The AnalyzeMed Project

Implementing Pharmacogenomics Into Clinical Practice and Research

Rekha Divakaran, PharmD
MPS Candidate, Biomedical and Health Informatics
University of North Carolina at Chapel Hill
Variations in Drug Response
Pharmacogenomics

- The scientific discipline that understands how genetic variability affects drug treatment outcomes
- Becoming prevalent in clinical decision making
- Integration of genomic data into EHRs and health IT systems
What is the AnalyzeMed Project?

- Pharmacogenomics database
  - Focus on African Americans
- Seeks to gather a deeper understanding of the potentially adverse interactions between genes/polymorphisms and prescription medications/molecules
- A system potentially utilized by:
  - Clinicians
  - Researchers
  - Patients
Creating the Database

- ER diagram → Relational mapping and schema
- Backend:
  - Python with Flask framework
  - PyCharm program
  - SQLite
- Frontend:
  - HTML and CSS concepts
Data Collection

- Collection period: 4 to 6 weeks
- Conduct literature review for the following:
  - Molecule or Drug Name
  - Associated Genetic Polymorphism
  - ICD10 code
  - Description of the adverse effect
  - Link to the supporting literature
- Exclusions:
  - No discussion of African Americans
  - No molecule-polymorphism pair
  - No full text accessibility
# Data Collection

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Polymorphism</th>
<th>Description of interaction</th>
<th>ICD-10 code</th>
<th>Supporting Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tacrolimus</td>
<td>CYP3A5*1</td>
<td>With IR-tacrolimus, peak concentrations were higher in CYP3A5 expressers vs nonexpressers resulting in risk for toxicity and adverse effects; this effect is attenuated with the use of once daily tacrolimus.</td>
<td>T45.1X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/29162334/">https://pubmed.ncbi.nlm.nih.gov/29162334/</a></td>
</tr>
<tr>
<td>Atenolol</td>
<td>rs201279313</td>
<td>Associated with diastolic blood pressure response to beta blockers</td>
<td>T44.7X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/26729753/">https://pubmed.ncbi.nlm.nih.gov/26729753/</a></td>
</tr>
<tr>
<td>Atenolol</td>
<td>rs11931667</td>
<td>Associated with systolic blood pressure response to beta blockers</td>
<td>T44.7X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/26729753/">https://pubmed.ncbi.nlm.nih.gov/26729753/</a></td>
</tr>
<tr>
<td>Cisplatin</td>
<td>rs1800371</td>
<td>Enhances tumor cell death and overall efficacy of medication in cancer patients</td>
<td>T45.1X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/30115697/">https://pubmed.ncbi.nlm.nih.gov/30115697/</a></td>
</tr>
<tr>
<td>Warfarin</td>
<td>rs4889606</td>
<td>Increased dose requirement</td>
<td>T45.5X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/26135054/">https://pubmed.ncbi.nlm.nih.gov/26135054/</a></td>
</tr>
<tr>
<td>Warfarin</td>
<td>rs785696</td>
<td>Lower dose requirement</td>
<td>T45.5X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/25079360/">https://pubmed.ncbi.nlm.nih.gov/25079360/</a></td>
</tr>
<tr>
<td>Warfarin</td>
<td>rs78132896</td>
<td>Increased risk of warfarin associated bleeding</td>
<td>T45.5X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/30357299/">https://pubmed.ncbi.nlm.nih.gov/30357299/</a></td>
</tr>
<tr>
<td>Warfarin</td>
<td>rs1786199</td>
<td>Lower dose requirement</td>
<td>T45.5X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/20716240/">https://pubmed.ncbi.nlm.nih.gov/20716240/</a></td>
</tr>
<tr>
<td>Warfarin</td>
<td>rs9923231</td>
<td>Lower dose requirement needed to maintain INR within therapeutic range</td>
<td>T45.5X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/29218998/">https://pubmed.ncbi.nlm.nih.gov/29218998/</a></td>
</tr>
<tr>
<td>HCTZ</td>
<td>rs6947309</td>
<td>Elevates uric acid and associated with hyperuricaemia; increased risk for gout</td>
<td>T50.2X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/24512202/">https://pubmed.ncbi.nlm.nih.gov/24512202/</a></td>
</tr>
<tr>
<td>HCTZ</td>
<td>rs12279250, rs4319915</td>
<td>Associated with change in plasma fasting triglycerides</td>
<td>T50.2X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/23400010/">https://pubmed.ncbi.nlm.nih.gov/23400010/</a></td>
</tr>
<tr>
<td>Chlorothalidone</td>
<td>rs9943921</td>
<td>Increase in blood glucose levels</td>
<td>T50.2X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/29523524/">https://pubmed.ncbi.nlm.nih.gov/29523524/</a></td>
</tr>
<tr>
<td>Metoprolol</td>
<td>rs1024323</td>
<td>Faster blood pressure response perhaps due to lower beta-adrenoreceptor activity</td>
<td>T44.7X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/19119263/">https://pubmed.ncbi.nlm.nih.gov/19119263/</a></td>
</tr>
<tr>
<td>Metoprolol</td>
<td>rs2960306</td>
<td>Lower blood pressure response when variant rs1024323 co-exists</td>
<td>T44.7X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/19119263/">https://pubmed.ncbi.nlm.nih.gov/19119263/</a></td>
</tr>
<tr>
<td>Amiodipine</td>
<td>CYP3A4-1B</td>
<td>Faster blood pressure response</td>
<td>T45.1X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/1967160/">https://pubmed.ncbi.nlm.nih.gov/1967160/</a></td>
</tr>
<tr>
<td>Albuterol</td>
<td>SPARTA1-AS1</td>
<td>Better response to short acting beta agonists</td>
<td>T44.5X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/24418663/">https://pubmed.ncbi.nlm.nih.gov/24418663/</a></td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>SBF2</td>
<td>Increased risk for taxane induced peripheral neuropathy</td>
<td>T45.1X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/27732968/">https://pubmed.ncbi.nlm.nih.gov/27732968/</a></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>rs11391147</td>
<td>Associated with a 55.7% increase in LDL-C reduction</td>
<td>T45.6X5A</td>
<td><a href="https://pubmed.ncbi.nlm.nih.gov/25602539/">https://pubmed.ncbi.nlm.nih.gov/25602539/</a></td>
</tr>
</tbody>
</table>
Improving User Interface and Database Features

