Advancing Disease Modeling in Animal-Based Research in Support of Precision Medicine: A Workshop

Linking Animal-Based Research to Precision Medicine: The Patient’s Perspective

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Personalized Medicine Coalition
“Trial-and-Error” Treatment
- Clinical symptom based taxonomy

Personalized Medicine Treatment
- Mechanism based taxonomy
Susceptibility, Mechanistic, and PGx biomarkers
-Risk, Efficacy, and Safety-

**Susceptibility biomarkers**
*Indicate the need for increased surveillance or prevention strategies*

- Flight planning

**Mechanistic biomarkers**
*Indicate that the candidate drug occupies the intended target*

- Navigation

**Pharmacogenetic (PGx) biomarkers**
*Indicate dose-dependent target modulation and/or pathway inhibition*

- Instrument landing

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*Can help predict risk of getting a disease*

*Can help select the right treatment*

*Can help to select the right dose and duration*
## Technology Advancement

<table>
<thead>
<tr>
<th>2005</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>$100 million</td>
<td>Cost of Sequencing a Human Genome</td>
</tr>
<tr>
<td>14</td>
<td>Personalized Medicine Products on the Market</td>
</tr>
<tr>
<td>1</td>
<td>Personalized Medicine U.S. Drug approvals that year</td>
</tr>
<tr>
<td>26 years (EGFR → cetuximab)</td>
<td>Example of Time Elapsed from Discovery to Market</td>
</tr>
</tbody>
</table>

42% of All Drugs in Development Are Personalized Medicines

73% of Oncology Drugs in Development Are Personalized Medicines

Technology Advancement

65,839
Genetic Testing Products Now on the Market
(as of September 2016)

(Cumulative growth)

More Than 5,500 New Genetic Testing Products Came to Market Between April 2015 and September 2016*

Data provided by: Concert Genetics. Available at concertgenetics.com.

*Methodological notes: Concert Genetics began publishing the first reliable data on the number of genetic testing products available in January of 2016. PMC has published a list of 127 genetic tests commonly associated with the 132 personalized medicines listed in the Appendix of this document at http://www.personalizedmedicinecoalition.org/Education Tests.
Technology Advancement

- Era of unprecedented discovery
- Ambitious major research projects around the world (publicly funded and private) to better understand human genetic variation, and elucidate more biomarkers that will further personalize medicine.

- U.S Precision Medicine Initiative
- All of Us Research Program
- Chinese Precision Medicine Initiative
- U.K.'s 100,000 Genomes Project
- The Qatar Genome Project
- IGSR: The International Genome Sample Resource
All of Us Research Program, Precision Medicine Initiative, NIH

We are building a research program of 1,000,000+ people

The mission of the All of Us Research Program is to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us.

Massive Cohort
Human subjects
Multiple types of data fields

Research focuses on the intersection of 3 factors:
- Environment
- Lifestyle
- Biology

Big Data
Discovery of Genetic Disease/Health Variants

• The “Big Data” study goal is to better understand human variation (especially genetic variants) and elucidate more biomarkers that will be useful in health care.

• However:
  - How genetic variants play a role in many common health conditions as well as some rare diseases, is largely unknown.
  - Should not look past research to elucidate mechanisms and molecular pathways of disease.
  - Clinical relevance of variants developed through animal-based and in vitro modelling studies.
  - Reproducibility concepts to improve understanding of clinical relevance of mechanistic studies and for pre- and co-clinical trials planning.
Comprehensive Research Strategies

Target variant discovery

Large shared Human Variant Database Studies

Traditional animal and in vitro modelling

Translational Research/Product Development

Reproducibility in humans concepts
Personalized Medicine: Has Turned a Corner

Challenges from Bench to Bedside

How do we Use Personalized Medicine In Patient Care?
Key Stakeholders

- Personalized Medicine
  - Researchers ✓
  - Dx Industry ✓
  - Rx Industry ✓
  - Providers
  - Payers
  - Regulators ✓
  - Patients

Access
Few have heard of personalized medicine and most do not know what it is.

