Global Leaders in Genomic Medicine: Genomic Medicine 6

U.S. Department of Health and Human Services
National Institutes of Health
National Human Genome Research Institute

Teri Manolio, M.D., Ph.D.
National Advisory Council on Human Genome Research
February 10, 2014

National Academy of Sciences Bldg

2101 Constitution Avenue, NW

Washington, DC

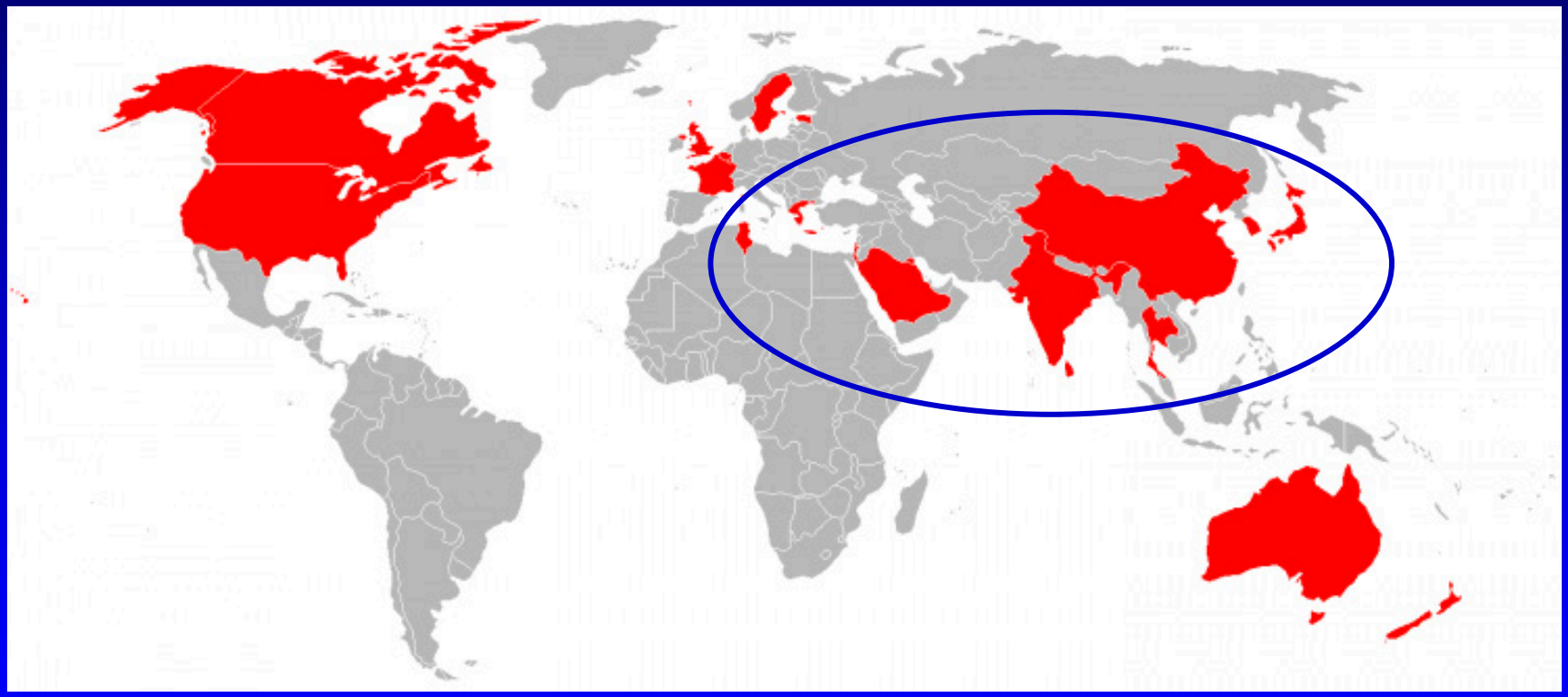

Building
Genomic tec
A report by the Hum

EUROPEAN SCIENCE FOUNDATION
ESF Forward Look
Personalise
for the Euro
Towards more pre
treatment and pre

