Systems Immunology at the Bedside

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DALLAS, TX

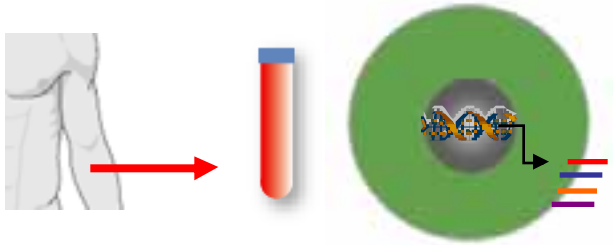
Human Systems Immunology

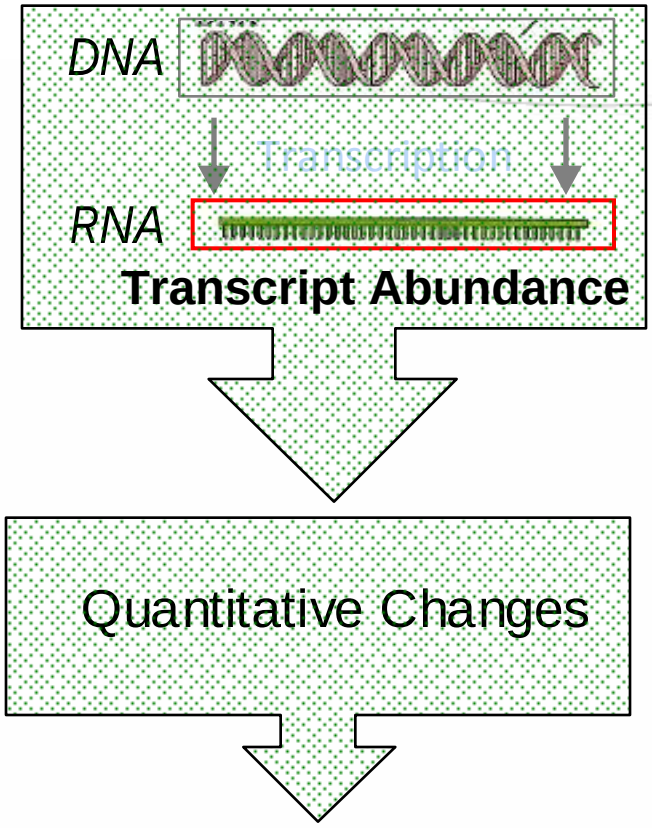
- Applying HT profiling platforms to the study of the human immune system
- Understand factors governing a system by studying its response to perturbation
- However: uncontrolled variables & limited ability to manipulate the system

Perturbations of the System

- First: obtain characteristics of variables measured at the steady state
- Unknown etiology: study diseases
- Known etiology:
  - Genetic: Primary Immune Deficiencies
  - Response to therapy, vaccines

