
An Extensible and Scalable Knowledge System Architecture for Cancer Research

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Thanks to Kristen Anton (Dartmouth), Heather Kincaid (JPL)



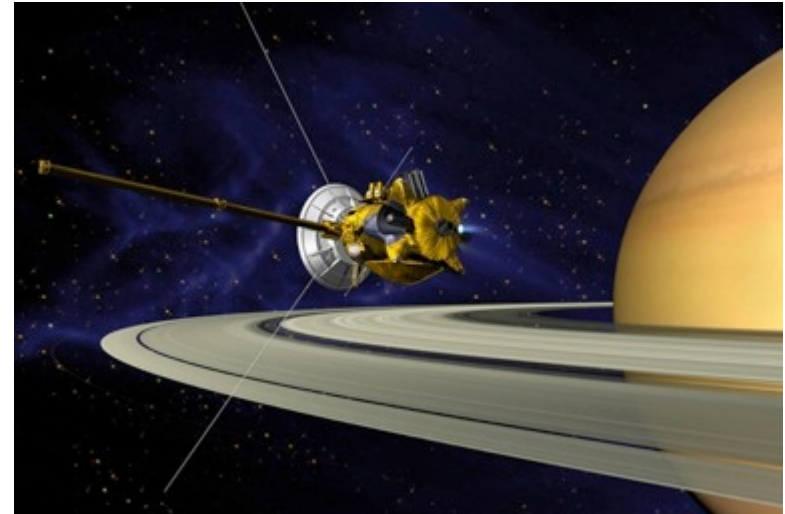
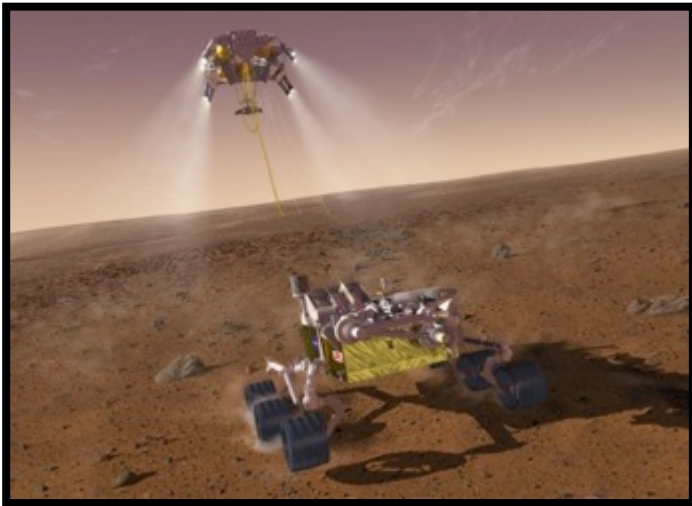
NATIONAL
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CANCER RESEARCH CENTER
A LIFE OF SCIENCE