Contents lists available at SciVerso ScienceDirect
journal homep
The policy of public health
Benedetto Simone[a], Walter Mazzu
Antonella Agodi[c], Domenico Coviel
Bruno Dallapiccola[f], Emilio Di Mari
Maurizio Genuardi[j,k], Liliana Vares
Stefania Boccia[a,m,*], for the GENISA
ARTICLE INFO
Article history:
Received 27 August 2012
Received in revised form 17 January 2013
Accepted 25 January 2013
Keywords:
Public health genomics
Policy
Italy
* Corresponding author at: Institute of Hygiene, Univer
fax: +39 06 35001522.
E-mail addresses: benedetto.simone@yahoo.it (B. Sim
agodi@unict.it (A. Agodi), coviello@unige.it (D. Covi
m.federici@hsanita.it (M. Federici), m.genuardi@dfc.unifi.it
sboccia@rm.unicatt.it (S. Boccia).
1 List of members of the GENISAP Network can be foun
0168-8510/$ – see front matter © 2013 Elsevier Ireland Lt
http://dx.doi.org/10.1016/j.healthpol.2013.01.015

GenomeCanada
About Genome Canada
Research Portfolio
Events and Sponsorships
Information for the Public
Media Gallery
GE³LS: Genomics & Society
GenomeCanada
Science that powers Innovation that powers Canada
2012 Large-Scale Applied Research Project Competition
In January 2012, Genome Canada in partnership with the Canadian Institutes of Health Research launched the 2012
Scale Applied Research Project Competition in Genomics and Personalized Health. This competition aimed to suppor
scale research projects that will demonstrate how genomics-based research can contribute to a more evidenc
approach to health and improving the cost-effectiveness of the health-care system.
Results of the competition were announced on March 26, 2013, Seventeen projects in total have been approved for
for a total budget of $149.8 million over four years with a maximum of $45.1 M from Genome Canada, $24.6 millic
CIHR, and $2.0 million from CSCC.
List of Approved Projects
Title
Sector
Lead Genome Centre/Co -Lead Centre
Project Leader(s)
Autism Spectrum Disorders: Genomes to Outcomes
Health
Ontario Genomics Institute
Scherer, Stephen
Szatmari, Peter
Biomarkers for Pediatric Glioblastoma through Genomics and Epigenomics
Health
Genome Quebec
Jabado, Nada
Majewski, Jacek
Clinical Implementation and Outcomes Evaluation of Blood-based Biomarkers for COPD Management
Health
Genome British Columbia
Sin, Don
Ng, Raymond
Early Detection of Patients at High Risk of Esophageal Adenocarcinoma
Health
Ontario Genomics Institute
Stein, Lincoln
Godfrey, Tony
Enhanced CARE for RARE Genetic Diseases in Canada
Health
Ontario Genomics Institute
Boycott, Kym
Mackenzie, Alex
IBD Genomic Medicine Consortium (iGenoMed): Translating Genetic Discoveries into a Personalized Approach to Treating Inflammatory Bowel Diseases
Health
Genome Quebec
Rioux, John
Bitton, Alain
Innovative Chemogenomic Tools to Improve Outcome in Acute Myeloid Leukemia
Health
Genome Quebec
Sauvageau, Guy
Hébert, Josée
PACE-'Omics: Personalized, Accessible, Cost-Effective Applications of 'Omics Technologies
Health/GE3LS
Genome Alberta
McCabe, Christopher
Bubela, Tania

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)

50 International Genomic Medicine Leaders

40 US Genomic Leaders and NHGRI Staff

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

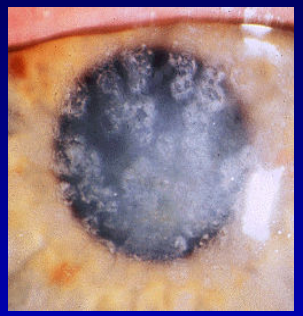
- UK: Genomics England to sequence 100K whole genomes and link to NHS medical record
- Belgium: Medical Genomics Initiative to create national framework for clinical exome sequencing
- Singapore: Pilot of *TGFB1* testing for disease diagnosis in stromal corneal dystrophies
- Estonia: Sequence 5K individuals, 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

