GENOMIC MEDICINE:
PHYSICIAN LITERACY IN CARDIOLOGY

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and
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President and CEO, University of Ottawa Heart Institute
Overview: Four Important Areas

• Diseases of Particular Interest to CV Medicine
• ACC – Personalized Medicine Survey
• ACC CME and MoC Offerings
• Future ACC Directions
Diseases & Conditions of Particular Genetic/Genomic Interest in CV Medicine

• Mendelian CV Diseases
  – Hypertrophic Cardiomyopathy
  – Long QT Syndromes
  – Marfan Syndrome
  – Familial Dilated Cardiomyopathy
  – Factor V Leiden

• Complex Genetic Diseases
  – CAD, HTN
  – Atrial fibrillation

• Pharmacogenetics
  – Warfarin metabolism
  – Clopidogrel activation
The Current Landscape of Personalized Medicine in Cardiology: 
Providers and Patients

Source: ACC’s CardioSurve panel
(Oct. 2010 survey of more than 150 cardiovascular professionals)
What is Personalized Medicine?

- Genetic Testing: 72%
- Age: 56%
- Gender: 56%
- Molecular Diagnostics: 53%
- Race: 52%
- Co-Morbidity: 49%
- Socio-Economics: 45%
- Other: 10%
### Percent of Patients Asking Cardiologists about Personalized Medicine

(n=144)

<table>
<thead>
<tr>
<th>Percent of Patients</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>0% of patients</td>
<td>33%</td>
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<tr>
<td>1% - 5% of patients</td>
<td>37%</td>
</tr>
<tr>
<td>6% - 10% of patients</td>
<td>17%</td>
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<tr>
<td>11% - 20% of patients</td>
<td>8%</td>
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<tr>
<td>More than 20% of patients</td>
<td>5%</td>
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<tr>
<td>Mean % of patients</td>
<td>6%</td>
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## Percent of Patients that Cardiologists are Using Personalized Medicine

(n=154)

<table>
<thead>
<tr>
<th>Percentage of Patients</th>
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<tbody>
<tr>
<td>0% of patients</td>
<td>29%</td>
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<tr>
<td>1% - 5% of patients</td>
<td>41%</td>
</tr>
<tr>
<td>6% - 10% of patients</td>
<td>14%</td>
</tr>
<tr>
<td>11% - 20% of patients</td>
<td>9%</td>
</tr>
<tr>
<td>More than 20% of patients</td>
<td>7%</td>
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<tr>
<td>Mean % of patients</td>
<td>7%</td>
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Future Use of Personalized Medicine

66% Not Sure
27% Yes
7% No
2 Future Role of Personalized Medicine

- Much Smaller: 0%
- Somewhat Smaller: 1%
- Same as Today: 5%
- Somewhat Larger: 54%
- Much Larger: 40%
Challenges to Clinical Implementation of Personalized Medicine

- Patient Outcome Data
- Payment Reform
- CME
- Guidance from Professional Societies
- Patient Education
- Guidance from Regulatory Bodies
- Updates to Medical School Curriculum
- Other
- None

Bar chart showing the percentage of challenges across various categories.
Importance of Genetics in Cardiovascular Medicine: New Discoveries & Realities

January 28 2013

Presented by:

Robert Roberts, MD, FRCPC, MACC, FRSM, Professor of Medicine
President and CEO, University of Ottawa Heart Institute
Director, Ruddy Canadian Cardiovascular Genetics Centre

Disclosure: Potential conflicts of interest have been resolved
- Cumberland Pharmaceuticals
- Celera Corporation
## Inherited Causes of Sudden Cardiac Death

<table>
<thead>
<tr>
<th>CARDIOMYOPATHIES</th>
<th>ARRHYTHMIAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophic Cardiomyopathy (HCM)</td>
<td>Long QT Syndrome (LQTS)</td>
</tr>
<tr>
<td>Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)</td>
<td>Short QT Syndrome</td>
</tr>
<tr>
<td>Dilated Cardiomyopathy (DCM)</td>
<td>Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)</td>
</tr>
<tr>
<td>Coronary Artery Abnormalities</td>
<td>Brugada Syndrome</td>
</tr>
<tr>
<td></td>
<td>Wolff-Parkinson-White (WPW) Syndrome</td>
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</table>
Clinical Screening For HCM

≥12 years:

- Family members should undergo physical examination
- ECG and echo at 12 to 18 month intervals

18 to 20 years:

- ECG and Echo every 5 years unless there is a clinical development
- Screening of first degree relatives are encouraged

Clinical Considerations

- Screening for causes of sudden cardiac death in the young
- History and physical examination detects less than 1%
- ECG exhibits abnormalities in over 80% of individuals with HCM, LQTS and WPW
- High % of false-positives
Role of Genetic Testing in Diagnosis of Cardiomyopathies

- HCM
- Fabry’s Disease
- Amyloidosis
- Other metabolic causes of hypertrophy
Role of Genetic Testing in Long QT Syndrome

- Long QTS-1 (Potassium Channel KV7.1) 35%
- Long QTS-2 (Potassium Channel KV11.1) 30%
- Long QTS-3 (Sodium Channel SCN5A) 10%

**Therapy**

- Long QTS-1  Beta Blockers
- Long QTS-2  Beta Blocker plus mexiletine, flecainide or ranolazine
- Long QTS-3
Benefits of Genetic Testing

- Genetic counseling
- Diagnostic
- Therapeutic implementation
- Cost effective
Sudden Death in Athletes

- 75% of all deaths in athletes is cardiac related and almost always precipitated by exertion.
- Familial hypertrophic cardiomyopathy (HCM) is the most common cause of sudden cardiac death below the age of 36 years.
- HCM is almost always asymptomatic, thus no warning precedes sudden death.

