Clinical Utility of Precision Medicine; Improving Quality & Reducing Costs Through Genomics

Jill Tapper, MHA, CG(ASCP)
Co-founder, Chief Operating Officer
Envision Genomics
Envision Genomics is committed to improving the quality & reducing the cost of healthcare by unlocking the utility and value of the genomic sequence for patient care.
**Envision Genomics** is not just a service provider – we are a comprehensive genomic medicine enabler.
~$40M to build infrastructure
Clinical care delivery is our strength

What do partner organizations get for working with Envision Genomics? A fully functioning genomic medicine program for rare & undiagnosed disease.

### Patient-Centric Resources
- **Genome Gateway** - online software tool for patient intake
- **Patient educational tools** - guidebooks, instructional/informational videos, etc.
- **An app** with illustrative findings from the patient’s clinical whole genome report

### Physician/Care Team
- **Genome Gateway Physician Portal** - Online software to assist physicians in collecting patient medical/family history & care planning can begin
- **Consultation with Envision in house genomics team**
- **Educational resources** - instructional guides, engagement support, educational sessions, symposia, conferences and other events

### Management
- **Data management tools/resources**
- **Economic models** and use cases from data sets collected across the network
- **Data dashboard** - decision support tool, quality metric monitoring
- **Access to a Clinical Partner Network** and genomic data resource
Exclusive License to Codicem (Codi) Analytics Platform
Build on existing enabling technology and expertise:

- Leading genomics research environment: NIH Undiagnosed Disease Network, Clinical Sequencing Exploratory Research (CSER), Oncology Research Information Exchange Network (ORIEN)
- Expertise in clinical application of genomic medicine: Smith Family Clinic, CAP/CLIA MDx lab
- We already practice medicine using genomic data derived knowledge
Evolution of Genomics & Genomic Medicine

2003
Human genome project completed

2005
2007
Innovation in technology support first rapid human resequencing

2010
First clinical genomics patient diagnosed & cured

2012
Genomic medicine hits mainstream

2013
International genomic medicine initiatives

2014
100's companies offering a variety of sequencing technologies (few to none in clinical whole genome)

2015
2016
Clinical genomics is standard of care in many rare disease settings

2016
US genomic medicine initiatives

2020
5%
35%
45%
5%
## Technology Timeline

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
<th>MDx</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>Exome sequencing</td>
<td>success</td>
</tr>
<tr>
<td>2012</td>
<td>First commercialized as a clinical test by Baylor College of Medicine</td>
<td>25%</td>
</tr>
<tr>
<td>2013</td>
<td>Envision founders showed WGS more powerful MDx</td>
<td>35%; price was too high</td>
</tr>
<tr>
<td>2015</td>
<td>HudsonAlpha acquires technological solutions; price now competitive</td>
<td>46%; 15% higher than WES</td>
</tr>
</tbody>
</table>
Exome sequencing

Whole Genome Sequencing
WGS Provides Superior Clinical Utility

Genome Coverage (nucleotides)