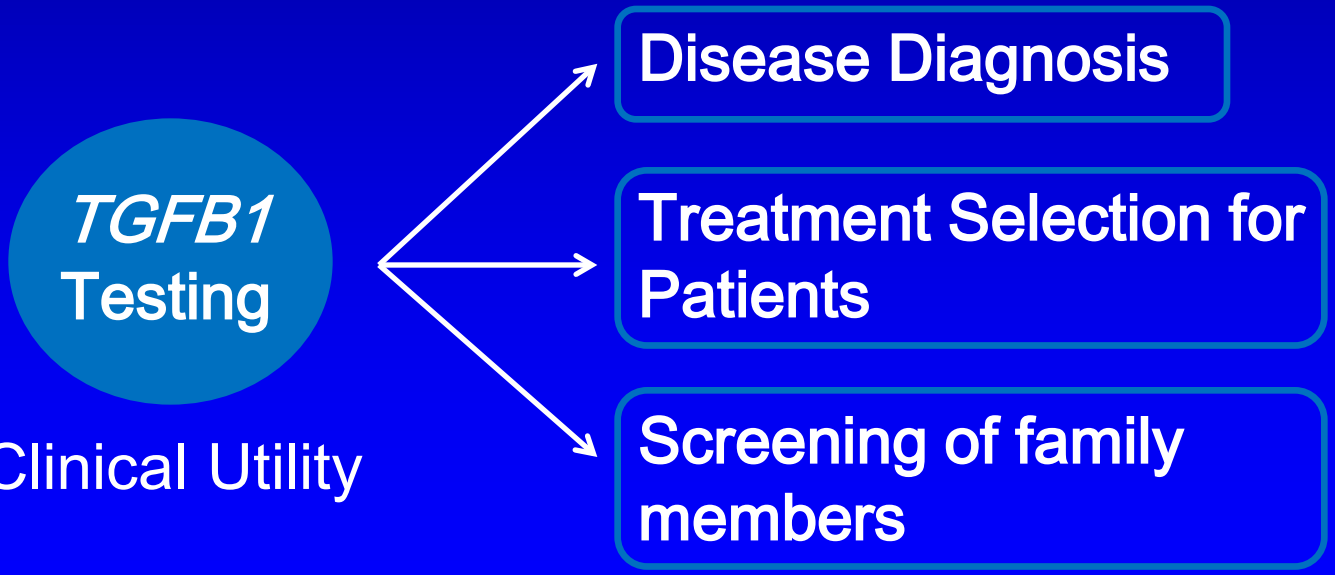
Plethora of Genomics Implementation Efforts

- 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.





Courtesy P Tan, Duke-Natl U Singapore

POLARIS

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

POLARIS

Estonian Program for Personal Medicine

Approved at the Estonian Government Research and Development Council on 17.12.2013.

- **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,

estonian genome center
university of tartu

U 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

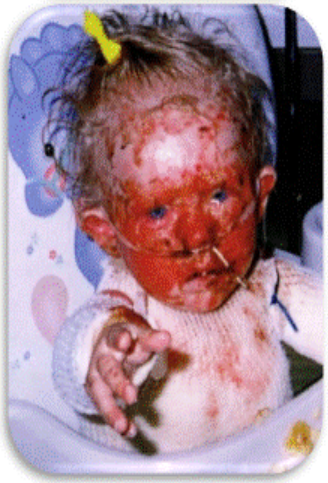
This system could be used as a additional "instrument" for physicians in diagnosing, treating and preventing disease, but also for research.,

