Using Pharmacogenetics Knowledge to Increase Accuracy of Alerts for Adverse Drug Events

(oral presentation)

Yossi Mesika - IBM Research Israel
Byung Chul Lee - IBM Korea
Yevgenia Tsimerman - IBM Research Israel
Haggai Roitman - IBM Research Israel
Heon Kyu Park - IBM Korea

MIE – Oslo Norway, Aug 2011
Why Adverse Drug Events (ADE)?

- ADE is the harm associated with the use of given medications

- ADEs annually result in more than 4 million* visits to the outpatient setting

- Between 11% to 50% of ADEs can be prevented based with currently available knowledge
  - the costs of preventable ADSs more than $4 billion* each year

Automatic systems can improve detection considerably

* statistics for United States
Genetic ADE

Decision Support System

Result (e.g. dosage)
Warfarin is an anticoagulant used for the prophylaxis and treatment of thromboembolic disorders.

The Warfarin drugs are implicated in 6.2%* of all reported ADEs in Emergency Departments.

Table 5: Range of Expected Therapeutic Warfarin Doses Based on CYP2C9 and VKORC1 Genotypes†

<table>
<thead>
<tr>
<th>VKORC1</th>
<th>CYP2C9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>*1/*1</td>
</tr>
<tr>
<td>GG</td>
<td>5-7 mg</td>
</tr>
<tr>
<td>AG</td>
<td>5-7 mg</td>
</tr>
<tr>
<td>AA</td>
<td>3-4 mg</td>
</tr>
</tbody>
</table>

* statistics for United States
Problem Statement

Decision Support System

Data -> Rule Engine -> Result

- Rules
- Medical expert?
- IT person?

Knowledge
- Intuitive
- Structured

Medical expert

IT person
- **Concept Mapping** is a method of representing knowledge in a way that allows information to be gathered, represented and understood visually.
  - Concepts = boxes or circles
  - Relationships among different concepts = labeled arrows
  - Can be used for learning, evaluation, planning, modeling

- **CmapTools** is a framework that allows construction, sharing and publishing of knowledge models represented as concept maps.
  - allows export to RDF
We want to allow the uniform rules definition

**Disease**
- disease_name
- disease_id
  - are
  - disease_name
  - disease_id_value
- has
- Disease
  - has
  - Phenotype
    - are
    - Positive
    - negative

**Dosage**
- dosage
  - has
  - range
    - has
    - min
      - is a
      - min_val
    - max
      - is a
      - max_val
  - unit
    - is a
    - unit_val

**Allele**
- gene_id
  - are
  - gene_id_value
- has
- Genotype
  - arc
  - Allele_object
    - has
    - allele_genotype
      - arc
      - *A/*B
Rule Example

drug
  has
  drug_generic
    is a
    Warfarin
  drug_brandname
    is a
    drug_brandname_value

snp_genotype
  are
  G, G, A

allele_genotype
  are
  1/1, 1/2, 2/2, 2/3, 3/3

condition 1
  implies
  dosage
    has
    range
      has
      min
        is a
        "mg"
      max
        is a
        "mg"
    unit

condition 2
  implies
  result 2

condition 3
  implies
  result 3
Summary

- Current usage
  - Intuitive model description

- Next steps
  - Automatic creation of rules in an appropriate format
  - Data sharing
  - Composition of clinical and genomic rules
Thank You
We want to allow the uniform rules transformation
Translation Example