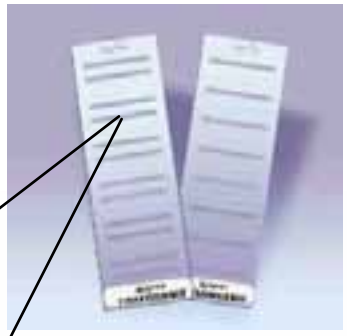
Transcript Profiling in Whole Blood

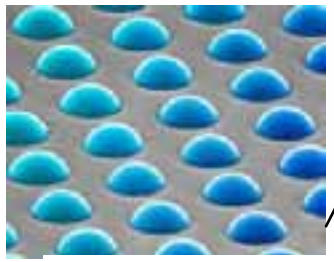




Detect Diseases Early
Monitor Activity

Microarray Beadchips

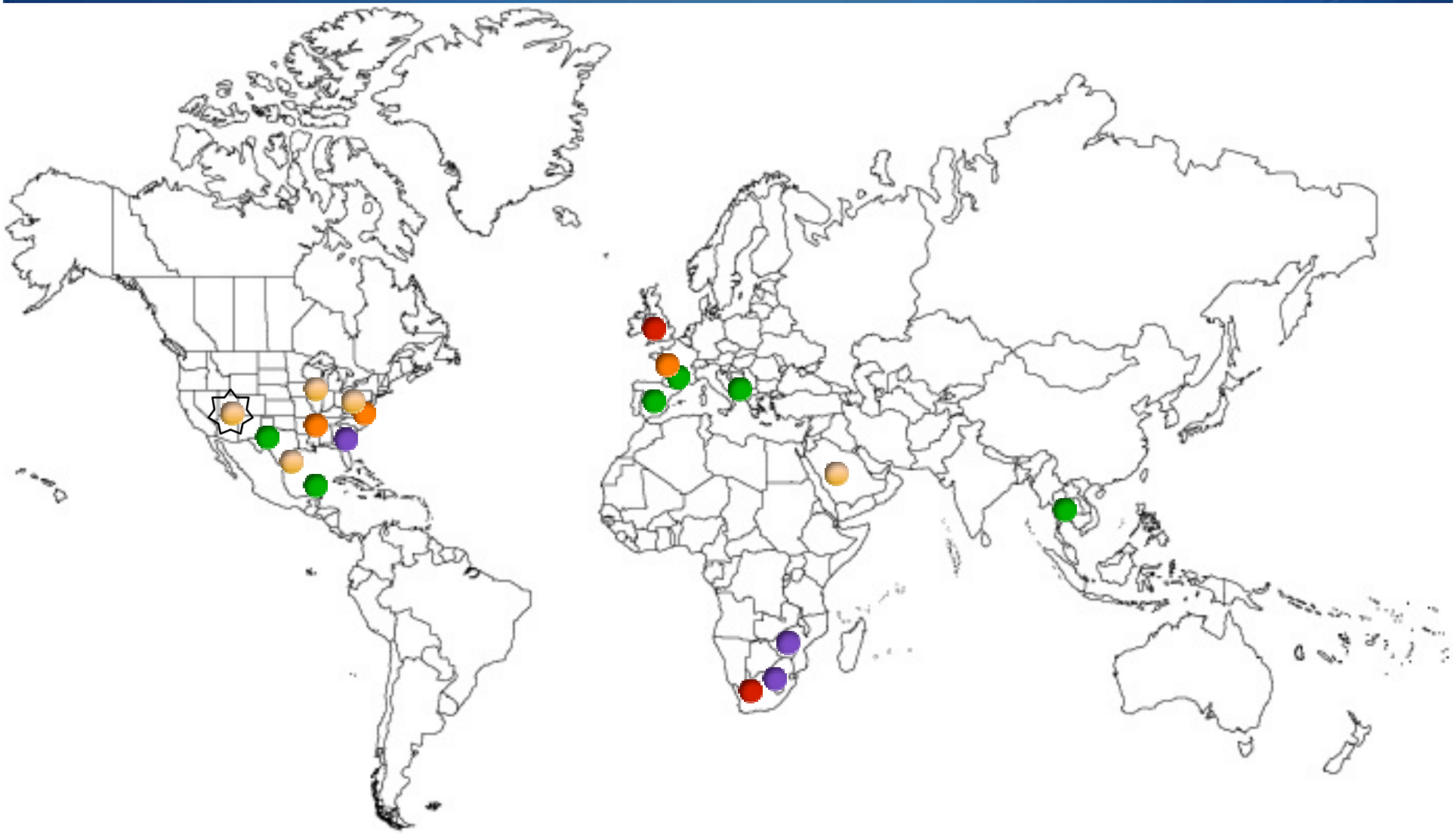




illumina
making sense

- ***3 micron beads***
- ***1.6 M beads/sample***
- ***Scans the activity of 48,000 transcripts***

Transcript Profiling in Whole Blood



- NIAID / CHAVI
- Primary Immunodeficiencies / Casanova
- TB / A. O'Garra - MRC
- NIAID / BioD

The Immune Profiling Arsenal

- High throughput molecular profiling platforms to study the human immune system “in nature”.
  - Polychromatic flow cytometry
  - RNA profiling (**mRNA**, miRNA, RNAseq)
  - SNP arrays (soon genome sequence)
  - Multiplex serum chemokines, cytokines profiles
  - Protein arrays
  - Mapping antigenic repertoire
  - “Other ex-vivo assays”
  - ….