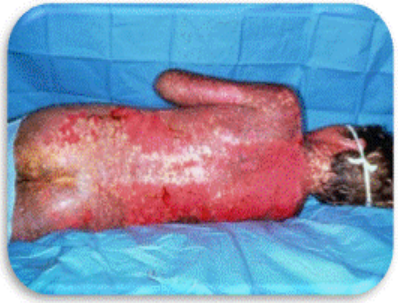
Courtesy A Metspalu,

estonian genome center
university of tartu

U Tartu

High Incidence of SJS/TEN in Thailand





Drug induced SJS/TENs in Thailand 1998-2008

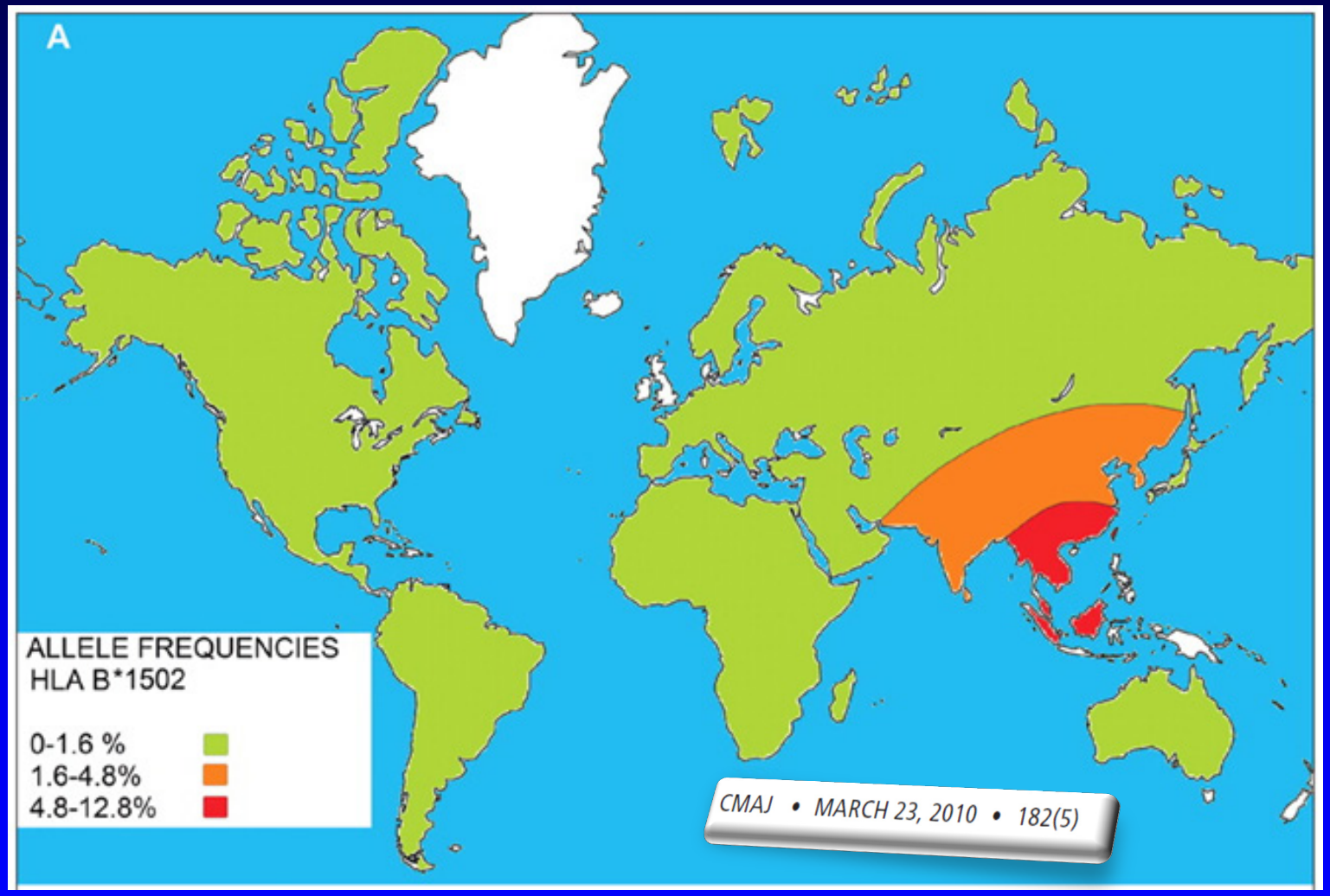
(Reference: Thai FDA 2008)

Drug name	Count
1. SULFAMETHOXAZONE+ TRIMETHOPRIM	1,234
2. CARBAMAZEPINE	703
3. ALLOPURINOL	664
4. PHENYTOIN	451
5. AMOXYCILLIN	342
6. STAVUDINE + LAMIVUDINE+NEVIRAPINE	313
7. PHNOBARBITAL	189
8. IBUPROFEN	156
9. NEVIRAPINE	122
10. TETRACYCLINE	113

