Immunosignatures: A Tool for Managing Disease

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Disclosure: N. Woodbury and S.A. Johnston are founders of HealthTell, Inc.
Changing the Healthcare Paradigm: Systems management vs. crisis management

A process engineer at a chemical manufacturing plant would not wait until this happened before intervening. Why do we?

We need both different tools and different thinking to apply process control principles to medicine.
Detecting Cancer Early Increases Survival

- Colon Cancer
- Pancreatic Cancer
- Prostate Cancer
- Lung Cancer
- Melanoma
- Breast Cancer
Immunosignatures

Downloading the Information From Your Immune System...

http://dxline.info/dictionary/finger-stick
http://www.turbosquid.com/3d-models/maya-mailbox-mail-box/640318
Characteristics of Immunosignatures

• Simple
  – Dilution is the only sample preparation

• Minimally invasive
  – One drop of blood dried on a piece of filter paper is all that is required. Can also use saliva

• Comprehensive
  – The peptide sequences are designed to profile antibody molecular recognition for any disease

• Can be used for animals as well as people
  – Just a matter of changing the secondary Ab

• Inexpensive at scale
  – Array technology based on electronics fabrication and the cost/volume scales as such
• High volume/low cost arrays and assays
• High resolution, multi-disease discrimination
• Building biological assays with electronics industry precision
Using Electronic Fabrication Equipment to Make Millions of Molecular Sensors

Downstream processing done entirely with commercially available liquid handlers and readers for microscope slides
The Commercial Effort is for Chronic Disease

- Current targets are primary cancers
- Multiple diseases per assay
- Adding a disease is just an informatics change
- Expect to launch first product (“One Test”) in 2016
- Probably start as either supportive diagnostic or interval testing
- Eventually health monitoring
Relating Signature to Pathology

100% accurate detection training and testing on samples taken years apart

Not only can immunosignaturing detect the brain tumor, it can distinguish accurately between the common types of brain tumors


Collaborator: Adrienne C. Scheck, BNI
Peptide Sequence Analysis: Brain cancer (GBM)

Peptide sequences from GBM immunosignaturing match frameshift sequences from cancer expressed sequence tag (EST) libraries.
Simultaneous Detection of 5 Cancers

- 5 cancers tested simultaneously
- 20 training samples/20 test samples
- Externally blinded

## Monitoring for 5 Cancers

<table>
<thead>
<tr>
<th>disease (SVM)</th>
<th>BC</th>
<th>GBM</th>
<th>EC</th>
<th>MM</th>
<th>ND</th>
<th>PC</th>
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<tr>
<td>Breast cancer</td>
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<tr>
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<tr>
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<td>Non-Disease</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>20</td>
<td>2</td>
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<tr>
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<td><strong>Sensitivity</strong></td>
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<td>0.95</td>
<td>1</td>
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<tr>
<td><strong>Specificity</strong></td>
<td>0.98</td>
<td>0.99</td>
<td>1</td>
<td>0.99</td>
<td>0.98</td>
<td>1</td>
</tr>
</tbody>
</table>

Example: Diagnosing Valley Fever
A Sonoran Desert Pathogen

- 90 blinded samples from patients presenting at the clinic
- Zero false positives (100% specificity)
- Zero false negatives (100% sensitivity)
- 100% accuracy on patients mis-diagnosed by standard methods

Collaborator: John Galgiani
Univ. of Arizona

Simultaneous Detection of 6 Infectious Diseases

Sensitivity Comparison vs. ELISA

Increased Sensitivity Allows Pre-symptomatic Detection of Infections

**Infected Mice: A/PR8/34 IgG ELISA**

**Infected Mice: A/PR8/34 IgG Immunosignaturing**

- **Absorbance (405 nm)**
- **Dilution**

Legend:
- Naive
- Day 3
- Day 7
- Day 21
Long Term Vision

• Regular monitoring
• Self normalized
• The more people the use it the better it gets
• Early detection of disease
• Enables the development of early intervention drugs
Potential Short Cut

• Do it in companion animals
• Many fewer restrictions
• Can often get people to pay to be in trials
Pre-IDE Submission to FDA

• Submission was based on Dengue Fever diagnostics
• Used DENV Detect™ IgM Capture ELISA as predicate
• ELISA was accepted as valid predicate
• Path opened for use of historical samples to validate
• So far no significant roadblocks identified
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