Thursday HPP Day Post-Congress Program
October 4, 2018

Stephen Pennington
UCD Conway Institute, School of Medicine
University College Dublin
Protein Biomarkers in Practice
Individual Markers
Imprecision medicine

Schork NJ. Nature 2015;520:609–611
Improved precision medicine

New protein based tests will be complimentary to genomics and add value.
New Era of Precision Medicine

• Precision healthcare and clinical diagnostics will reflect:
  – the heterogeneity of 'individual' diseases, and
  – the variability of individual patients – including their co- and multi-morbidities

• Environmental exposures and lifestyle behaviors influence health.
  – New diagnostic tests will have the capability of incorporating these important factors
Proteogenomics

Welcome address: https://youtu.be/Szi6Y1W3HxM
Biden’s speech: https://youtu.be/IUmSFLjqWaw
VP Biden's Messages

Speak clearly – engage with public/patients
Change your culture
Have impact – do something

**Do it now**

You (we) have a huge opportunity and responsibility

“Knowing is not enough, we must apply
Willing is not enough, we must do”

Johann Goethe
Multiple Markers
How can we discover, develop and deliver protein biomarkers of clinical utility & impact?
Protein Biomarker Development

Discovery → Confirmation → Evaluation → Approval & Adoption

- Discovery
- Confirmation
- Evaluation
- Approval & Adoption

- Sample Numbers
- Statistical Methods

- Clinical Test
- Regulatory Authorities
- Clinician Adoption
- Impact Measurement
Protein Test Development

- Biomarker Candidate Panel
- Analytical Validation
- Clinical Validation
- Clinical Utility

Clinical Test
Ascent in Stages
Some Key Questions

For use who does:
  Implementation?
What samples?
How to promote awareness and use?
What markers?
Who:
How many?
Uses?
How to combine?
Pays?

Which platform?
Regulatory path?
Discovery
Clinical Evaluation?
Verification
Statistical Methods?
Use
Analytical performance?
Cost?
Throughput?
Healthcare impact?
“It’s simple”

Dean Griffiths, Cambridge Consultants 2014
Need

Solution

Scale it

Dean Griffiths
Some Key Questions

- Who does:
  - Implementation?
  - Awareness?
  - Use?
  - What?
  - Use?
  - Pays?
  - Regulatory?
  - Healthcare impact?

- What samples?
  - What markers?
  - How many?
  - How to combine?

- Clinical Evaluation?
  - Statistical Methods?

- Which platform?
  - Discovery
  - Verification
  - Use
  - Analytical performance?
  - Cost?
  - Throughput?

- START at the END
- Some Key Questions

- Who pays:
  - Implementation?
  - Awareness?
  - Use?
  - What?
  - Use?
  - Pays?
  - Regulatory?
  - Healthcare impact?

- Clinical Evaluation?
  - Statistical Methods?

- Which platform?
  - Discovery
  - Verification
  - Use
  - Analytical performance?
  - Cost?
  - Throughput?
Start With Unmet Clinical Needs

Identify the clinical need and the clinical test (that will address the need)

Develop and evaluate against intended use
Evolution of Translational Omics

Lessons Learned and the Path Forward

Committee on the Review of Omics-Based Tests for Predicting Patient Outcomes in Clinical Trials

Board on Health Care Services
Board on Health Sciences Policy

Christine M. Michiel, Sharyl J. Nass, and Gilbert S. Omenn, Editors

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<table>
<thead>
<tr>
<th>Clinical Biomarker Use</th>
<th>Clinical Objective</th>
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<tbody>
<tr>
<td>Disease risk stratification</td>
<td>Assess the likelihood that disease will develop (or recur)</td>
</tr>
<tr>
<td>Screening</td>
<td>Detect and treat early-stage disease in the asymptomatic population</td>
</tr>
<tr>
<td>Diagnosis/Differential Diagnosis</td>
<td>Definitively establish the presence and precise description of disease</td>
</tr>
<tr>
<td>Classification&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Classify patients by disease subset</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Estimate the risk of or the time to clinical outcomes.</td>
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<tr>
<td>Prediction/treatment stratification&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Predict response to particular therapies and choose the drug that is mostly likely to yield a favorable response in a given patient.</td>
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<tr>
<td>Therapy-related risk management</td>
<td>Identify patients with a high probability of adverse effects of a treatment</td>
</tr>
<tr>
<td>Therapy monitoring&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Determine whether a therapy is having the intended effect on a disease and whether adverse effects arise</td>
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<tr>
<td>Posttreatment monitoring</td>
<td>Early detection and treatment of advancing disease or complications</td>
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<sup>a</sup> Companion diagnostic biomarkers include features from several of these categories. These tests identify whether an individual’s molecular profile associated with a disease pathophysiology is likely to respond favorably to a particular therapeutic. Examples include KRAS– cetuximab, HER2– Herceptin, and estrogen receptor– tamoxifen.

<sup>b</sup> Dose optimization is a subset of this category.

SOURCE: Adapted from IOM (2007, 2010).
Identify the Mountain
Psoriatic Arthritis (PsA)
Some Key Challenges in PsA

1. We don’t understand the *mechanism* of bony changes in PsA
2. There are no diagnostic criteria or laboratory tests to discriminate PsA from RA or other arthropathies
3. We don’t know how to predict clinical outcome (e.g. radiographic damage)
4. Lots of new treatments but we have no way of knowing which patient will respond to which treatment
Next steps

Organized exclusively for educational and scientific purposes, specifically to facilitate sharing of information related to psoriasis and psoriatic arthritis, networking among different medical disciplines that see & treat psoriasis and psoriatic arthritis patients.

To enhance research, diagnosis and treatment of psoriasis and psoriatic arthritis

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
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<tbody>
<tr>
<td>Dermatologists</td>
<td>192</td>
</tr>
<tr>
<td>Rheumatologists</td>
<td>372</td>
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<tr>
<td>Non-medical scientists</td>
<td>23</td>
</tr>
<tr>
<td>Patient Research Partners</td>
<td>21</td>
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<tr>
<td>Industry</td>
<td>206</td>
</tr>
<tr>
<td>Others</td>
<td>41</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>855</strong>*</td>
</tr>
</tbody>
</table>

(1) Biomarkers of development of PsA in patients with psoriasis
(2) Biomarkers predicting treatment response in patients with early PsA
(3) Biomarkers of disease Activity in PsA
A Recipe for Biomarker Success?

• Identify clinical need
• Validate clinical need
• Conceive product to fulfill clinical need
• Design test to be 'fit for purpose'
• Evaluate potential clinical value of test
• Identify monetary value and reward (and the route by which it may be achieved)

• And then begin……..
Bottom Up
Assemble Kit

Top Down
Identify Challenge
Bottom Up
Assemble Kit

Top Down
Identify Challenge
(Choose Route)
Some thoughts

Medics

Clinical Labs

Science