Data Management: Why Bother?

Managing data at the bench

- Immunology has become a data-intensive field
- Currently information generated for a single experiment is scattered between CDs, hard drives, servers, notebooks, printouts etc…
- Public repositories are necessary but not sufficient
- The data management challenge must be met at the bench

Key Goals

- Preserving interpretable datasets; for years to come
- Integrating data within and across projects
- Facilitating data exploitation: Make integrated datasets available for mining. Enable large-scale data meta analyses.
- Data Sharing: Results can be seamlessly shared with collaborators; and the scientific community at large

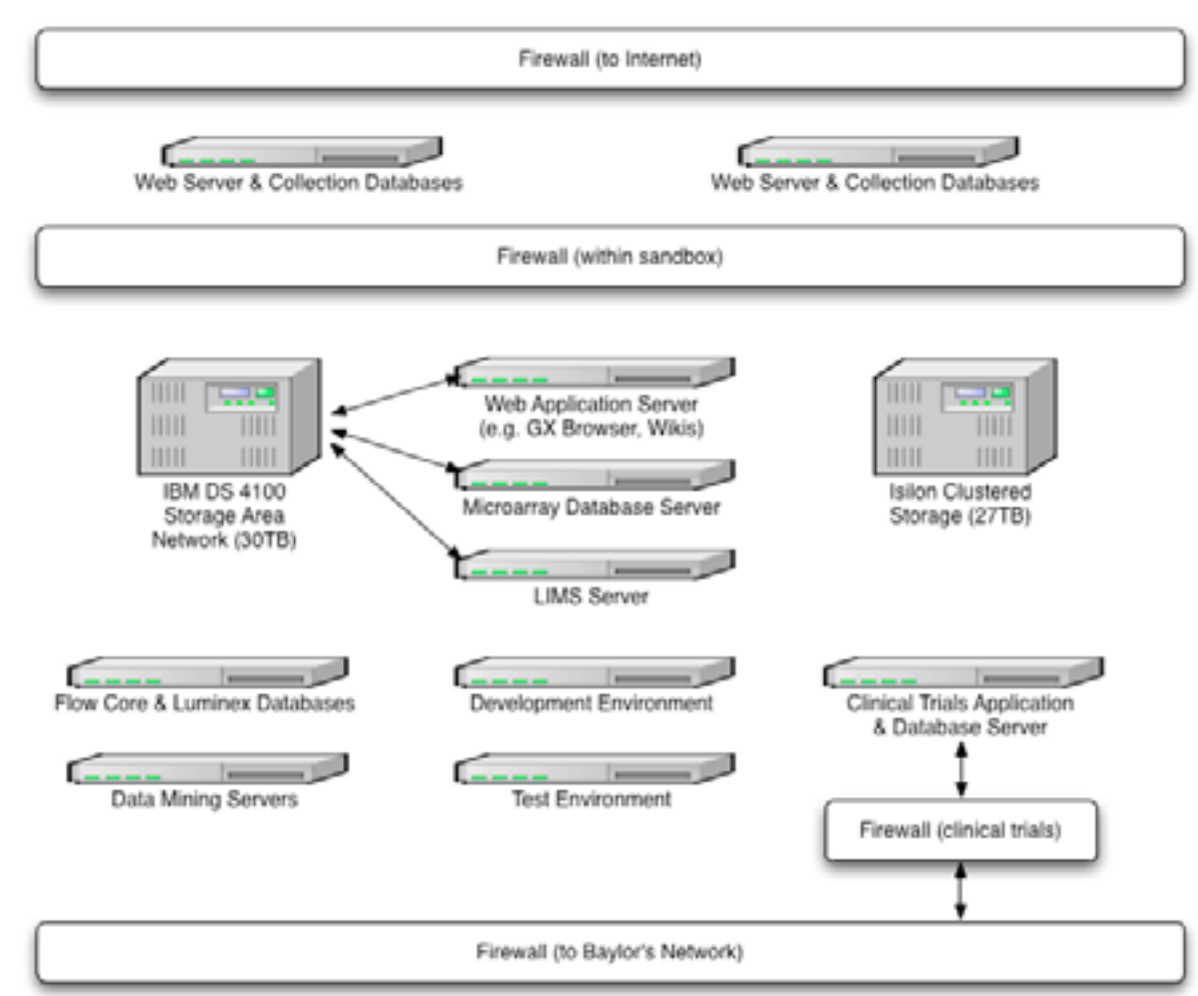
Step 1: Capturing Information

- Information about the experiment: title, aims, variables, materials, methods.
- Information about the samples: attributes (stimulation, time point, study group etc…)
  - Sample tracking information
  - Clinical information
  - Quality control information (sample processing)
- Instrument output (genomics, flow, imaging, luminex cores…); raw data files, processed results etc…

Step 2: Data Curation

- Implement a review process for experiment annotation
- Develop codebook (definition of variables)
- Periodic quality checks, double entry etc..
- Compliance with minimum information standards

