The Duke Center for Applied Genomics & Precision Medicine
1. Discovery and development of innovative approaches to disease detection, diagnosis, and prediction
2. Translation and implementation of them to improve patient outcomes
Programs in Applied Genomics

Programs in Precision Medicine

Center for Applied Genomics & Precision Medicine

Early Disease Detection and Diagnostics

Systems and Clinical Pharmacogenomics

Predictive Analytics

Biomarker Discovery

Clinical Sequencing

Major Discovery Programs: Exposures, the Exposome, Exposomics

- Exposome
  - Reactive electrophiles
  - Metals
  - Endocrine disrupters
  - Immune modulators
  - Receptor-binding proteins

- Internal chemical environment
  - Xenobiotics
  - Inflammation
  - Preventing disease
  - Lipid peroxidation
  - Oxidative stress
  - Gut flora

- Multi-dimensional Models of Health and Disease

- Time

Gene Expression

Protein Expression

Metabolite Expression

Phenotypic Data

APPLIED GENOMICS & PRECISION MEDICINE
Pathogen Exposures in Humans
Viral Challenge Studies (Rhino, RSV, H3N2, H1N1)

Healthy Volunteers → Standard Viral Challenge → 5 day observation

- **R** = Blood RNA expression profiling
- **P** = Blood/urine/saliva/breath proteomics profiling
- **M** = Blood/urine/saliva/breath metabolomics profiling

Physiologic Zones in the Challenge Model

- Pre-challenge
- Post-challenge
- A symptom post-challenge
- Sx symptom post-challenge

References:
- Zaas et al, Cell, Host and Microbe, 2009
- Chen et al, BMC Bioinformatics, 2011
- Huang et al, PLoS Genetics, 2011
- Bazot et al, BMC Bioinformatics, 2013
- Zaas et al, Science Translation Medicine, 2014
H3N2 Influenza: Early Detection Using A Phenotype-Associated Model

Ongoing Programs

- Predicting Health and Disease (PHD)
- Austere Environment Consortium For Enhanced Sepsis Outcomes (ACESO)
- Fieldable Tests for Early Viral Exposure Response (FEVER)
- Biochronicity
Systems Pharmacogenomics: Aspirin

Healthy Volunteers → Aspirin 325 mg → Repeat @ 3 hours & 14 days

= Nine platelet function non-COX1 assays

= RNA expression profiling (whole blood and PLTs)

Bayesian Factor Regression Modeling

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose</th>
<th>Outcome</th>
<th>n</th>
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<tbody>
<tr>
<td>Discovery</td>
<td>325mg/day</td>
<td>PFS</td>
<td>50</td>
</tr>
<tr>
<td>Validation</td>
<td>325mg/day</td>
<td>PFS</td>
<td>50</td>
</tr>
</tbody>
</table>

Voora et al, JACC 2013

Discovery: A set of co-expressed genes is associated with platelet function on aspirin

Factor 14:
- 72 probe sets
- 60 unique genes

Voora et al, JACC 2013
Transcripts associated with Death/MI

Adjustment variables:
- Sex
- Race
- Log(PLT)

Voora et al, JACC 2013

Biochronicity Pilot Study: Experimental Challenge Design

3X Daily Collections
Day 1 Day 2 Day 3 Day 4
Blood RNA Expression
Blood DNA Exomes
Blood Plasma Metabolomics
Self Reported Symptoms
Physiologic Monitoring
Cognitive Assessments

HRV Challenge

3X Daily Collections
Day 5 Day 6 Day 7 Day 8
Blood RNA Expression
Blood Plasma Metabolomics
Self Reported Symptoms
Physiologic Monitoring
Cognitive Assessments

Prototype Models
- Health Profiles
- Circadian Patterns
- Time-dynamic Classifiers
- Susceptibility Prediction

Analytical Modeling

DARPA
**Data+ / PDC / Accenture**

A collaborative research program with vertical and horizontal integration

- **Focus:** Improve Patient Care and Health System Efficiency
- EHR Centralization and Record Linking
- Returning Patient Patterns
- Pharmaco genotyping
- Appointment No-Show Prediction
- Clinical Risk Assessments

<table>
<thead>
<tr>
<th>Faculty and Clinician</th>
<th>Direct Research Efforts, Oversee Students</th>
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<tbody>
<tr>
<td>Graduate Students</td>
<td>Research, Oversee Undergraduates</td>
</tr>
<tr>
<td>Undergraduate Students</td>
<td>Research</td>
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</tbody>
</table>

- Data Science Seminar/Forum
- Clinical Seminar/Student Presentation Forum
- Occasional Social Gatherings
- Project Design and Planning
- Poster Session

**President Obama’s State of the Union Address:** January 20, 2015
The US Precision Medicine Initiative: 1 Million + Person Cohort

Genomics

EHRs

Technologies

Data Science

Patient Partnerships

Precision Medicine: Data Sciences Driven Opportunities

Time Series Data Repository

Sensor Data

FHH and EHRs

Exposure Data

Omics, Imaging Data

Social Network Data

Geo-spatial Data

Discovery

Modeling Simulation

Algorithms
Precision Medicine: A Cross Campus University-wide Opportunity

Duke’s Strengths: Precision Medicine

- Strength and differentiator: strong partnership of the scientific and clinical enterprises → expand to campus scientific expertise
- DCRI trials and MURDOCK samples, data, and outcomes
- Family health history/risk assessment platform and EMR integration and full DUHS deployment → student health?
- Diagnostics and devices at the point of care
- mHealth for patient and provider decisions
- Analysis of EMR data for predictive models
Duke’s Opportunities in Precision Medicine

- Cross institutional strategic initiative for student and faculty for data driven innovation in health and society
- Enhance health system/SOM and campus to sync with national objectives in precision medicine
- Engage of students, faculty, and staff campus wide
- Recruit to fill key gaps
- MEDx prototype
- Innovative training and education
- Public-partnerships
- Precision medicine accelerator