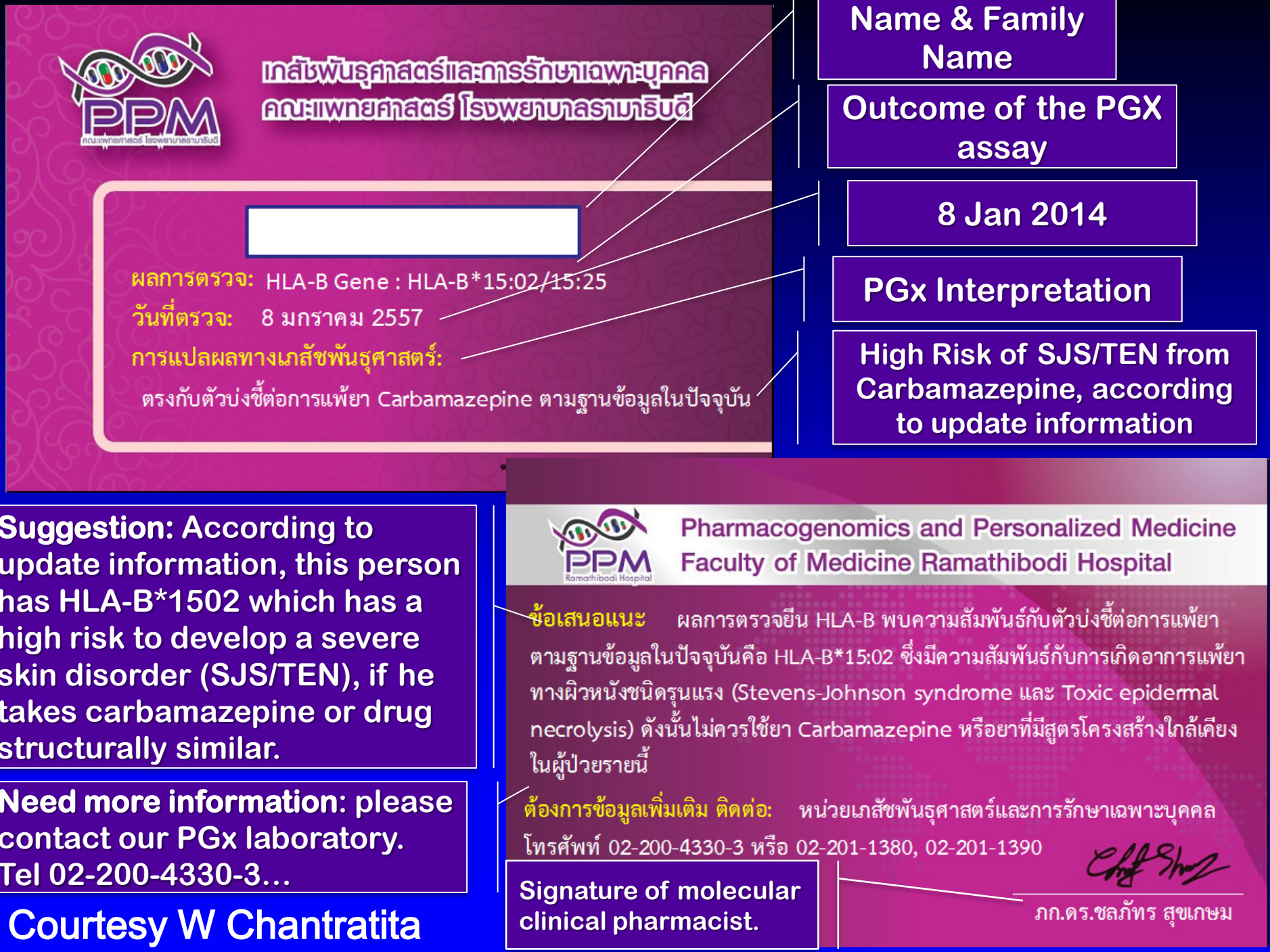
Genomic markers have been found and utilized as predictive tools by our group.

