Global leaders in Genomic Medicine 2014

National Academy of Sciences Bldg
2101 Constitution Avenue, NW
Washington, DC
2012 Large-Scale Applied Research Project Competition

In January 2012, Genome Canada in partnership with the Canadian Institutes of Health Research launched the 2012 Large-Scale Applied Research Project Competition in Genomics and Personalized Health. This competition aimed to support several projects that will demonstrate how genomics-based research can contribute to a more evidence-based approach to health and improving the cost-effectiveness of the health-care system.

Results of the competition were announced on March 28, 2013. Savanna projects in total have been approved for a total budget of $149.6 million over four years with a maximum of $45.1 M from Genome Canada, $24.6 million from CIHR, and $2.0 million from CSCC.

List of Approved Projects

<table>
<thead>
<tr>
<th>Title</th>
<th>Sector</th>
<th>Lead Genome Centre/Co-Lead Centre</th>
<th>Project Leader(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autism Spectrum Disorders: Genomes to Outcomes</td>
<td>Health</td>
<td>Genome Quebec</td>
<td>Jordan, Stephen, Stephen</td>
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<tr>
<td>Biomarkers for Pediatric Glioblastoma</td>
<td>Health</td>
<td>Genome Quebec</td>
<td>Janssen, Nadia, Majewski, Jacek</td>
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<td>Clinical Implementation and Outcomes</td>
<td>Health</td>
<td>Genome British Columbia</td>
<td>Sin, Don, Ng, Raymond</td>
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<td>Evaluation of Blood-based Biomarkers for COPD Management</td>
<td>Health</td>
<td>Genome British Columbia</td>
<td>Sin, Don, Ng, Raymond</td>
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<td>Early Detection of Patients at High Risk of Esophageal Adenocarcinoma</td>
<td>Health</td>
<td>Genome British Columbia</td>
<td>Sin, Don, Ng, Raymond</td>
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<td>Enhanced CARF for RARE Genetic Diseases in Canada</td>
<td>Health</td>
<td>Genome Canada</td>
<td>Rieuw, John, Bliton, Alain</td>
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<td>IBD Genomic Medicine Consortium (GenMed)</td>
<td>Health</td>
<td>Genome Quebec</td>
<td>Rieuw, John, Bliton, Alain</td>
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<tr>
<td>Innovative Chemogenomic Tools to Improve Outcomes in Acute Myeloid Leukemia</td>
<td>Health</td>
<td>Genome Quebec</td>
<td>Rieuw, John, Bliton, Alain</td>
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<tr>
<td>PACE-Oms: Personalized, Accessible, Cost-Effective Applications of 'Omers Technologies</td>
<td>Health</td>
<td>Genome Alberta</td>
<td>McCabe, Christopher, Bubela, Tanya</td>
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</table>
50 International Genomic Medicine Leaders
25 Countries

Courtesy, G Ginsburg, Duke U
Global Leaders International Attendees

- Canada (CIHR, GenomeCan)
- UK (MRC, WT, Genom Engl)
- Belgium (U Brux, U Leuven)
- Estonia (Eston Genom Ctr)
- France (INSERM)
- Greece (U Patras)
- Luxembourg (Ctr Syst Biomed)
- Sweden (Swed Res Council)
- European Commission
- Israel (Hadassah U, Clalit Med)
- Kuwait (Kuwait U)
- Saudi Arabia (Pr Salman Ctr)
- Tunisia (Tunis U)
- India (Min Sci Tech, Natl Inst Biomed Genomics)
- Sri Lanka (U Colombo)
- China (Chinese Acad Med Sci)
- Japan (U Tokyo, Ctr Integ Med, Min Science)
- Korea (NIH Kor, Seoul Natl U)
- Singapore (National U)
- Thailand (Mahidol U, Min Hlth)
- Australia (MRC)
- New Zealand (Natl Hlth Cmte)
Objectives of GMVI: Global Leaders in Genomic Medicine

• Identify areas of active translation and implementation
• Prioritize common barriers to implementation in healthcare
• Frame a policy agenda to advance the field
• Highlight nations with unique capabilities
• Discuss opportunities for international collaborations
Plethora of Genomics Implementation Efforts

- UK: Genomics England to sequence 100K whole genomes and link to NHS medical record
- Belgium: Medical Genomics Initiative to create national framework for clinical exome sequencing
- Singapore: Pilot of $TGF\beta 1$ testing for disease diagnosis in stromal corneal dystrophies
- Estonia: Sequence 5K individuals, develop Estonian chip and offer to all 35-65 yo (~500K)
- Thailand: PGx card identifying risk for top ten SJS-TEN drugs, clinical exomes and genomes
- Israel: Push family hx data into EMR of relatives
Plethora of Genomics Implementation Efforts