Step 3: Data Storage



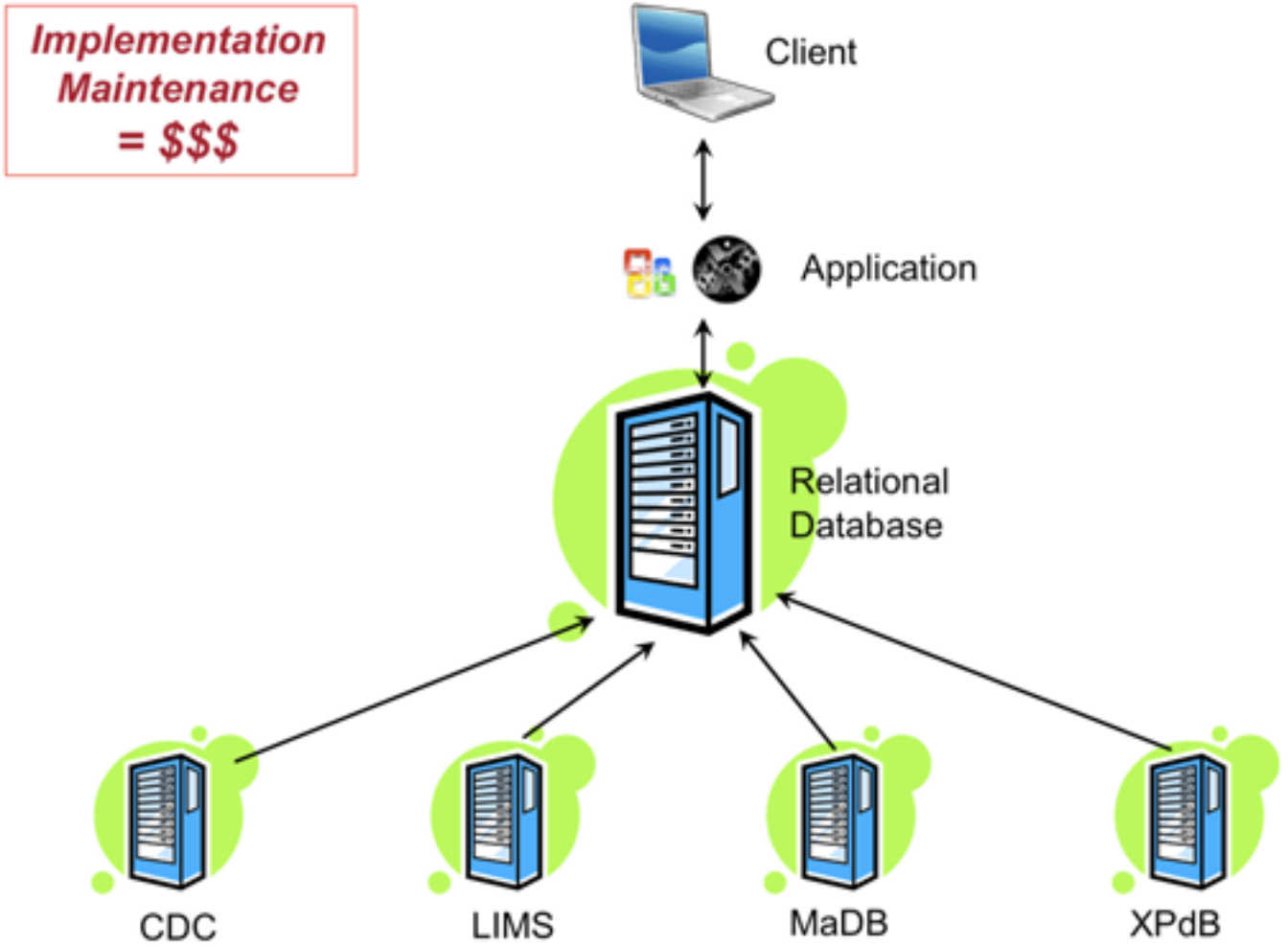
Step 4: Data Integration

- Data integration is not only a buzzword
- Ability to integrate data from multiple technology platforms
- Ability to integrate data from multiple projects
- Difficult to achieve without bioinformatics infrastructure in place

Step 5: Data Exploitation

