 M build, operate provincial genome centres
$63 M develop new technologies and applications
$33 M legal, ethical & socio-economic research (GE³LS)

Health Research Funded

$700 M fundamental research
$24 M target ID and drug discovery
$210 M biomarker ID
$46 M biomarker validation, diagnostic development
$30 M clinical stage pharmacogenomics

An enabling infrastructure is in place

- DNA sequencing
- Microarray and gene-chip expression analysis
- Proteomics
- Bioinformatics
Laboratory developed tests (LDT) are most often used for PM

- Subject only to provincial regulation and oversight (no national standard)
- Regulation is variable across provinces - even lacking in some or differentially enforced
- Absence of regulation to ensure clinical validity
- Funding decisions are not coordinated nationally or often even provincially

As a result, delivery, access, QC vary across the provinces and even within provinces
### Regulated Practices by Province

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Source: Quality Issues in Clinical Genetic Services, Kristoffersson et al, 2010
Standardization of genetic tests needed

Published at www.cmaj.ca on Sept. 14

Evolving knowledge of the genetic indicators of disease is rapidly changing medical care, and overwhelming the ability of regulatory agencies to ensure the quality and accuracy of such tests.

“We’re doing [genetic testing] for lung cancer, for colon cancer, for breast cancer, for melanoma, myeloma,” says Dr. Suzanne Kamel-Reid, head of laboratory genetics and director of molecular diagnostics at the University Health Network in Toronto, Ontario, and head of the Molecular Oncology Task Force which is sponsored by Cancer Care Ontario. “It’s used much, much more frequently than it used to be.” According to the task force, referrals for cancer-related genetic testing rose 61% in 22 clinics surveyed between 2002 and 2008.

The increased use is also evident in the United States, so much so that the US Food and Drug Administration (FDA) says about 10% of pharmaceuticals are now labelled as being especially useful — or not so useful — for patients with specific genetic conditions.

But a lack of standardization in the field is leading to a patchwork of practices that can ultimately cost patients more, according to Dr. Kamel-Reid.

A decade ago, she said, it was possible to generate a genetic test for many diseases, but there were not enough clients to make it worthwhile for the lab.

“I would test maybe a couple of patients a month, and my lab would do a test I hadn’t done before,” she said. “So I would have to go through the whole process of designing that test.”

In recent years, however, the number of patients for whom genetic tests are performed in Ontario and across Canada has grown exponentially, with more genetic testing being performed on a day-to-day basis.

“We’re starting to see labs, and even the drug companies, totally immerse themselves in genetic testing as opposed to testing an occasional patient,” said Dr. Kamel-Reid.

Standardization is critical in the field, she said, not only so that the results of the test can be compared across patients and laboratories, but also to provide the information that is needed.

“We need to have a national system to ensure our results are comparable across the country,” she said. “If we have a system that provides basic, foundational information, that’s going to be much more useful to patients.”

But the current system doesn’t offer that level of detail, she said, and that could be devastating for patients.

“Imagine you have a cancer genetic test, and you have a specific gene mutation,” she said. “But you don’t get back the information that says you have this mutation. And you say, ‘What do I do with this?’ That’s the kind of issue that needs to be solved.”

The task force is dedicated to solving that problem, she said, and has already created a comprehensive database of genetic tests for cancer.

It has also made a number of recommendations to improve the field, including standardizing the language used to describe genetic tests, improving the accuracy of the tests, and making sure that the results are communicated clearly to patients.

“Genetics is a very rapidly changing field, and we’re trying to keep up with that change,” she said. “But we need to do it in a way that’s meaningful for patients.”
### Commercialization in Oncology: CA vs. US

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**M**-testing mandatory; **R**-testing recommended; **C**-testing mentioned

LDT-laboratory developed test; D-diagnostic device
Pharmacogenomic info. on drug labeling is similar (US v. CA)
– Consideration, incorporation of pharmacogenomics by regulatory agencies is similar in Oncology

More commercialization approved devices in the US (9 US, 5 CA)
– Standardized tests available as companions to approved drugs - commercialization of clinical validated tests
– Facilitates development of standardized practices
– Support commercial activity - recognizes value of ‘diagnostic’ technologies
– Foster competition between companies selling similar products – expertise, innovation

Tests are increasingly available only through exclusive foreign providers (i.e. Oncotype DX, Amplichip®, BRACAnalysis®)
– Exclusive provider strategy maybe necessary for ROI
– Difficulties in enforcing IP impact commercialization strategies
– Test interpretation requires proprietary database, proprietary algorithms
– Potential negative impact on Canadian HC system, expertise, commercial activity....
Access to PM through Private Companies in Canada

Routes of Access

- Testing & PM services via physicians, geneticists and genetic counselors at private clinics
- Tests carried out by licensed private CA labs (not publically funded) with physician req.
- Foreign testing services via private lab or clinic
- Direct-to-consumer genetic testing companies (usually foreign testing services)

Related Developments

- Private CA clinics and labs are expanding genetic testing-PM services
- CA insurance companies are being lobbied to increase coverage of diagnostic testing
- Private CA health care payors are aware and interested (CHLIA statement on genetic testing)
THIS IS ONLY THE BEGINNING