- Sri Lanka: Carrier screening for thalassemia and modifier genes to convert to manageable illness
- Luxembourg: National Centre of Excellence in Early Diagnosis and Stratification of Parkinson’s
- Japan: Implementation of Genomic Medicine Project including genomic prediction of drug response, efficacy and cost-effectiveness studies
- Genomic Medicine Alliance bridging developed and developing/low-income countries, combining 8 national/ethnic genetic databases
- Economic evaluations in Croatia, Serbia, Greece
Singapore: Stromal Corneal Dystrophies and *TGFB1* Testing

- Inherited disorders leading to loss of corneal transparency.
- *TGFB1* mutations underlie the majority of stromal corneal dystrophies.

**Clinical Utility**

- Disease Diagnosis
- Treatment Selection for Patients
- Screening of family members

Courtesy P Tan, Duke-Natl U Singapore
Challenges in Developing a Singapore Framework for Genetic/Genomic Testing

- Legal and licensing agreements across institutions and ministries are often complex
- Reimbursement options for genetic assays that cross medical centres
- General lack of genetic counsellors and advisors
- Official polices on patient consent, incidental findings and aggregation of genetic/genomic data

Courtesy P Tan, Duke-Natl U Singapore
Estonian Program for Personal Medicine


- **Health care**
  - Educating health care professionals
  - Educating the patients
  - Further development of the eHealth incl. decision support systems

- **Research and Development**
  - Sequencing 5000 individuals, Estonian Chip and analysis software
  - International collaboration

- **Commercialization**
  - Business agreements
  - IPR

Courtesy A Metspalu, University of Tartu
Estonian Program: Research and Development

PILOT PROJECT
- Sequence 5000 – we’ll get SNV up to 0.1%
- Estonian chip – ca 0.7 – 1.0 million SNVs
- Pilot with 50,000 gene donors from the Estonian Biobank during one year using PCP, eHealth database, and decision support software

MAIN PROJECT
- Offer to everyone 35-65 years old as a disease risk and drug response prediction test (75-80% will accept)
- We’ll have ca 500 000 people in the database with EMR, genotypes, samples and longitudinal prescription data

This system could be used as a additional “instrument” for physicians in diagnosing, treating and preventing disease, but also for research.

Courtesy A Metspalu, U Tartu
High Incidence of SJS/TEN in Thailand

Drug induced SJS/TENs in Thailand 1998-2008

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Count</th>
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<tbody>
<tr>
<td>1. SULFAMETHOXAZONE+ TRIMETHOPRIM</td>
<td>1,234</td>
</tr>
<tr>
<td>2. CARBAMAZEPINE</td>
<td>703</td>
</tr>
<tr>
<td>3. ALLOPURINOL</td>
<td>664</td>
</tr>
<tr>
<td>4. PHENYTOIN</td>
<td>451</td>
</tr>
<tr>
<td>5. AMOXYCILLIN</td>
<td>342</td>
</tr>
<tr>
<td>6. STAVUDINE + LAMIVUDINE+NEVIRAPINE</td>
<td>313</td>
</tr>
<tr>
<td>7. PHENOBARBITAL</td>
<td>189</td>
</tr>
<tr>
<td>8. IBUPROFEN</td>
<td>156</td>
</tr>
<tr>
<td>9. NEVIRAPINE</td>
<td>122</td>
</tr>
<tr>
<td>10. TETRACYCLINE</td>
<td>113</td>
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</tbody>
</table>

Genomic markers have been found and utilized as predictive tools by our group.

Courtesy W Chantratita, Ramathibodi Hospital
Carbamazepine and SJS/TEN: Allele Frequency of HLA-B*15:02

Courtesy W Chantratita, Ramathibodi Hospital
Name & Family Name

Outcome of the PGX assay

8 Jan 2014

PGx Interpretation

High Risk of SJS/TEN from Carbamazepine, according to update information

Suggestion: According to update information, this person has HLA-B*1502 which has a high risk to develop a severe skin disorder (SJS/TEN), if he takes carbamazepine or drug structurally similar.

Need more information: please contact our PGx laboratory. Tel 02-200-4330-3...