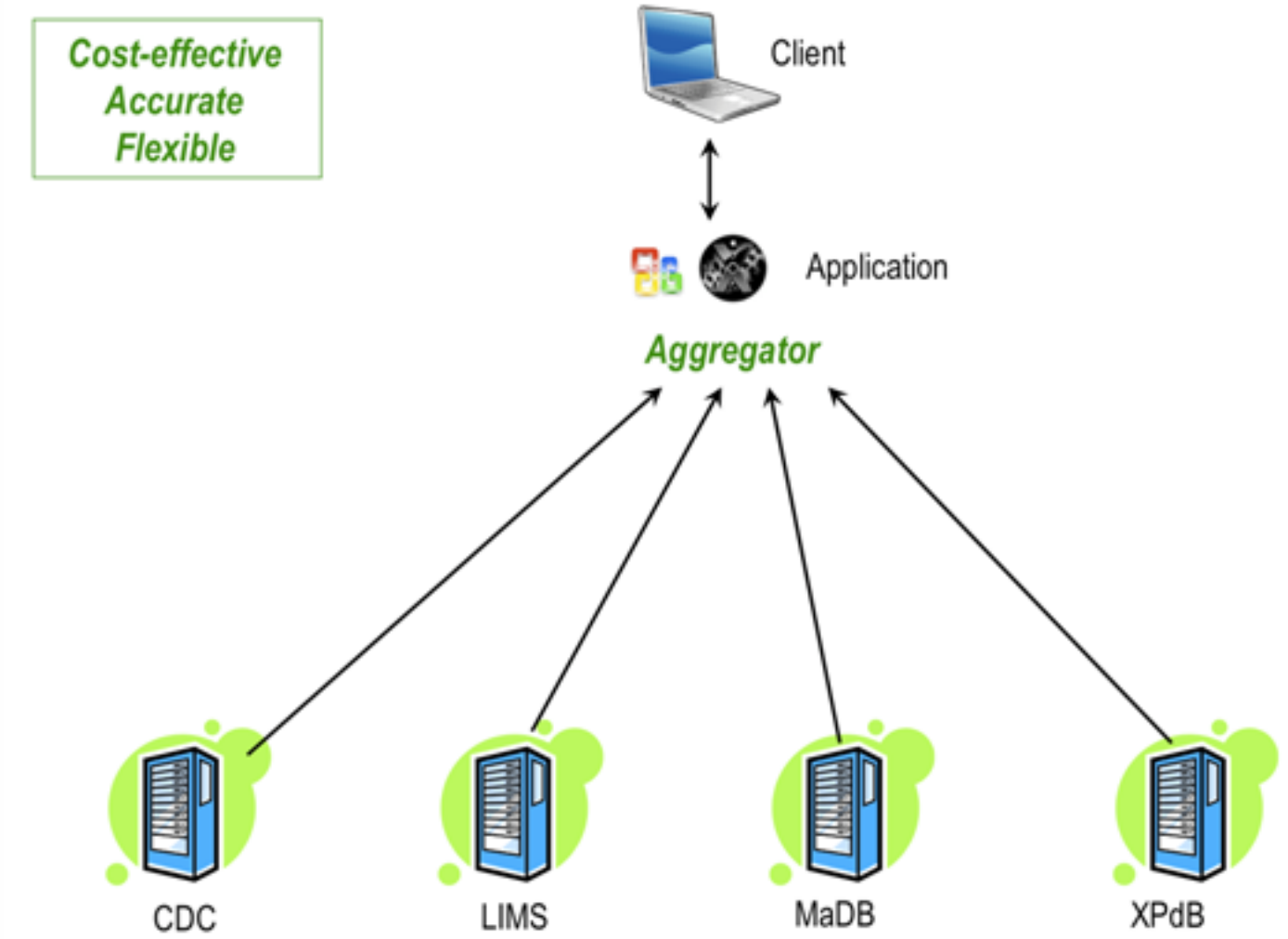
- Emphasis on data dissemination / high availability
- For downstream analyses by biostat / bioinformatics teams
- For access/query by investigators: promote insight
- Sharing data with study participants, collaborators, consortia members, scientific community
- Streamline data export to public repositories