25% of FDA approved drugs have PGx information on the label*
• 10%+ specify genetic based sub-populations

26+ drugs in development have an associated companion diagnostic

Many widely prescribed drugs are efficacious only in 40-60% of patients

*Frueh F. et al., Pharmacotherapy 28(8) 2008
Genetic Non-Discrimination – Canadian Landscape

Current Protections
Canadian Human Rights Act (Art. 3) prohibits discrimination based on disability (including real or perceived ailment)

Personal Information Protection and Electronic Documents Act (PIPEDA 2000) has provisions relating to consent, privacy, limited use, reasonable use

Public Awareness
90% of Canadians feel that insurance companies and employers should not have access to their genetic information

40% of physicians surveyed report that their patients are concerned about genetic discrimination

Many not aware of the potential implications of consent given to employers as part of benefits/employment agreements

2. Cepmed Data
Recent Developments - Genetic Non-Discrimination

**Canadian Developments**
Private members bill C-508, introduced Apr. 2010, proposes to amend the Human Rights Act to specify genetic characteristics as a prohibited ground of discrimination.

Little pressure otherwise to adopt legislation in Canada for this purpose.

**Foreign Developments**
US Genetic Non-Discrimination Act (GINA) enacted in 2008 prohibits genetic discrimination by healthcare insurance providers (Title I) and employers (Title II).

In addition, 45 states have genetic non-discrimination statutes.

Massachusetts Genetic Bill of Rights, introduced in Jan. 2011, aims to address gaps in GINA with respect to property rights, sale, transfer or use of personal genetic information.


THANK YOU

Katherine Bonter
KBONTER@CEPMED.COM
CANADIAN LANDSCAPE OF PM

Recognize Value
Infrastructure for Adoption
Translate into practice
Implement & standardize

GENETIC PRIVACY AND LEGAL PROTECTIONS
INSURANCE COVERAGE AND REIMBURSEMENT
TECHNOLOGY AND TOOLS
LABORATORY INFRASTRUCTURE
REGULATION
HEALTHCARE INFORMATION TECHNOLOGY
MEDICAL EDUCATION
“PERSONALIZED MEDICINE IS A TECHNOLOGY ENABLER WHICH IS TRANSFORMING MEDICINE FROM INTUITIVE, TO EMPIRICAL, TO PRECISION MEDICINE”*

- Healthcare costs represent almost 50% of many provincial budgets and rising
- This is an issue being faced by all industrialized countries
- Demographic changes and technological advances are inevitable
- Trend to control cost has often been to ration care rather than rationalizing treatment based on evidence
- Medical advances and new technologies can be adopted to improve healthcare; increase efficacy and safety (reducing cost), enable prevention (reducing cost)

*Christenden Clayton M, The Innovator’s Prescription (2009)
Examples of high impact health research funded

A Haplotype Map of the Human Genome
- International research network (CA CN JP NG UK US)
- massive data set generated had major commercial impact
- successful use of open innovation
- Canadian efforts led by Dr. Thomas Hudson (McGill)

Genotype-Specific Approaches to Therapy in Childhood
- large cohort multi-site study in translational medicine
- network of 2,300 pediatricians and 10 Canadian hospitals
PI: Dr. Bruce Carlton (UBC)

Public Population Project in Genomics - P3G Observatory
- International harmonization of project designs, biobanks to enable large cohorts for population genomics studies
PI: Dr. Bartha Maria Knoppers (McGill)
ONE SIZE DOES NOT FIT ALL

Figure 1 shows the % of the patient population for which the drug class indicated is ineffective.

Genetic differences are a key element to understanding and identifying an individual’s response to a drug.

A COMMERCIALIZATION STORY

Macula-Risk®, developed by ArticDX (Toronto): a genetic prognostic test for Age-related Macular Degeneration (ADM)

- 1 of 5 patients with AMD will progress to severe vision loss (affects 1/10 over age 60 and 1/4 over 75)
- Patients with AMD or with a high risk of vision loss can be ID using Macula Risk®
- Treatment with Lucentis® (anti-VEGF antibody) which prevents or arrests the development in 95% of patients (early stage, vision mostly intact)
- Preventative vitamin therapy and other interventions (ie. smoking cessation, blood pressure control) can delay vision loss
- Macula-Risk® is currently reimbursed in the US at $450 but not commercialized in Canada
MULTI-DISCIPLINARY STAKEHOLDER GROUPS

Health Canada established PM working group in 2010
- includes representatives from: Health Canada, Public Health Agency of Canada, CIHR, Patented Medicines Prices Review Board
- Mandate: to develop a harmonised ‘Health Portfolio’ response to personalised medicine
  - facilitate collaborative interactions amongst Portfolio members on initiatives related to personalised medicine

Centre for Advancement of Health Innovation
- coalition of public and private Stakeholders
- Mandate: to publish in-depth analysis innovation and commercialization in Canada’s health-care system
  - engage stakeholders and leaders in policy discussions
  - identify best practices in health