

What is translational bioinformatics?

- Translational bioinformatics
 - Development of analytic, storage, and interpretive methods
 - Optimize the transformation of increasingly voluminous genomic and biological data into diagnostics and therapeutics for the clinician
- Includes
 - Research on the development of novel techniques for the integration of biological and clinical data
 - Evolution of clinical informatics methodology to encompass biological observations
- End product of translational bioinformatics
 - Newly found knowledge from these integrative efforts that can be disseminated to a variety of stakeholders, including biomedical scientists, clinicians, and patients

Why translational bioinformatics?

Eight reasons

1. There is an increasing call for translational medicine: Universities, Congress, NIH, and elsewhere: “What did we get for our money?”
2. Many tools now exist that enable the large-scale parallel quantitative assessment of molecular state
 - Premier example is RNA expression detection microarray
 - High-bandwidth measurement tools; not just big, but nearly comprehensive
 - Low-cost
 - Quantitating every gene in the genome: ~\$300 per sample
 - Measuring 1.8 million human polymorphisms: ~\$300 per sample
 - Knocking out every gene in the worm: ~\$4500 for the kit



Why translational bioinformatics?

3. Incredible amounts of publicly-available data

- GenBank: Hundreds of organisms have been completely sequenced, including man and mouse; 260,000 species have had SOME sequence measured
- GEO has 236,000 samples today from 9080+ experiments
- ArrayExpress has 118,000 samples today from 6650+ experiments
- EBI Pride: 7900+ samples yielding over 7.4+ million mass spectra
- NCBI dbGAP (genotype and phenotype): 25 genetic studies with 50,000+ human samples
- Doubling or tripling in size each year

Why translational bioinformatics?

4. New community of sharing: tools, data, publications
 - Journals require this; NIH is starting to require this
 - Along with communities comes contention and agreement: “What is the name for this gene?”
 - Increasing standardization in names, abbreviations, codes, and file formats
 - Where standards have not been reached, there is at least the understanding that it must be reached

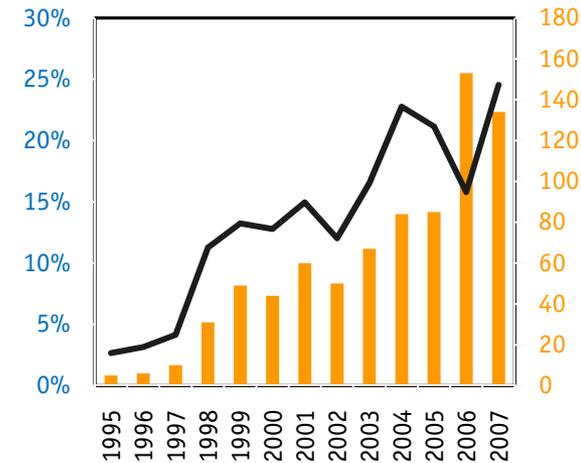
Why translational bioinformatics?

5. Change in role of the bioinformatician from service provider to question asker
 - Each high-bandwidth measure yields sizeable amount of raw data
 - Distilling raw data and filtering out noise through the proper use of bioinformatics
 - Bioinformatics clearly plays a role in the storage, retrieval, and sharing of measurements, and relating to clinical outcomes
 - However, role for bioinformatics in genomic medicine is now beyond that of providing a service, and in enabling new and interesting questions to be asked in biomedical research
 - A researcher, whether clinical, experimental, or theoretical, can ask questions no one else can ask today, when powered by bioinformatics

Why translational bioinformatics?

6. Increased funding for this line of work

- NIH Roadmap started in May 2002; Dr. Zerhouni's roadmap for medical research in the 21st century
- "At no other time has the need for a robust, bidirectional information flow between basic and translational scientists been so necessary."
- Three major themes
 - New Pathways to Discovery: addresses Bioinformatics and Computational Biology
 - Research Teams of the Future: cell biologists and computer programmers working to accelerate movement of scientific discoveries from the bench to the bedside
 - Re-engineering the Clinical Research Enterprise: transforming basic research discoveries into drugs, treatments, methods for prevention.
- Clinical and Translational Science Award (CTSA): 60 funded at ~\$30M
 - RFA mentions "informatics" 38 times
 - Recognition that the problem of translational medicine will not go away without the help of informatics



Why translational bioinformatics?