Option #1: Relational Database

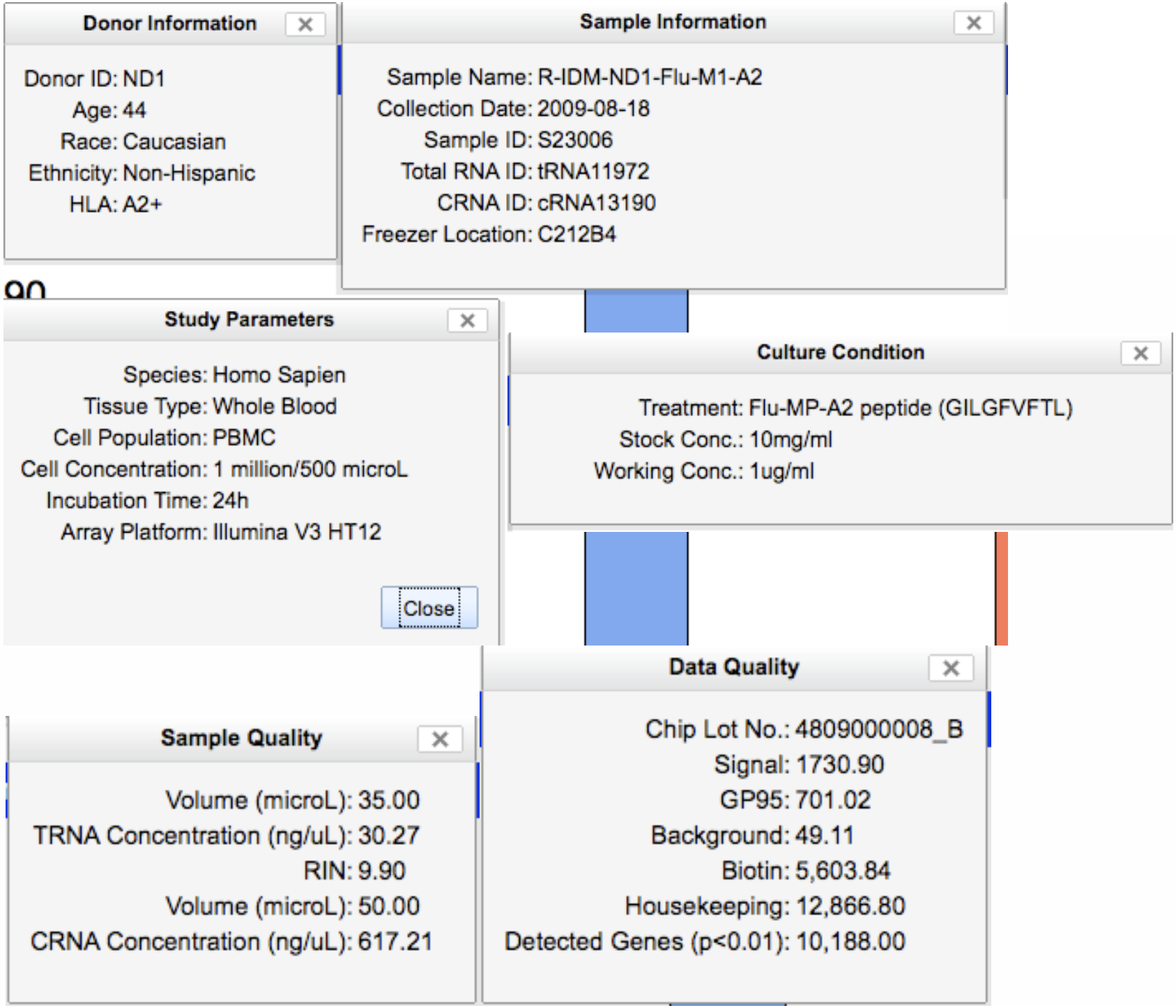


Option #2: Information Aggregator

Cost-effective
Accurate
Flexible




Sample Information
Quality Information
Associated Results
BAYLOR
Institute for Immunology Research
Data Management: Starting at t
CCL7
Signal: 1542.70
1900
0
Display Mode
Sample Information
Quality Information
Associated Results
Study Information
Study Parameters
Study Report
Supplemental Information
Gene Information
Files
Help
Contributors
Gene Expression Signal
Control
FLU-M1-A2
CMV-A2
Flow Cytometry
6.63
<PE-A> CD8
<CFSE-A>
CD3+CD8+
ND2_CMV-3.fcs
Event Count: 11396
View Image
Luminex Data
Sample ID ND2-CMV ND2-CMV ND2-CMV
IP-10 (pg/ml) *6676.31 *8253.66 7400.77
MIP-1a (pg/ml) 519.41 548.36 637.83
Rantes (pg/ml) *0.00 *0.00 *0.00
MCP-1 (pg/ml) 2798.81 2752.4 2530.01
Eotaxin (pg/ml) 17.8 25.96 14.73
TNF-a (pg/ml) 9.22 8.76 7.26
IFNg (pg/ml) 9.26 11.24 10.67
GM-CSF (pg/ml) *0.22 *0.33 *0.10
IL-15 (pg/ml) *0.47 *0.15 OOR <
IL-13 (pg/ml) OOR < OOR < OOR <
IL12p70 (pg/ml) OOR < OOR < OOR <
IL12p40 (pg/ml) OOR < OOR < OOR <