- **Genome**: ~98%
- **Exome**: ~2%
- **Array**: ~0.03%

### MDx per technology in patients with severe ID

- **Array**
  - Conclusive cause: 12%
  - No cause: 98%
  - Total: n = 1,489

- **WES**
  - Conclusive cause: 27%
  - No cause: 73%
  - Total: n = 100

- **WGS**
  - Conclusive cause: 42%
  - No cause: 58%
  - Total: n = 50

# of variants
- **Array**: ~5M
- **Exome**: ~18K
- **Array**: ~500

### Others Find the Same Benefits

<table>
<thead>
<tr>
<th>Approach</th>
<th>Disorder</th>
<th>n</th>
<th>MDx rate</th>
<th>Site</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WES</strong></td>
<td>Various</td>
<td>250</td>
<td>24.8%</td>
<td>Baylor College Medicine</td>
<td>24088041</td>
</tr>
<tr>
<td></td>
<td>Various</td>
<td>2000</td>
<td>25.2%</td>
<td>Baylor College Medicine</td>
<td>25326635</td>
</tr>
<tr>
<td></td>
<td>Intellectual disability</td>
<td>100</td>
<td>27%</td>
<td>Radboud, Nijmegen</td>
<td>24896178</td>
</tr>
<tr>
<td></td>
<td>Intellectual disability</td>
<td>1133</td>
<td>27%</td>
<td>DDD STUDY, UK</td>
<td>25529582</td>
</tr>
<tr>
<td></td>
<td>Various</td>
<td>3040</td>
<td>28.8%</td>
<td>GeneDx</td>
<td>26633542</td>
</tr>
<tr>
<td><strong>WGS</strong></td>
<td>Various - Pediatric</td>
<td>100</td>
<td>34%</td>
<td>Toronto</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ID – CSER</td>
<td>240</td>
<td>40%</td>
<td>HudsonAlpha</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intellectual disability</td>
<td>50</td>
<td>42-62%</td>
<td>Radboud, Nijmegen</td>
<td>24896178</td>
</tr>
<tr>
<td></td>
<td>Autism spectrum disorder</td>
<td>170</td>
<td>42.4%</td>
<td>HSC, Toronto</td>
<td>27525107</td>
</tr>
<tr>
<td></td>
<td>Hereditary spastic paraplegia</td>
<td>9</td>
<td>44%</td>
<td>Garvan Institute</td>
<td>27679996</td>
</tr>
<tr>
<td></td>
<td>Various – genetics</td>
<td>190</td>
<td>46%</td>
<td>HudsonAlpha</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Various - NICU</td>
<td>35</td>
<td>57%</td>
<td>Children’s Mercy, Kansas City</td>
<td>25937001</td>
</tr>
<tr>
<td></td>
<td>neurodevelopmental disorders</td>
<td>15</td>
<td>73%</td>
<td>Children’s Mercy, Kansas City</td>
<td>25473036</td>
</tr>
<tr>
<td></td>
<td>AD Polycystic kidney disease</td>
<td>28</td>
<td>86%</td>
<td>Garvan Institute</td>
<td>27165007</td>
</tr>
</tbody>
</table>
## Building the Economic Case for WGS

### The NICU Example

<table>
<thead>
<tr>
<th>Case - Infant</th>
<th>Diagnostic Success</th>
<th>Successes per 100 cases</th>
<th>Total Cost of Test(s)</th>
<th>Cost per Success</th>
<th>Avg Time for Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMA Alone</td>
<td>8.7%</td>
<td>9</td>
<td>$900</td>
<td>$10,345</td>
<td>21</td>
</tr>
<tr>
<td>CMA+Gene Panels</td>
<td>13.8%</td>
<td>14</td>
<td>$4,500</td>
<td>$32,609</td>
<td>96</td>
</tr>
<tr>
<td>CMA+Gene Panels +Exome</td>
<td>26.0%</td>
<td>26</td>
<td>$8,500</td>
<td>$32,692</td>
<td>145</td>
</tr>
<tr>
<td>CMA+Exome</td>
<td>34.7%</td>
<td>35</td>
<td>$4,900</td>
<td>$14,121</td>
<td>45</td>
</tr>
<tr>
<td>Envision CMA/Genome</td>
<td>45.0%</td>
<td>45</td>
<td>$6,500</td>
<td>$14,444</td>
<td>21</td>
</tr>
</tbody>
</table>
Reflex from WES to WGS cost consideration

- Based on reported MDx rates reflex to WGS would be required in ~70% of WES cases (i.e. 30% WES MDx success rate).

- Using $6,500 WGS and $5,000 WES per sample price points and for 100 patients (with 70% WES MDx rate) it would cost:
  - $650,000 for WGS first versus $955,000 for WES with WGS reflex.
  - 1.5x as much for the WES with a WGS reflex plan as compared to the WGS first approach.

- You need to have an 77% WES MDx success rate for this strategy to be financially sensible.
WGS provides significant benefits to all stakeholders versus the current SOC.
A rare disease is defined in the U.S. as one affecting fewer than 200,000 patients.

