Towards an interoperable information infrastructure providing decision support for genomic medicine

**Matthias Samwald**, Holger Stenzhorn, Michel Dumontier, M. Scott Marshall, Joanne Luciano, Klaus-Peter Adlassnig

Section for Medical Expert and Knowledge-Based Systems  
Center for Medical Statistics, Informatics, and Intelligent Systems  
Medical University of Vienna  
Austria

+  
University of Technology,  
Vienna, Austria

MIE 2011, 30. August 2011, Oslo, Norway
Medical practice is far from perfect

Adults in the U.S. receive only about half of recommended care,¹ and up to 98,000 Americans die each year as the result of preventable medical errors.²

The development and clinical establishment of new therapies, e.g. drugs
Most promising drugs fail at some point and never reach widespread clinical practice

> 17 years
> 1 billion €
People are different

“If it were not for the great variability among individuals, medicine might as well be a science and not an art”

Sir William Osler, 1892
Drug → Drug → Drug → Drug → Drug

Patient with Disease X

> 17 years
> 1 billion €
Great variability in effectiveness and safety among patients
This costs lots of lives and money
Great variability in effectiveness and safety among patients
Stratified Medicine
A considerable part of the differences might be caused by genetic variation (such as SNPs)

- rs7412 – 10x risk of Alzheimer's disease
- rs9939609 - risk of obesity and type-2 diabetes
- rs1799971 - stronger alcohol cravings
- rs1051730 - nicotine dependence
- rs3057 - perfect musical pitch
- rs4988235 - lactose intolerance
Genotyping is becoming very cheap

- > 500,000 SNPs
- Cost < 400 €
- Data is valid for the entire lifetime of each individual
Pharmacogenetic information is becoming available for many different drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>System</th>
<th>Enzyme</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenylbutyrate</td>
<td>Gastroenterology</td>
<td></td>
<td>Description, Clinical Pharmacology</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>Oncology</td>
<td>Estrogen receptor</td>
<td>Indications and Usage, Precautions, Medication Guide</td>
</tr>
<tr>
<td>Terbinafine</td>
<td>Antifungals</td>
<td>CYP2D6</td>
<td>Drug Interactions</td>
</tr>
<tr>
<td>Tetrabenazine</td>
<td>Neurology</td>
<td>CYP2D6</td>
<td>Dosage and Administration, Warnings, Clinical Pharmacology</td>
</tr>
<tr>
<td>Thioguanine</td>
<td>Oncology</td>
<td>TPMT</td>
<td>Dosage and Administration, Precautions, Warnings</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>Psychiatry</td>
<td>CYP2D6</td>
<td>Precautions, Warnings, Contraindications</td>
</tr>
<tr>
<td>Timolol</td>
<td>Ophthalmology</td>
<td>CYP2D6</td>
<td>Clinical Pharmacology</td>
</tr>
<tr>
<td>Tiotropium</td>
<td>Pulmonary</td>
<td>CYP2D6</td>
<td>Clinical Pharmacology</td>
</tr>
<tr>
<td>Tolterodine</td>
<td>Reproductive and Urologic</td>
<td>CYP2D6</td>
<td>Clinical Pharmacology</td>
</tr>
<tr>
<td>Tramadol and Acetaminophen</td>
<td>Analgesics</td>
<td>CYP2D6</td>
<td>Clinical Pharmacology</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>Oncology</td>
<td>Her2/neo</td>
<td>Indications and Usage, Precautions, Clinical Pharmacology</td>
</tr>
<tr>
<td>Tretinoin</td>
<td>Dermatology and Dental</td>
<td>PML/RARα translocation</td>
<td>Boxed Warning, Dosage and Administration, Precautions</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>Psychiatry</td>
<td></td>
<td>Contraindications, Precautions, Adverse Reactions</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Psychiatry</td>
<td>CYP2D6</td>
<td>Drug Interactions</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>Antifungals</td>
<td>CYP2C19</td>
<td>Clinical Pharmacology, Drug Interactions</td>
</tr>
<tr>
<td>Warfarin (1)</td>
<td>Hematology</td>
<td>CYP2C9</td>
<td>Dosage and Administration, Precautions, Clinical Pharmacology</td>
</tr>
</tbody>
</table>
Still very difficult to make this useful for clinical practitioners
An extended view of personalized/stratified medicine

- „Blockbuster drugs“
  Drugs
- „Personalized medicine“
  Drugs + Diagnostics
- „Computer-assisted personalized medicine“
  Drugs + Diagnostics + **Computer-based decision support**
W3C Health Care and Life Science Interest Group - Task force: „Clinical decision support for effective and personalized medicine“

http://www.w3.org/wiki/HCLSIG/CDS/Introduction
The W3C group is developing the 'Translational Medicine Ontology'
Knowledge Base based on W3C standards powering CDS systems based on HL7 standards (e.g. Arden, Gello)
Project initiated at the Medical University of Vienna

Vienna General Hospital:
> 2200 beds