Courtesty W Chantratita
Incremental cost-effectiveness ratio of universal HLA-B*15:02 screening estimated at 222,000 THB ($6,660)/QALY gained for epilepsy pts; 130,000 THB/QALY for neuropathic pain pts

Test 343 patients to prevent one case of SJS/TEN

Courtesy S Mahasirimongkol, Ministry of Public Health
Products – Agreement, Committee Structure, White Paper

Continued international communication and collaboration valuable; facilitate through Steering Committee, Working Groups

- IT/bioinformatics
- Education/workforce
- Pharmacogenomics
- Evidence
- Policy
- Communications

*Leadership must be multinational...* seeking willing volunteers!
Five Break-out Groups’ Top Ideas

• **IT/bioinformatics**
  - Define key elements to be stored in EMR
  - Identify most robust and generalizable solutions for potential wider adoption
  - Global resource for actionable variants

• **Education:**
  - Define workforce needs
  - Develop existing/new educational tools that can be widely shared
  - Develop region-specific teaching materials, perhaps common templates
Five Break-out Groups’ Top Ideas

- **Evidence Generation**
  - Evidence Generation
  - Catalog evidence-generating projects
  - Identify poolable/extendable projects
  - Develop systems to capture evidence; federated network, standardized APIs (e-tools)

- **Pharmacogenomics**
  - Global eradication of SJS/TEN
  - PGx card

- **Policy**
  - Share efforts in consent, results reporting
  - Study economics, cost-effectiveness
Genomic Medicine Alliance Aims

- Encourage multidisciplinary collaborative research, particularly from emerging countries
- Facilitate introduction of PGx and advanced omics into mainstream clinical practice
- Propose guidelines and recommendations in all areas pertaining to genomic medicine
- Develop and coordinate educational activities in genomic medicine

http://www.genomicmedicinealliance.org/
Genomic Medicine Alliance and GM6...

http://www.youtube.com/watch?v=rwnd3PY46-g
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Next Steps

• Distribute meeting summary and exec summary

• Establish steering group and working groups, assess what’s feasible

• Engage and leverage related groups such as GA4GH, IRDiRC, EPMA

• Draft white paper and circulate

• Share with other NIH Institutes/Centers, encourage participation

• Re-assess GMWG opportunities and priorities
IT/Bioinformatics/CDS Top Ideas

- Define key elements to be stored in EMR
- Identify most robust and generalizable solutions for potential wider adoption (e.g., CDS, variant databases, informatics pipelines)
- 10 Global resource for actionable clinical variants
- Collection/aggregation of variant/phenotype associations
- Define necessary federated databases to implement genomic medicine
- Phenotype ontology (including inventory)
- Clearinghouse of implementation guidelines
Education/Workforce Top Ideas

• Three types: genomics professionals, other healthcare providers, public

• Genomics professionals:
  • Collect data on genomic professional workforce and training in different countries
  • Conduct formal workforce studies
  • Share competencies and training paradigms
  • Genomics academy
Education/Workforce Top Ideas

- Other healthcare providers:
  - Deploy new educational tools
  - Develop region-specific teaching materials, perhaps common templates
  - Use existing professional workforce to educate other physicians/providers

- Public:
  - Provide clearinghouse for information
  - Consider novel educational paradigms
  - Customize culturally-specific materials
  - Extend DNA Day to be international educational event
Evidence Generation Top Ideas

- Evidence epistemology (pre-evidence)
  - Catalog evidence generating projects
  - Standards for a test
  - Definition of evidence
  - Encourage adoption of genomic medicine applications with sufficient existing evidence
- Opportunities for action
  - Identify countries/systems willing to enable patient data sharing
  - Develop systems to capture evidence—federated network, standardized APIs (e-tools)
- Next steps: discuss areas of overlap with others particularly poolable or extendable projects
Pharmacogenomics Top Ideas

- Endorse desire for quality of evidence base for PGx implementation
- Emphasize cheap drugs with treatment failure or extreme ADRs (metformin, vaccines)
- Add drug/PGx component to all iPS initiatives (lack of basic mechanistic science)
- Global effort to develop value around cancer NGS-- expensive test generates use of very expensive drugs
- Global eradication of SJS/TEN via PGx-- systematic approach
Policy Top Ideas

• Engaging stakeholders
• Data sharing
  • Privacy
  • Informed consent
  • Legal issues
• Regulatory oversight
  • Map activities and issues addressed, gap analysis
  • Encourage network of networks (consent, data-sharing groups, etc)
• Cost benefit assessments– improve capacity for doing them; engage payers