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

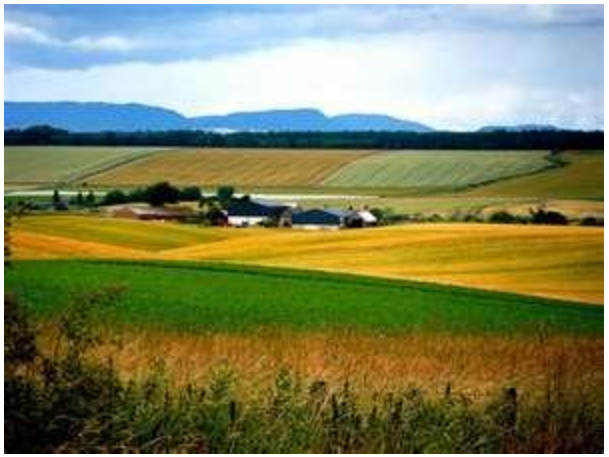
Our goal:
to explore the boundaries between research and clinical practice

- 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



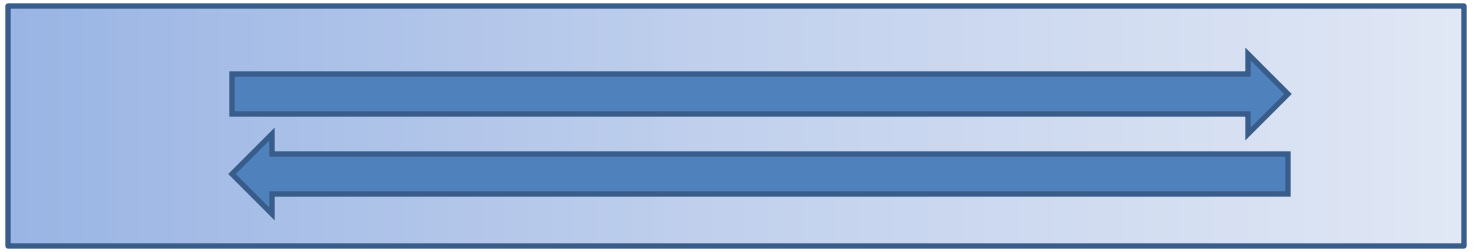
- Knowledge-driven ecosystem
  - Open sharing of ideas and problems
  - Complementary efforts
    - Close collaboration between clinicians, researchers and patients
  - Maximizing output
  - Advances in health
  - Everyone loves and support$ us

