Genomic Medicine Working Group Update

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 9, 2015
Genomic Medicine Working Group of National Advisory Council on Human Genome Research

Assist in advising NHGRI on research needed to evaluate and implement genomic medicine

- Review current progress, identify research gaps and approaches for filling them
- Identify and publicize key advances
- Plan genomic medicine meetings focusing on timely themes
- Facilitate collaborations, coordination
- Explore models for long-term infrastructure and sustainability of groups arising from genomic medicine meetings.
NACHGR Genomic Medicine Working Group Members

Rex Chisholm Northwestern
Geoff Ginsburg Duke
Howard Jacob Med Coll Wisconsin
Howard McLeod Moffitt
Mary Relling St. Jude
Dan Roden Vanderbilt
Marc Williams Geisinger

Eric Green
Teri Manolio
Laura Rodriguez
NHGRI Genomic Medicine Meetings, 2014-2015

• GM VI, Jan 8-9, 2014, Bethesda MD
  – Engage international agencies
  – Explore current activities, needs, obstacles
  – Identify common research gaps to ensure evidence only need be generated once
  – Develop plans for international collaboration
Inherited disorders leading to loss of corneal transparency.

*TGFBI* 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
Estonian Program for Personalized Medicine


- Health care
  - Educating health care professionals
  - Educating patients
  - Further development of the eHealth including decision support systems

- Research and Development
  - Sequencing 5,000 individuals, Estonian Chip and analysis software
  - International collaboration

- Commercialization

Courtesy A Metspalu, U Tartu
Carbamazepine and SJS/TEN: Allele Frequency of HLA-B*15:02

Courtesy W Chantratita, Ramathibodi Hospital
## High Incidence of SJS/TEN in Thailand

### Drug induced SJS/TENs in Thailand 1998-2008

(Reference: Thai FDA 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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</table>

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

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…

**Signature of molecular clinical pharmacist.**

Courtesy W Chantratita

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ผลการตรวจ: HLA-B Gene : HLA-B*15:02/15:25
วันที่ตรวจ: 8 มกราคม 2557
การแปลผลทางมOLEKULAR ผู้วิเคราะห์:
ตรงกับคำงั้นชี้ของการหากยา Carbamazepine ตามฐานข้อมูลในปัจจุบัน

**Pharmacogenomics and Personalized Medicine**

Faculty of Medicine Ramathibodi Hospital

ข้อเสนอแนะ ผลการตรวจยืน HLA-B พบความเสี่ยงสูงถึงด้านปัจจัยการแพทย์ตามฐานข้อมูลในปัจจุบันคือ HLA-B*15:02 ซึ่งมีความเสี่ยงกับการเกิดอาการแพ้ทางผิวหนังชนิดรุนแรง (Stevens-Johnson syndrome และ Toxic epidermal necrolysis) ดังนั้นไม่ควรใช้ยา Carbamazepine หรือยาที่มีสตรีโครงสร้างใกล้เคียงในกลุ่มปัญหา

ต้องการข้อมูลเพิ่มเติม ติดต่อ: หน่วยเภสัชพยาธุศาสตร์และการวิเคราะห์พยาธุศาสตร์ โทรศัพท์ 02-200-4330-3 หรือ 02-201-1390, 02-201-1390

ภ.ดร. ฉัตรศักดิ์ สุทธกัศมี
Objectives:

1. Review current state of knowledge of surveillance, pathogenesis, and treatment
2. Examine role of genomics and PGx in etiology, treatment, and eradication of preventable cases
3. Identify gaps, unmet needs, and priorities for future research to eliminate SJS/TEN globally

Mark Avigan, FDA
Ricardo Cibotti, NIAMS
Robert Davis, U Tenn
Josh Denny, Vanderbilt

Carolyn Hutter, NHGRI
Lois La Grenade, FDA
Neil Shear, U Toronto
Lisa Wheatley, NIAID
50 International Genomic Medicine Leaders

Global Leaders in Genomic Medicine
Washington, DC, USA
January 8, 2014

40 US Genomic Leaders and NHGRI Staff
Facilitating Collaborations

GA4GH

Global Alliance for Genomics Health

G2MC

Global Genomic Medicine Collaborative
Goals of the Global Genomic Medicine Collaborative (G2MC)

An international genomic medicine community hosted by the Institute of Medicine and formed to:

- Serve as nexus, clearinghouse, and knowledge base for GM activities globally
- Develop opportunities for global GM demonstration projects (implementation and outcomes research)
- Capture and disseminate best practices for GM (IT, education, evidence, Pgx, policy) across the global GM community
- Develop a financial model for sustained efforts
Inter-Society Coordinating Committee for Practitioner Education in Genomics (ISCC)
Educational Products Available on G2C2, Site Re-Designed, Mapped to Competencies
The TRIG Model: A structured approach to teaching...

- Needs assessment
  - Targeted learner

- Objectives/Teaching Strategies
  - Knowledge-based
  - Performance-based
  - Affective

- Evaluation

- Dissemination/Research

Curriculum available at www.ascp.org/TRIG
Online Supplement

A Curriculum in Genomics and Personalized Medicine for Pathology Residents

Richard L. Haspel, MD, PhD,1 Ramy Arnaout, MD, DPhil,1 Lauren Briere, MS,2 Sibel Kantarci, PhD,1 Karen Marchand, MS,2 Peter Tonellato, PhD,1,3 James Connolly, MD,1 Mark S. Boguski, MD, PhD,1,3 and Jeffrey E. Saffitz, MD, PhD1

Am J Clin Pathol 2010;133-35.

We have taken a structured approach to develop a practical curriculum in genomics and personalized medicine that would also generate resident enthusiasm and interest in the subject.1,2

The second lecture, entitled “Next-Generation Sequencing,” includes the limitations of conventional (Sanger) sequencing and the concept of next-generation sequencing. The lecturer reviews the advantages and disadvantages of the

• Objectives
  – Define ideal state of genomic CDS, identify gaps and strategies to close them
  – Identify and engage health IT initiatives that would support recommended strategies
  – Define a prioritized research agenda for GCDS

• Potential collaborative projects
  – GCDS Use Cases
  – GCDS Sandbox
  – Open CDS Knowledge Library
  – End-to-End Project
  – Role of the Patient/Caregiver
Genomic Medicine VIII: NHGRI’s Genomic Medicine Programs, June 8-9, 2015

• Objectives
  – Review NHGRI’s genomic medicine portfolio, identify gaps, opportunities for collaborations
  – Identify related programs of other NIH ICs or other funders and opportunities for collaborations
  – Identify research needs in genomic medicine for NHGRI and partner agencies to pursue
  – Enhance approaches to capturing and disseminating best practices
  – Examine potential methods for assessing impact of programs

• GM IX, Winter 2016? Bethesda MD
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<thead>
<tr>
<th>Alice Bailey</th>
<th>Heather Junkins</th>
<th>Rex Chisholm</th>
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<tr>
<td>Ebony Bookman</td>
<td>Rongling Li</td>
<td>Geoff Ginsburg</td>
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<td>Joy Boyer</td>
<td>Nicole Lockhart</td>
<td>Howard Jacob</td>
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<td>Cati Crawford</td>
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<td>Lucia Hindorff</td>
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<td>Jean Jenkins</td>
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<td>Anastasia Wise</td>
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