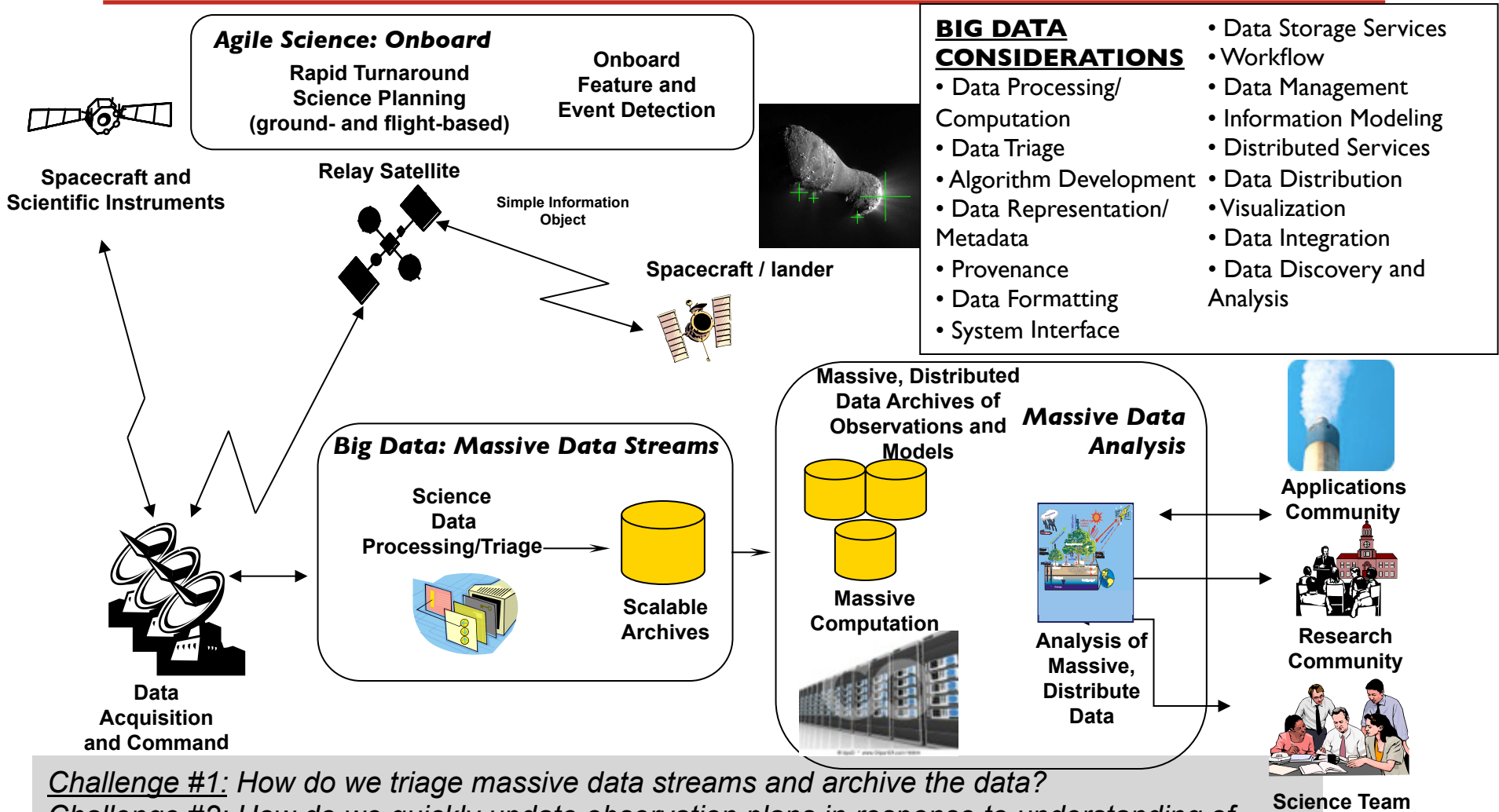


NASA Big Data Challenges



- Scientific missions that explore the Earth and solar system return a wealth of data
- Capturing and archiving these data are essential for preserving these data and supporting research and analysis
- Federal research analysis programs at NASA require data be from public archives

NASA/JPL Big Data Research Areas



Challenge #1: How do we triage massive data streams and archive the data?

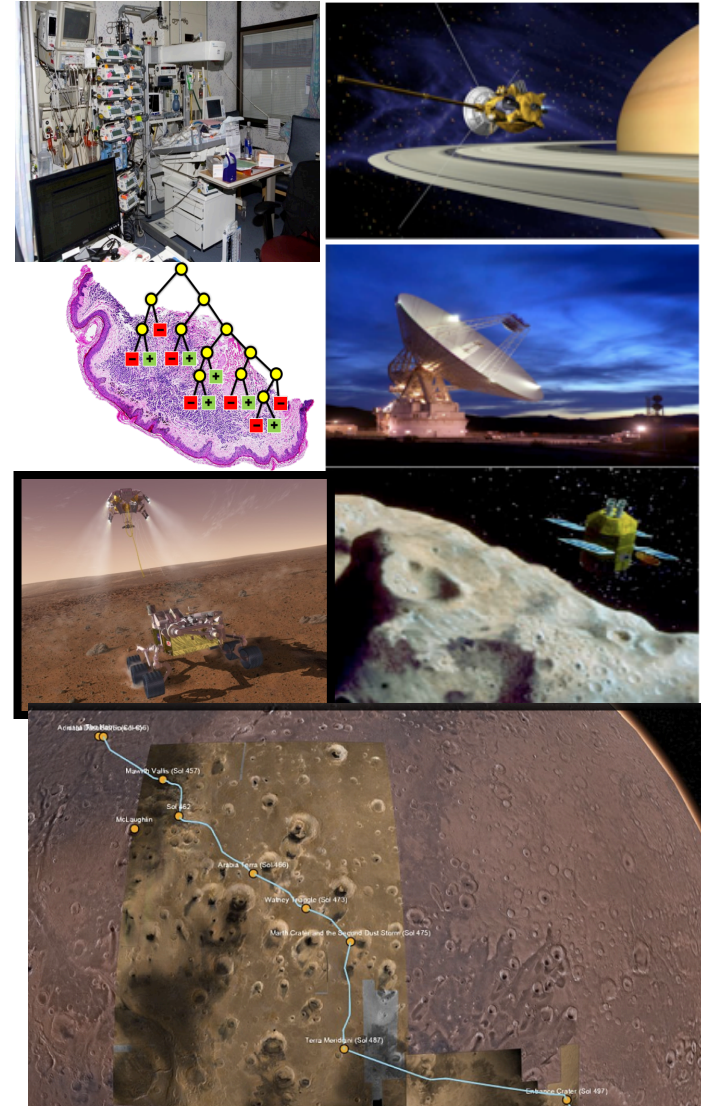
Challenge #2: How do we quickly update observation plans in response to understanding of newly acquired science data, especially for time-limited missions?