7. It's incredible how much bioinformatics you need to know just to read the *New England Journal of Medicine*!
 - "Shrunken centroid", "Unsupervised cluster analyses", "gene-expression signature"
 - "global scaling, or normalization"
 - "q value for each gene represents the probability that it is falsely called significantly deregulated"
 - "class-prediction analyses", "10-fold cross validation"
 - "implemented in the PLINK tool set as a Cochran-Mantel-Haenszel stratified analysis"

Doctors are not at all trained to know about this.

8. Paucity of people trained to make use of these resources

Think out of the box in looking for students: MD/PhD, medical fellows, etc.



Summit on Translational Bioinformatics
March 10-12, 2008
San Francisco, California

First annual meeting to explore topics in translational bioinformatics

Sponsor: **American Medical Informatics Association (AMIA)**

Co-Sponsor: **International Society for Computational Biology**



Track Chairs: **Atul Butte** (Stanford), Chair; **Yves Lussier** (U Chicago);
Marco Ramoni (Harvard Med); **Neil Sarkar** (MBL); **Olga Troyanskaya** (Princeton)

InterContinental Mark Hopkins Hotel, San Francisco, California

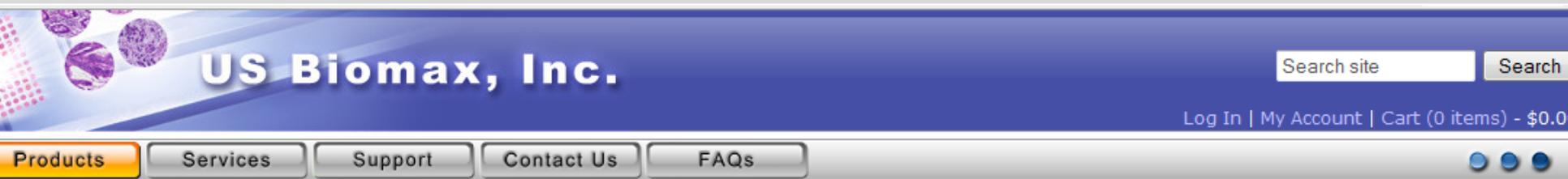
Keynote: **Alan Krensky**, Director, Office of Portfolio Analysis
and Strategic Initiatives (OPASI) and
Deputy Director, National Institutes of Health



www.amia.org/meetings/stb08/
www.amia.org

Discussion points

- Need for tools is diminishing
 - Academic versus commercial, commercial versus outsourcing
 - Is it academic to build a database-backed web-site?
Academic to build infrastructure to integrate databases?
 - Is it still useful to improve on certain methods (gene expression differences, sequence search, etc)?
 - Importance of finding new questions to ask, not just answering the old questions more efficiently.
 - My heroes are those in CS who enable new questions, and even ask those questions, driving novel findings
- What is the difference between KIAA12345 and p53?
 - Is it heresy to have some domain expertise and interest?
 - What is easy for collaborators for to validate, and what is hard?
- How to outsource back the biology?
 - Public availability of data empowers computationalists
 - How to outsource the validation?