Proposed changes:

- Improve the overall visual appeal of the web application and database
- Have a filter and sort feature that displays search results by molecule name, polymorphism, most recent study, etc.
- Be able to search by drug class or other key words especially in cases where one is conducting a more general search
- The database should include a column containing pertinent information and/or recommendations that may affect clinical decision making
- Have a feature that allows a clinician or patient to input a patient's medication list and retrieve all relevant results
- Devise a way in which the web application can be connected directly to PubMed and conduct searches to retrieve supporting literature and automatically extract data to input into database
Medication List Search Feature
AnalyzeMed Pharmacogenomics Database

AnalyzeMed Project
Linking PubMed to AnalyzeMed

```python
author = 'Rekha Divakaran, rdarsh@live.unc.edu, Onyen = rdarsh'

import Bio
from Bio import Entrez, Medline
Entrez.email = 'ccbe@ge0ce4296b1f22dc12eef3956307680'
Entrez.email = 'rdarsh@live.unc.edu'

# search PubMed
pubmed_id_handle = Entrez.esearch(db='pubmed', term="african americans [MeSH] AND genetic polymorphism [MeSH]")

# handle
record = Entrez.read(pubmed_id_handle)

# how many records with this handle
for row in record["eQueryResult"]: if row["DbName"] == "pubmed": print(row["Count"])

pubmed_id_handle.close()

# ID records of all articles with above search terms
idlist = record["IdList"]

# Medline records
medline_handle = Entrez.efetch(db='pubmed', id=idlist, rettype='medline', retmode='text')
records = Medline.parse(medline_handle)

# save as list
records = list(records)
for article in records:
    print(article)
```
Moving Forward

- Easy accessibility
  - Working within CHIP server to manipulate and revise database
- Continue to collect more data
  - Other ethnic groups
- Clinician vs. Researcher Interface
  - Testing for Usability and Improvements to Features
- Direct information retrieval from PubMed
- Future EHR and Health IT system integration
  - Clinical decision support and improved health outcomes
Internship Experience

• Overall, it was a rewarding experience
  • Create a foundation for the future of pharmacogenomics and health IT
  • Opportunity to apply both pharmacy and informatics knowledge and skillset
    • Refine literature review, data collection, and Python skills
    • From a clinician perspective, propose changes valuable and beneficial to clinical practice and research

• Challenges
  • Delay in transition and on-boarding of technical aspects for project
  • Navigate and learn about creating a web application and database using Python, Flask, Entrez, etc.

• Lessons Learned
  • The process of learning and developing informatics knowledge and skillset will continue
  • Look forward to being a part of initiatives that continue to add value to healthcare technology and improve patient care and support clinical practice
Questions?