IL1-10 (pg/ml) *0.28 *0.31 *0.35
IL-8 (pg/ml) OOR > OOR > OOR >
IL-7 (pg/ml) 61.8 62.65 55.96
IL-6 (pg/ml) 217.45 333.46 301.53
IL-5 (pg/ml) OOR < OOR < OOR <
IL-4 (pg/ml) 36.53 34.39 32.85
IL-3 (pg/ml) *0.45 *0.45 *0.07
IL-2 (pg/ml) *0.79 *1.64 *0.49
IL-1b (pg/ml) 42.7 50.8 60.29
IL-1a (pg/ml) OOR < *2.31 OOR <
*Value extrapolated beyond standard range
OOR = Out of Range / OOR> = Out of Range Above / OOR< = Out of Range Below
Interactive Figure 1: Induction of CCL7 gene expression in response to antigen-specific stimulation of peripheral blood mononuclear cells (PBMCs). Gene expression levels of the chemokine CCL7 were measured by microarrays in PBMCs isolated from three donors. Cells were cultured alone or in the presence of Influenza, CMV or MART peptides for 24 hours. Associated results: a) Flow cytometry analysis was performed after 8 days of culture to measure proliferative responses following antigenic exposure; b) Protein levels were measured in supernatants after 48 hours of culture for a panel of 22 cytokines and chemokines.
http://www.biir.net/gxb/ccl7.htm


