Clinical/Research Interface
From whence we came

• Initially *Miscellanea Group*
  – Disconcerting and uninviting in its vagueness
• Initial discussions were IRB-centric
  – Escaped that trap!
• Evolved…to

  Research/Clinical Interface
Our goal:
to explore the boundaries between research and clinical practice

• What/where are the boundaries?
• How and why they overlap.
• What do we know about each side and the middle?
• Is genomic information different than other emerging clinical information/technology?
• Is there a relevant research agenda to better understand how to bi-directionally navigate across this space?
Why this exploration is relevant

• Because the boundary threatens to be a gap
• We are not where we wish we would be:
Where we wish we were

- Knowledge-driven ecosystem
  - Open sharing of ideas and problems
  - Complementary efforts
    - Close collaboration between clinicians, researchers and patients
  - Maximizing output
  - Advances in health
  - Everyone loves and supports us
Where we wish we were

• Clinicians collaborating with researchers to identify the problems that need attention
  – Robust clinical contextualization
• Researchers working on those problems and course correcting in concert with clinicians
• Clinicians anxiously awaiting research findings and actively incorporating into care
• Quality processes for communicating appropriate results
• Seamless bidirectional flow between research and clinical
Bi-directional Flow
Remember important modulators:

- Patients
- Advocacy groups
- Local institutional pressures
- A variety of industries
- Research funding
- Laws and strong suggestions
The reality

- Warp speed from karyotyping to WG or WE sequencing and still moving

- Difficulty keeping up with the technology and avalanche of uncertain information
  - Doable for geneticists and their close friends
  - Many non-geneticist clinicians and researchers feel left in the dust
The reality

• “Anyone who thinks they understand it all is delusional”

Research-clinical interface committee member with first name of Marc
A few ‘gap-inducers’

• Presentation of genetic data is not user friendly for most
• Uncertainty of data and analyses
  • Esp difficult when binary decision of ‘act/don’t act’ is the desired outcome
• Concern that genetic ‘oh wows’ fail to consider the importance of environment and clinical setting
  – Lack of clinical conceptualization
  – Have little to no relationship to the pressing problems (or needs) of clinicians
A few ‘gap-inducers’

• Impression that the focus is on HOW to get genetic info into the clinic with not enough attention to SHOULD, WHEN etc.
• The evolving role of the patient
  • Expectations: e.g., DTC, social media
  • Medical record transparency
The gap

• Must better define the gap
• Must better understand both sides of the gap
  – Who lives there?
  – How do they think?
  – Can they see the other side of the gap?
  – How have others traversed similar gaps?
The gap we must avoid

WOW!
Look what we discovered!
The gap we must avoid

WOW!
Look what we discovered!

And you think I care because…
# The clinical context gap

*(exaggerated extremes)*

<table>
<thead>
<tr>
<th><strong>Bench Researchers</strong></th>
<th><strong>Clinicians</strong></th>
</tr>
</thead>
</table>
| Limited or no experience of interacting with patients: do not appreciate complexity of:  
  - obtaining specimens/data  
  - communicating risk | “Fiduciary responsibility”  
  Overwhelmed with questions from patients re:  
  - use of their ‘stuff’  
  - genetics  
  Role of information filter |
| May over-rate their own research finding and lack ‘big-picture’ context | Await guidance from institution/subspecialty societies/guidelines.  
  Suspicious of individual ‘oh wows’ |
| Oversimplified view of what it takes (or means) to create new practice knowledge | Difficulties ordering, understanding and being reimbursed for genetic tests or genetic-based therapies |
The clinical context gap
(exaggerated extremes)

