Translational Medicine Ontology: A Patient-Centric Ontology for Drug Development and Clinical Practice

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Introduction

• The aim of personalized medicine is for patients to receive the right treatment at the right time and at the right dose

• Development of personalized medicines require the translation of preclinical science into patient studies and involves people in varied roles, e.g. the medicinal chemist to develop compounds with the desired activity to the strategic portfolio manager who prepares a marketing plan for the drug

• Such translational medicine strategies require that traditionally separate data sets from early drug discovery through to patients in the clinical setting be integrated, and presented, queried and analyzed collectively

• Ontologies, a formal representation of domain knowledge, can be used to drive such capabilities; however, at present few ontologies exist that bridge genomics, chemistry and medicine.

• The Translational Medicine Ontology (TMO), an application ontology that bridges the diverse areas of translational medicine, draws on existing domain ontologies where appropriate and provides a light-weight framework that spans the roles involved in the drug development process

Goals

• The Translational Medicine Ontology will facilitate data integration from diverse areas of translational medicine such as discovery research, hypothesis management, formulation, clinical trials, and clinical research

• It will serve as a framework that can be extended further for additional use cases, enabling scientists to answer interesting and currently difficult questions more easily, especially those about data that are typically hosted by different functional areas

• The ontology will provide a framework for the modeling of patient-centric information, which is essential for tailoring drugs.

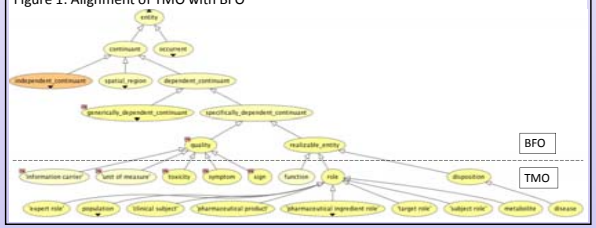
Methodology

- Identify roles of people involved in the drug development process (Table 1)
  - Cellular and Molecular Biologist
  - Medicinal Chemist
  - Clinical Trial Formulator/Lead Physician
  - Strategic/Portfolio Manager
- Identify questions of interest from people in these roles
  - Area of focus
  - Entities of interest within the focus area
- Identify entities of interest and whether there already exists an ontology for them:
  - Disease --> Disease Ontology
  - Drug --> ChEBI
  - Patient --> EPOC Patient Ontology
- Build ontology
  - Card sorting
  - Define the relations
  - Align with the Basic Formal Ontology (Fig. 1)

Table 1: Roles played by individuals across health care and the life sciences and their relevant interests.

Role	Primary Interest
Strategic/portfolio manager	Assessing market opportunities
Project manager	Prioritizing activities and resources
Immunologist	Developing large molecules for therapeutic purposes
Cheminformatician	Analyzing chemical data and making predictions
Systems physiologist	Understanding the biological system
Cellular and molecular biologist	Assessing target viability
Medicinal chemist	Exploring structural patterns and properties of compounds
In vitro biologist	Predicting success of compounds to be tested in vivo
In vivo biologist	Performing toxicology and efficacy studies in animals
Clinical trial formulator	Designing clinical trials
Clinical decision support	Analyzing response to therapies
Sales and marketing	Driving sales
Primary care clinician	Treating broad range of patients
Specialty medical provider	Treating patients with specific diseases
Health plan provider	Providing insurance coverage to individuals
Statistician	Testing scientific hypotheses using statistical approaches

Figure 1: Alignment of TMO with BFO



Alzheimer's Disease Use Case

Significance

• 106.8 million people will have AD by 2050
• Relatively few medications available to treat the disease
• AD is influenced by a range of genetic, environmental and other factors

Data Sources

• ClinicalTrials.gov
• Diagnostic criteria for Alzheimer's
• Disease
• DailyMed
• Diseaseome
• DrugBank
• Medicare Formulary
• Patient records
• PharmGKB
• SIDER

Data Mappings

• Same identifier, e.g. Shared Names
• Third-party information, e.g. Bio2RDF
• Semantic link discovery tool, e.g. LinQuer, Silk

Data Queries using TMO

Physician

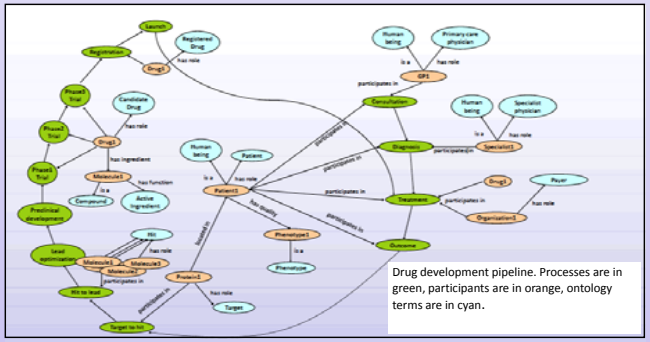
• How many patients experienced side effects while taking Donepezil?
• What is the diagnostic criteria for AD?
• Is Donepezil covered by Medicare Part D?
• Have any of my patients been treated for neurological conditions that might impact the diagnosis?

Clinical

• Are there other clinical trials that my patient can enroll in that are testing a drug with a different mechanism of action compared to the patient's current drug?
• Are there any patients missing the APOE4 allele who would therefore be a good candidate for treatment with Bapineuzumab?
• What active trials are ongoing that would be a good fit for Patient 1?
• Do I have suitable patients for an AD trial where the eligibility criteria includes females over the age of 55 with the APOE variant and low ADAS COG scores?

Discovery Research

• What genes are associated or implicated with AD?
• What biomarkers are associated or implicated with AD?
• An APOE variant is strongly correlated with AD predisposition. Is there a drug class that targets APOE?
• Which existing marketed drugs might be successfully used as an off-label treatment for AD?



Drug development pipeline. Processes are in green, participants are in orange, ontology terms are in cyan.

Future Work

• Further refine ontology
• Develop role-based user interface

Acknowledgements

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References

[1] http://translationalmedicineontology.googlecode.com
[2] http://www.ifomis.org/bfo