Challenge #3: How can we use advanced data science methods to systematically derive scientific inferences from massive, distributed science measurements and models?

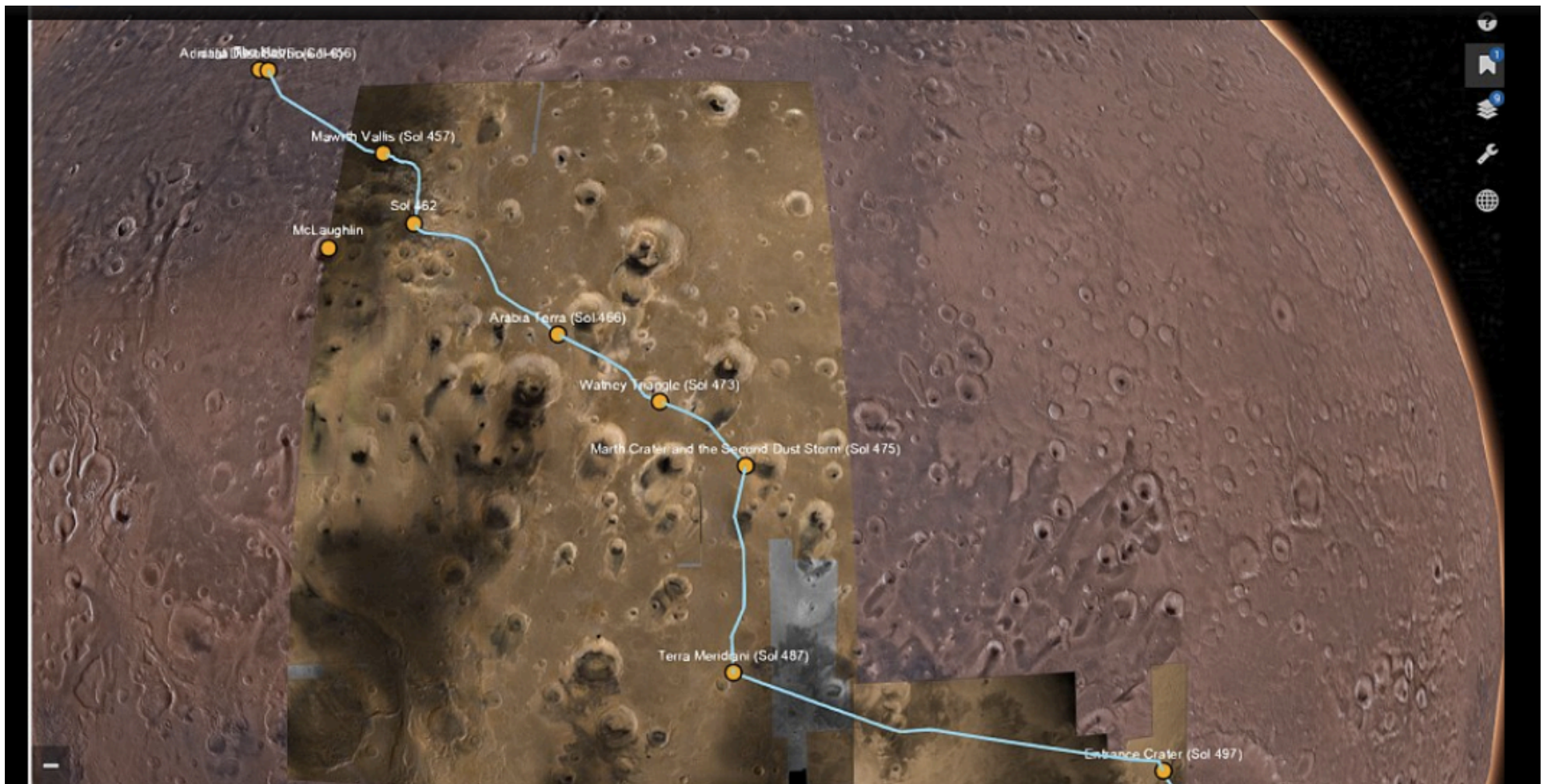
NASA/JPL Informatics Center: Crossing Disciplines to Support Scientific Research