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

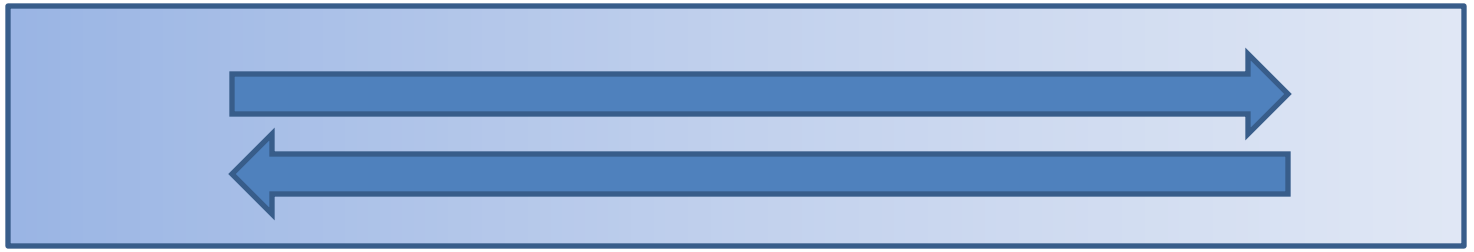
Bi-directional Flow

Research Clinical



Bi-directional Flow

Research Clinical



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

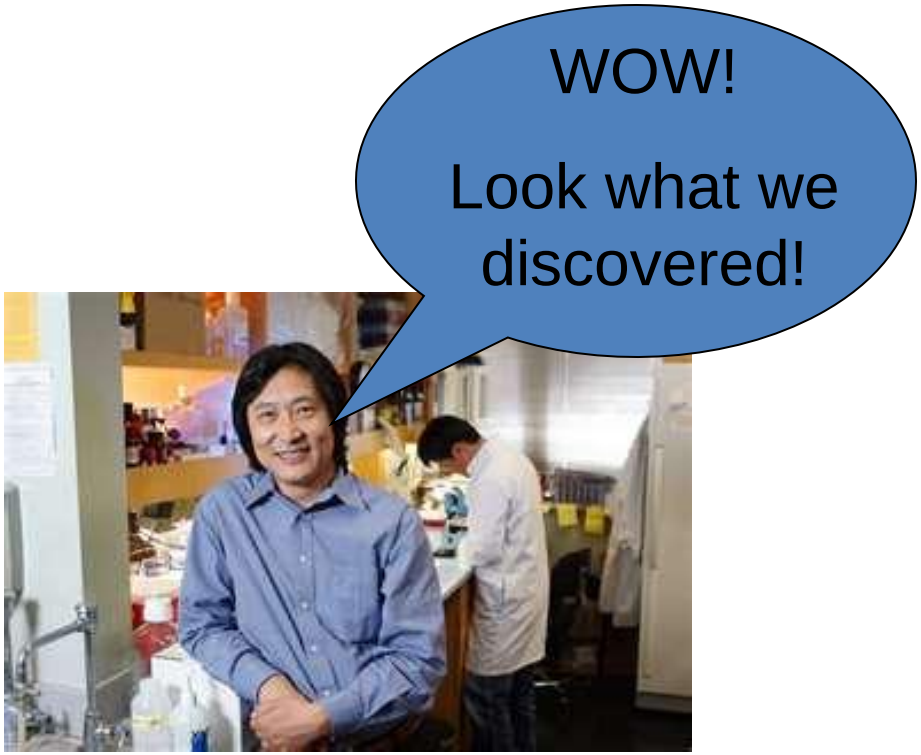
A few ‘gap-inducers’