<table>
<thead>
<tr>
<th>Bench Researchers</th>
<th>Clinicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>The scope of information is a benefit</td>
<td>I order specific tests to rule in/out candidate diagnoses that are relevant to my patient</td>
</tr>
<tr>
<td></td>
<td>Uninvited information is not welcome</td>
</tr>
<tr>
<td>WGS can limit diagnostic crusades</td>
<td>Uninvited information causes diagnostic crusades</td>
</tr>
<tr>
<td></td>
<td>Who will provide the pre-testing counseling as well as the post-testing counseling</td>
</tr>
<tr>
<td></td>
<td>(remember, 72% of us report poor genetic understanding)</td>
</tr>
<tr>
<td>Basic Researchers</td>
<td>Clinicians</td>
</tr>
<tr>
<td>-------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Urgency to move research findings forward – perhaps into clinical care</td>
<td>Waiting for robust evidence for change – little time/energy or expertise to assess/implement ‘oh wows’</td>
</tr>
<tr>
<td>Urgency to ‘prove’ importance in order to obtain and sustain funding. Possible push for IP – note role of institutions.</td>
<td>Belief that hands tied by regulations, legal issues</td>
</tr>
<tr>
<td>‘On to the next thing.’”</td>
<td>The “next thing” is another patient in 15 minutes.</td>
</tr>
</tbody>
</table>
# The genetic info gap

*(exaggerated)*

<table>
<thead>
<tr>
<th>Researchers</th>
<th>Clinicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>This is the most important information – use it NOW! Genomics is different</td>
<td>Genetics is over-hyped. (Soccer quote)</td>
</tr>
<tr>
<td></td>
<td>If that important it would be required</td>
</tr>
<tr>
<td></td>
<td>Genomics is different</td>
</tr>
<tr>
<td>A one-time WGS – and you are set for the life of the patient!</td>
<td>You expect me to use test results from 20 years ago? Can’t find anything</td>
</tr>
<tr>
<td></td>
<td>from that long ago!</td>
</tr>
<tr>
<td></td>
<td>Easier to repeat it.</td>
</tr>
<tr>
<td></td>
<td>Liability concerns for omission or commission</td>
</tr>
<tr>
<td></td>
<td>Criteria for placement into the medical record</td>
</tr>
</tbody>
</table>
## The ‘bad press’ gap (exaggerated)

<table>
<thead>
<tr>
<th>Researchers</th>
<th>Clinicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinicians know nothing about genetics</td>
<td>Researchers have no concept of clinical care – there is a process for assessing new findings. Not all findings are earth-shattering</td>
</tr>
<tr>
<td>We need to develop ‘Genetics for Dummies’ courses</td>
<td><em>Personalized medicine</em>…this is what we do. It is off-putting to hear geneticists think they have discovered the concept. “So do I practice impersonal medicine?”</td>
</tr>
</tbody>
</table>
Suggestions for Next Steps

• Identify and collaborate with others in this space  
  – See last slide
• Better understand evidentiary medicine and the process for “routinization”  
  – Evidentiary piece – what standards?  
  – How triaged?  
  – How communicated  
  – Development of guidelines
• Needs assessments for clinicians
• Needs assessments for the “system”
• Patient expectations in clinical care and research  
  – Are they different? (how?)
Suggestions for Next Steps

• Better understand the medical chart and process
  – Legal and/or institutional considerations
  – Downstream implications (e.g., access by others)

• Maximize collaborations for ‘clinical-trial-genomics’
  – Provide different opportunity than observational genetics
Who else is in this space?

<table>
<thead>
<tr>
<th></th>
<th>CSER</th>
<th>Return of Results Consortium</th>
<th>eMERGE</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Informed consent</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Actionable variants</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td></td>
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<tr>
<td>Sequencing</td>
<td>YES</td>
<td></td>
<td>YES</td>
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<tr>
<td>Phenotyping</td>
<td>YES</td>
<td></td>
<td>YES</td>
<td>YES</td>
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<tr>
<td>Electronic records</td>
<td>YES</td>
<td></td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Instruments &amp; Measures</td>
<td></td>
<td>YES</td>
<td></td>
<td></td>
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