Donor Information
Donor ID: ND1
Age: 44
Race: Caucasian
Ethnicity: Non-Hispanic
HLA: A2+
Sample Information
Sample Name: R-IDM-ND1-Flu-M1-A2
Collection Date: 2009-08-18
Sample ID: S23006
Total RNA ID: tRNA11972
CRNA ID: cRNA13190
Freezer Location: C212B4
Study Parameters
Species: Homo Sapien
Tissue Type: Whole Blood
Cell Population: PBMC
Cell Concentration: 1 million/500 microL
Incubation Time: 24h
Array Platform: Illumina V3 HT12
Close
Culture Condition
Treatment: Flu-MP-A2 peptide (GILGFVFTL)
Stock Conc.: 10mg/ml
Working Conc.: 1ug/ml
Sample Quality
Volume (microL): 35.00
TRNA Concentration (ng/uL): 30.27
RIN: 9.90
Volume (microL): 50.00
CRNA Concentration (ng/uL): 617.21
Data Quality
Chip Lot No.: 4809000008_B
Signal: 1730.90
GP95: 701.02
Background: 49.11
Biotin: 5,603.84
Housekeeping: 12,866.80
Detected Genes (p<0.01): 10,188.00

EpiGen: Peptide Specific T-cell Immune Response

Project Manager: Durgha Nattamai
Platform: HT12 V3

Dataset Files

Contributors

Experiment Coordination & Execution:	Durgha Nattamai
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Data Aquisition	Laure Bourdery Jill Plants
Experiment Design & Data Interpretation	Damien Chaussabel Hide Ueno Jacques Banchereau
Affiliation	All contributors are affiliated with the Baylor Institute for Immunology Research and Baylor Reseach Institute
Grant Support:	Supported by the Baylor Health Care System Foundation and the National Institutes of Health (U19 AIO57234-02, U01 AI082110).
Correspondence:	Charles Quinn (email: charlieq@baylorhealth.edu)

<< first < prev 1 2 3 4 5 next > last >>

Close

you may want to use additional RNase free 1XPBS to thoroughly rinse the well of the culture plate to recov
4C. f. Using a pipette tip, remove as much PBS as possible without disturbing the pellet. 6. Resuspend the

Experience so far…

- Setup LIMS for genomics core; ~50,000 samples tracked,
- Microarray database: 233 experiments, 11,460 whole genome profiles, 749,865,378 unique data points (~3% of the size of NCBI GEO).
- "Distributed" data management. Information contributed to the system by independent groups that are distinct:
  - Operationally: Independent core facilities
  - Geographically: Multiple sites with multiple roles

Managing Data at the Bench

- Data driven science: ability to accumulate interpretable data over time is key
- We must learn from past successes and failures
- Difficult problem to tackle
- Need for a strong rationale: how data is managed may be more important than how it is analyzed
- Data sharing is a different debate

The Bottom Up View

- Data Management

Translational Genomics & Bioinformatics

Genomics

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BRI

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BIIR

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