- >7,500 Types of rare disease are known
- 10% (350m people) Pop. has rare or rare form of disease
- 35% Deaths in 1st year are due to rare disease
- >7 yrs Average time until diagnosis
- 3 Average # of misdiagnoses/patient
- 8 Average # of diagnostic attempts

30% of children with a rare disease will not live to see their 5th birthday.
Significant Impact on Clinical Care Delivery

Rare disease touches every hospital system and every specialty
Initial target market: Rare disease cases in US Children's Hospitals

- >60% Rare disease patients receive conflicting treatment options
- 6.6x More expensive to treat a rare disease patient
- >10% Inpatient costs come from the 2% rare disease patients
- 92% physicians state these patients req more & longer office visits
- 95% Rare diseases have no FDA approved drug treatment
- 76% Physicians spent more time coordinating specialist care
Impact of WGS-based Genomic Medicine on Patient Care

1. End a Diagnostic Odyssey:
   In the case of Nic Volker (XIAP), >$7,000,000 in medical costs would have been avoided and Nic would still have his colon. If Nic’s genome was sequenced earlier on in his course of care, the cord blood transplant would have taken place sooner and resolved his issues years earlier.

2. Informed Treatment Decisions/Avoid Wrong Treatment:
   DNA diagnosis found a new variant causing liver failure and progressive neurological symptoms in a 3-month old patient. Neuro-decay would be lethal. Child died at 6-months. Savings >$500,000 for this patient’s family through one avoided liver transplant plus 180 days post-transplant care costs. Donor liver went to another child.

3. Inappropriate Therapeutic Treatment:
   Three children within a family have recessive atypical hemolytic-uremic syndrome due to mutations in DGKE NOT a complement problem meaning the children would not have responded to Eculizumab—the care team’s initial therapeutic inclination. Administration of Eculizumab costs ~$600,000 per child, per year. This family would have been burdened with ~$2.0M in costs each year for a drug that would have NO efficacy on the children’s health.

4. Delayed Treatment, Missed Chance to Cure:
   Patient presented with unusual learning delay and missing milestones. Standard of care test failed to detect a treatable biochemical defect. Three years later, clinical presentation revealed cause but permanant neurological damage was done during this time. Damage could have been abated or preventend if genome had been sequenced early on.
These 4 cases resulted in $9.3M in testing & other procedures due to not having an accurate/definitive MDx.

These examples occurred in the first 200 cases:
- Cost to do WGS on 200 cases: 200 x $6,500 = $1.3M
- Savings: $8M minimal savings (or 6x reduction)

These families are no longer going place to place looking for an answer.
Opportunities Beyond Rare Disease

- Cancer
- Cardiovascular Disease
- Disease Risk
- Executive Medicine/Wellness
- Population Health
- NICU/PICU
- Infectious Disease
- Pharmacogenomics
**Imprecision Medicine**

For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

1. **Abilify** *(aripiprazole)*
   - Schizophrenia
2. **Nexium** *(esomeprazole)*
   - Heartburn
3. **Humira** *(adalimumab)*
   - Arthritis
4. **Crestor** *(rosuvastatin)*
   - High cholesterol
5. **Cymbalta** *(duloxetine)*
   - Depression
6. **Advair Diskus** *(fluticasone propionate)*
   - Asthma
7. **Enbrel** *(etanercept)*
   - Psoriasis
8. **Remicade** *(infliximab)*
   - Crohn’s disease
9. **Copaxone** *(glatiramer acetate)*
   - Multiple sclerosis
10. **Neulasta** *(pegfilgrastim)*
    - Neutropenia

*Based on published number needed to treat (NNT) figures. For a full list of references, see Supplementary Information at go.nature.com/4dr78f."

**FDA-approved medications**

- 7% Affected by actionable pharmacogenes
- 93% Not affected by actionable pharmacogenes

**Prescriptions in the United States**

- 18% Affected by actionable pharmacogenes
- 82% Not affected by actionable pharmacogenes
Clinical Partner Network - Cracking the Code on Rare Disease

- Population Health Companies
- National Genomic Initiatives/Datasets
- Payor Datasets

Data Resource "Intelligent Hub"

- Research Opportunities
- Tool Development
- Diagnoses/Disease Understanding
- Commercial Development Opportunities (Pharma, Biotech)
Thank You

info@envisiongenomics.com
jtapper@envisiongenomics.com
envisiongenomics.com