The following professional sporting organizations endorse ECG screening followed by other tests if abnormal:

- National Football League (NFL)
- Major League Baseball (MLB)
- National Basketball Association (NBA)
- National Hockey League (NHL)
- Major League Soccer (MLS)
Role of Genetic Testing in Cardiovascular Pharmacogenomics

- Anticoagulation
- Platelet Therapy
9p21: The First Genetic Risk Factor For CAD

9p21 genetic risk variant is extremely common with one or two copies occurring in 75% of the population.

**Homozygotes** carry increased risk of 50% for CAD
**Heterozygotes** carry increased risk of 25% for CAD

9p21 locus risk is independent of known risk factors for CAD, namely: cholesterol, hypertension or diabetes.

9p21 risk allele is estimated to be present in 4.5 billion people.


Genetics Of Coronary Artery Disease and Myocardial Infarction

50 genetic risk variants for CAD of genome-wide significance have been identified and replicated in independent populations

CARDIoGRAMplusC4D Consortium.
Nature Genetics: Jan 2013;Vol.45
Distribution of Genetic Risk Variants Associated with CAD

Ottawa Heart Genomic Study (n=14,495)

Genetic Risk Score (cGRS) based on 21 genetic variants

Percent of Population
Directives for Cardiology

- The time for genetic testing of cardiovascular Mendelian disorders is now.
- Genetic screening is ultimately necessary for comprehensive prevention of Coronary Artery Disease.
- Personalized Medicine is in large part dictated by genetic predisposition.

Structured education of Genetics is a prerequisite to enable our cardiologists to be proactive.
ACC Educational Offerings in Genetics/Genomics
ACC CME and MoC Offerings

• ACCSAP 8 (ACC Self Assessment Program) “Cardiovascular Genetics”
  – CME and MOC (maintenance of certification) offering
  – Mendelian CV Diseases
  – Complex Genetic Diseases
  – Pharmacogenetics
• Annual ACC Scientific Sessions
  – ACC.11
    • 3 sessions on translational research in genetics, pharmacogenetic tailored antiplatelet therapy, and functional genomics in CV disease
  – ACC.12
    • 7 sessions on personalized medicine, genome sequencing, translational research, genetic testing, gene therapy for heart failure, and the genetics of sudden cardiac death
3 ACC CME and MoC Offerings

• Live Programs – Genetic/Genomic Topics
  – 2011
    • “Genetics and genomics”
    • “Careers in Genetics and Proteomics”
  – 2012
    • “Addressing LV Dysfunction by Gene Therapy Upgrading of Metabolism”
    • “Genetics and Arrhythmias”
New Lifelong Learning & MOC

ACC Cardiosource
ACC Digital Strategy

Optimize Delivery of Knowledge & Decision Support tools
Appropriate Use Criteria (AUC)

- SPECT-MPI
- CCT/MRI
- TTE/TEE
- Stress Echocardiography
- Coronary Revascularization: PCI/CABG
- SPECT-MPI Update

Imbed Appropriateness of Genetic testing in Disease Entities & Clinical Scenarios?

- Pacemaker/ICD (2013)
- Multimodality (2013)
Knowledge & Decision Support Tools at the Point of Care

- Migration towards point-of-order
- Embedded clinical decision support
- Tracking/data registry
- Reporting/feedback
Future ACC Direction

ACC BoT Basic Science Advisory Task Force

• Dr. Geoffrey Ginsberg (Chair)
• Dr. Thomas Caskey
• Dr. Robert Roberts
• Dr. Christine Siedman
• Dr. Jennifer Hall
• Dr. Pat O’Gara
• Dr. Deepak Srivastava
Future Goals

• To develop whitepapers on basic and translational science anticipated to affect cardiovascular practice in the next 10 years.

• To recommend goals for training the next generation of cardiologists (in training and early career) as well as at the current practitioner based on the emerging science and technologies that will impact the practice of cardiovascular medicine.

• To advise the ACC on scientific questions, research strategy, and partnerships with other organizations.
“It’s far more important to know what person the disease has than what disease the person has.”

– Hippocrates
Thank You
Appropriate Use Criteria (AUC)

Define the “when to do” and “how often to do” a test or procedure in the context of scientific evidence, the healthcare environment, the patient’s profile and a physician’s judgment.