- 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

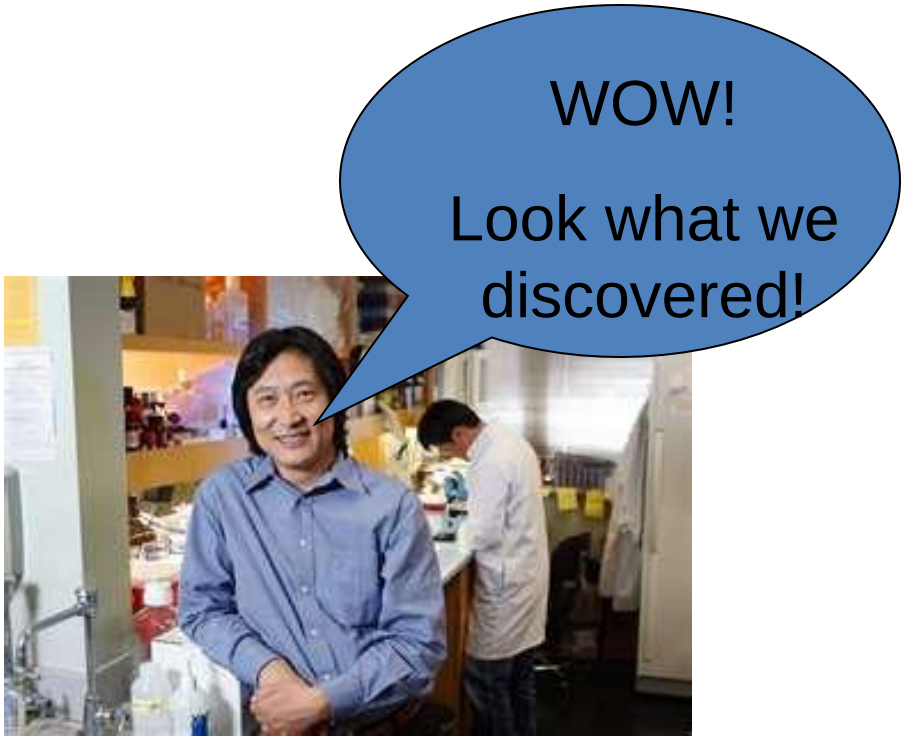
The gap

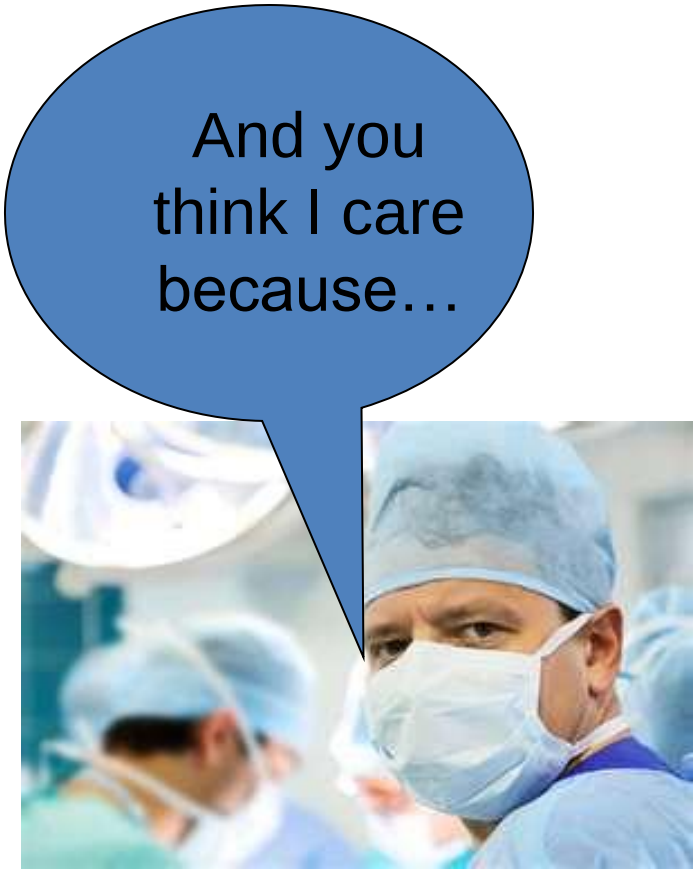
- Must better define the gap
- Must better understand both sides of the gap
  - Who lives there?
  - How do they think?
  - Can they see the other side of the gap?
  - How have others traversed similar gaps?

The gap we must avoid



The gap we must avoid





The clinical context gap

(exaggerated extremes)

Bench Researchers	Clinicians
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)

Bench Researchers	Clinicians
The scope of information is a benefit	I order specific tests to rule in/out candidate diagnoses that are relevant to my patient Uninvited information is not welcome
WGS can limit diagnostic crusades	Uninvited information causes diagnostic crusades
	Who will provide the pre-testing counseling as well as the post-testing counseling (remember, 72% of us report poor genetic understanding)

The motives gap

(exaggerated extremes)

Basic Researchers	Clinicians
Urgency to move research findings forward – perhaps into clinical care	Waiting for robust evidence for change – little time/energy or expertise to assess/implement ‘oh wows’
Urgency to ‘prove’ importance in order to obtain and sustain funding. Possible push for IP – note role of institutions.	Belief that hands tied by regulations, legal issues
‘On to the next thing.”	The “next thing” is another patient in15 minutes.

The genetic info gap

(exaggerated)

Researchers	Clinicians
This is the most important information –use it NOW! Genomics is different	Genetics is over-hyped. (Soccer quote) If that important it would be required Genomics is different
A one-time WGS – and you are set for the life of the patient!	You expect me to use test results from 20 years ago? Can't find anything from that long ago! Easier to repeat it.
	Liability concerns for omission or commission Criteria for placement into the medical record

The ‘bad press’ gap

(exaggerated)

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

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?

	CSER	Return of Results Consortium	eMERGE	PAGE
Informed consent	YES	YES	YES	
Actionable variants	YES	YES	YES	
Sequencing	YES		YES	
Phenotyping	YES		YES	YES
Electronic records	YES		YES	YES
Instruments & Measures		YES		