- Just over 1 in 10 say their doctor talked to them about or recommended personalized medicine.
- Knowledge among those who have heard the term is shallow.
- Few associate it with genetic testing or genetic medicine.

Base: Total (N=1024)
Q5: I’m going to read you a list of words and terms. For each one, tell me if you have heard or read anything about that term before today. Here’s the first one: [ASK ALL ABOUT PERSONALIZED MEDICINE; FOR OTHER TERMS, SPLIT THE SAMPLE IN HALF AND ASK EACH RESPONDENT HALF OF THE TERMS. RANDOMIZE AND READ LIST; RECORD ALL HEARD RESPONSES.]
Consumers quickly see major benefits.

Knowledge to prevent illness and to pick the right treatments seen as major benefits.

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Major</th>
<th>Minor</th>
<th>Not</th>
<th>Not sure</th>
</tr>
</thead>
<tbody>
<tr>
<td>The information could help me and my doctor choose the treatment that is most likely to be effective</td>
<td>76%</td>
<td>15%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>The information could give me more control to prevent or treat illness</td>
<td>72%</td>
<td>18%</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>The information could help reduce or avoid treatment side effects</td>
<td>71%</td>
<td>20%</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>The information could result in less invasive procedures</td>
<td>69%</td>
<td>19%</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>The information could help avoid trial and error medicine</td>
<td>68%</td>
<td>19%</td>
<td>6%</td>
<td>6%</td>
</tr>
</tbody>
</table>

**Base:** Total (N=1024)

Q18-22: I'm going to read you a list of some of the benefits of personalized testing. For each one, tell me if that would be a major benefit, a minor benefit, or not a benefit for you personally. First, [READ ITEM] – is that a major benefit, a minor benefit, or not a benefit? [RANDOMIZE]
# Personalized Medicine: Impacts Care

## "Disease of the Blood"

<table>
<thead>
<tr>
<th>60 Years Ago</th>
<th>50 Years Ago</th>
<th>40 Years Ago</th>
<th>Today</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Disease of the Blood&quot;</td>
<td>Leukemia or Lymphoma</td>
<td>Chronic Leukemia</td>
<td>~38 Leukemia types identified:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute Leukemia</td>
<td>Acute myeloid leukemia (~12 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Preleukemia</td>
<td>Acute lymphoblastic leukemia (2 types)</td>
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<td></td>
<td></td>
<td></td>
<td>Acute promyelocytic leukemia (2 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Acute monocytic leukemia (2 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Acute erythroid leukemia (2 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Acute megakaryoblastic leukemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Acute myelomonocytic leukemia (2 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic myeloid leukemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic myeloproliferative disorders (5 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Myelodysplastic syndromes (6 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mixed myeloproliferative/myelodysplastic syndromes (3 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Indolent Lymphoma</td>
<td>~51 Lymphomas identified:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aggressive Lymphoma</td>
<td>Mature B-cell lymphomas (~14 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mature T-cell lymphomas (15 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Plasma cell neoplasm (3 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Immature (precursor) lymphomas (2 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hodgkin's lymphoma (5 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Immunodeficiency associated lymphomas (~5 types)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Other hematolymphoid neoplasms (~7 types)</td>
</tr>
</tbody>
</table>

5 Year Survival

- ~0%
- 70%


Source: Mara G. Aspinall, former President, Genzyme Genetics
“I’m here and I’m doing very well three years after my stage IV lung cancer diagnosis, and most of the time…my life feels pretty good….”

“I’ve been taking trips with my son that I never thought I would be able to take… what I’ve been trying to do is give him some good memories…and in the process, I’ve found that my life is more complete than ever before…”

- Deb Smith, EGFR+ Stage IV Lung Cancer Survivor
  (Tarceva clinical trial)
  (AZD9291 clinical trial)