Courtesy W Chantratita, Ramathibodi Hospital

Carbamazepine and SJS/TEN: Allele Frequency of HLA-B*15:02



Courtesy W Chantratita, Ramathibodi Hospital


เภสัชพันธุศาสตร์และการรักษาเฉพาะบุคคล
คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี
ผลการตรวจ: HLA-B Gene : HLA-B*15:02/15:25
วันที่ตรวจ: 8 มกราคม 2557
การแปลผลทางเภสัชพันธุศาสตร์:
ตรงกับตัวบ่งชี้ต่อการแพ้ยา Carbamazepine ตามฐานข้อมูลในปัจจุบัน
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…
Courtesy W Chantratita
Pharmacogenomics and Personalized Medicine
Faculty of Medicine Ramathibodi Hospital
ข้อเสนอแนะ ผลการตรวจยีน HLA-B พบความสัมพันธ์กับตัวบ่งชี้ต่อการแพ้ยาตามฐานข้อมูลในปัจจุบันคือ HLA-B*15:02 ซึ่งมีความสัมพันธ์กับการเกิดอาการแพ้ยาทางผิวหนังชนิดรุนแรง (Stevens-Johnson syndrome และ Toxic epidermal necrolysis) ดังนั้นไม่ควรใช้ยา Carbamazepine หรือยาที่มีสูตรโครงสร้างใกล้เคียงในผู้ป่วยรายนี้
ต้องการข้อมูลเพิ่มเติม ติดต่อ: หน่วยเภสัชพันธุศาสตร์และการรักษาเฉพาะบุคคล
โทรศัพท์ 02-200-4330-3 หรือ 02-201-1380, 02-201-1390
ภก.ดร.ชลภัทร สุขเกษม
Signature of molecular clinical pharmacist.

Cost Effectiveness Analysis

Epilepsia, **(*):1–11, 2013
doi: 10.1111/epi.12325

FULL-LENGTH ORIGINAL RESEARCH

Economic evaluation of HLA-B*15:02 screening for carbamazepine-induced severe adverse drug reactions in Thailand

*Waranya Rattanavipapong, *Tanunya Koopitakkajorn, *†Naiyana Praditsitthikorn, ‡Surakameth Mahasirimongkol, and *Yot Teerawattananon

*Health Intervention and Technology Assessment Program (HITAP), Nonthaburi, Thailand; †Bureau of AIDS TB and STIs, Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand; and ‡The National Institute of Health, Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand

- 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

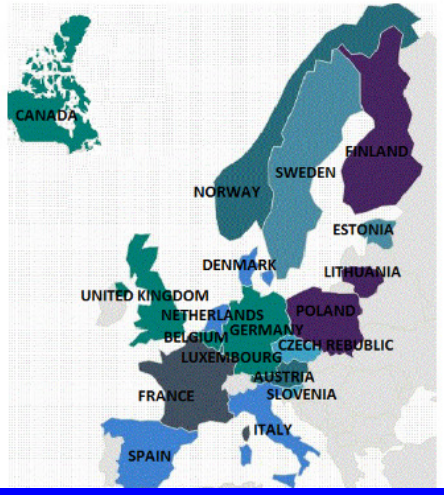
- Evidence Generation

HOME ABOUT INSIGHTS OBSERVATORY EUROBIOFORUM 2014 NEWS EVENTS CONTACT

EURO BIO FORUM | Forum for research funders and performers in Personalised Medicine

PERSONALISED MEDICINE OBSERVATORY

Insight into key people and key initiatives in Personalised Medicine



The aim of the Observatory – initiated by EuroBioForum – is to give insight into the 'key players' in Personalised Medicine in Europe. The online database is publicly available and presents an overview of initiatives per country and/or topic – all related to Personalised Medicine.

Currently featuring:

18 countries in Europe

28 Bioregions and clusters in Europe - Since January 2013 we worked on a thorough research audit on the Bioregion and cluster landscape in Europe. These have now been added to the Observatory.

Specials:

Canada

Miss something?

We are in continuous process of updating and expanding the content in the Observatory, so please feel free to contact us and share your additional information with us.