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Colon Tissue Microarray

Tissue Arrays

Cat No.	Tissue Microarray Description	Cores1	Cases2	Slides3	Unstained4	Trial5	H&E6	C
BC05011	Multiple types of colon carcinoma tissue array, replaced by CO804	80	80	1	\$195 ●	\$55 ●	\$195 ●	<input type="checkbox"/>
BC050112	Colon metastatic carcinoma tissue array	63	23	1	\$195 ●	-	\$195 ●	<input type="checkbox"/>
BC05012	Colon carcinoma (multi-tissue combined panel) tissue array	72	70	1	\$195 ●	-	\$195 ●	<input type="checkbox"/>
BC05021	Colon adenocarcinoma (combination of adjacent and normal) tissue array, no overlapping with BC05022	54	18	1	\$195 ●	-	\$195 ●	<input type="checkbox"/>
BC05022	Colon adenocarcinoma (combination of adjacent and normal) tissue array, no overlapping with BC05021	54	18	1	\$195 ●	-	\$195 ●	<input type="checkbox"/>
BC05023 NEW!	Colon adenocarcinoma (combination of adjacent and normal) tissue array	54	18	1	\$195 ●	\$55 ●	\$195 ●	<input type="checkbox"/>
BN05011	Normal colon tissue (multi-sites) array	63	23	1	\$120 ●	-	\$120 ●	<input type="checkbox"/>
BN05012	Normal colon tissue (multi-sites) array, replaced by CO806	72	69	1	\$120 ●	-	\$120 ●	<input type="checkbox"/>
BS05011	Colon adenocarcinoma tissue array	63	23	1	\$120 ●	-	\$120 ●	<input type="checkbox"/>
BS05021	Colon adenocarcinoma (grade I) tissue array	63	23	1	\$120 ●	-	\$120 ●	<input type="checkbox"/>
BS05031	Colon adenocarcinoma (grade II) tissue array	63	21	1	\$120 ●	-	\$120 ●	<input type="checkbox"/>
BS05041	Colon adenocarcinoma (grade III) tissue array	63	23	1	\$120 ●	-	\$120 ●	<input type="checkbox"/>
CO1002 NEW!	Colon and rectum carcinoma and normal tissue array	100	73	1	\$195 ●	\$55 ●	\$195 ●	<input type="checkbox"/>

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BC050112
Colon metastatic carcinoma tissue array

Unstained: \$195.00
Trial (BC050112*): \$55.00

Overview Specification Sheet Core Image Overlapping Cases Print Export for Excel

Microarray Panel: Each three (3) cores from three different tissue spots represents one single specimen that was selected and pathologically confirmed

Cores: 63

Cases: 23

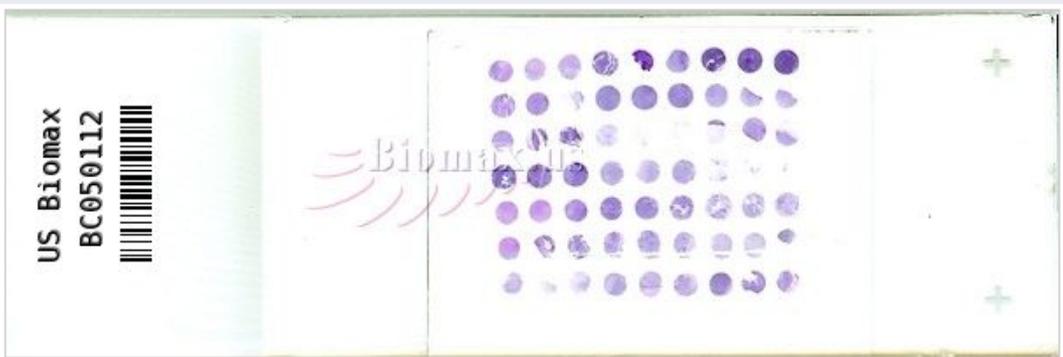
Layout: 9 cols x 7 rows

Core Diameter: 1.5 mm

Thickness: 5 µm

Quality Control: Anti-Cytokeratin (Low-MW) confirmed

Applications: Routine histology procedures including ImmunoHistochemistry (IHC) and In Situ Hybridization (ISH), protocols which can be found on our support page.



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Options...

Support

- Lucille Packard Foundation for Children's Health
- Howard Hughes Medical Institute
- NIH: NLM, NIGMS, NHGRI, NCI
- Hewlett Packard
- California Institute for Regenerative Medicine
- PhRMA Foundation
- Stanford Cancer Center

- Tarangini Deshpande
- Mark Musen and Alan Krensky
- Isaac Kohane

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