Genomic Medicine Alliance Aims

http://www.genomicmedicinealliance.org/

Genomic Medicine Alliance and GM6…

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

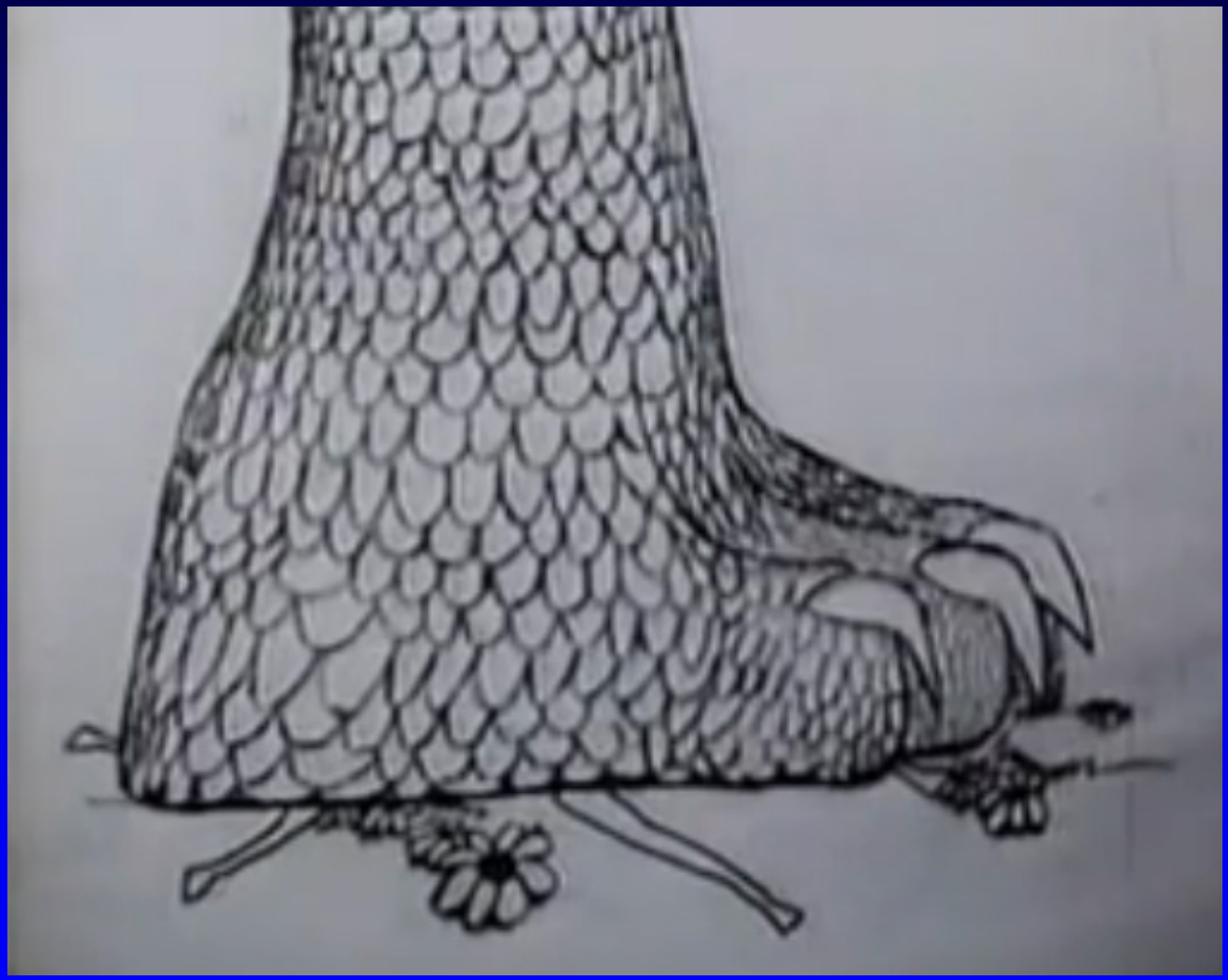
Genomic Medicine Alliance and GM6…

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

Genomic Medicine Alliance and GM6…

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

Genomic Medicine Alliance and GM6…



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

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