- Development of an advanced Knowledge System to *capture, share* and support *reproducible analysis* from the biomarker data results
 - Supporting EDRN program since 2001
 - Supporting MCL program since 2015
- NASA-NCI partnership, leveraging informatics and data science technologies from planetary and Earth science
 - Reproducible, Big Data Systems for exploring the universe
 - 2011 NASA Group Award for “*innovative use of NASA software technologies to support cancer research*”

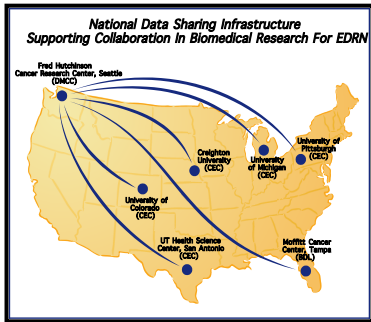


Creating Knowledge from Big Data: Exploring Mars Imaging Data with Mars Trek

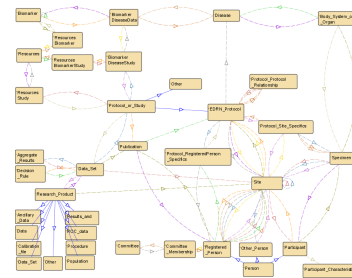


Derived from about 800 TBs of Imaging Data in the NASA Planetary Data System

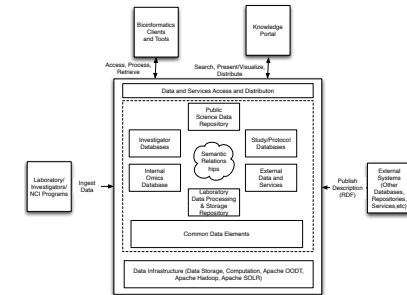
Informatics and Data Science Needs and Capabilities



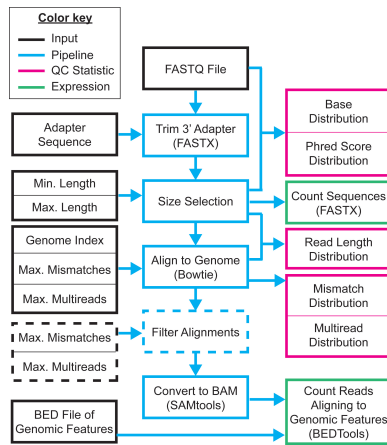
National Data Sharing Architectures



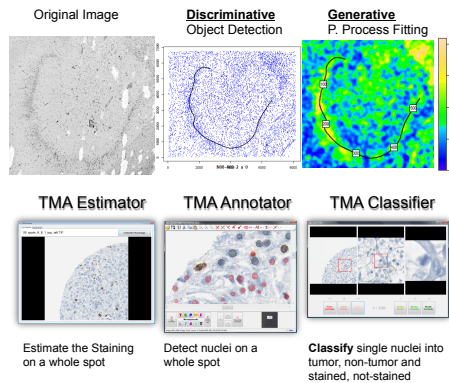
Common Data Elements & Models



Big Data Infrastructure



Analytical Data Pipelines



Intelligent Data Algorithms

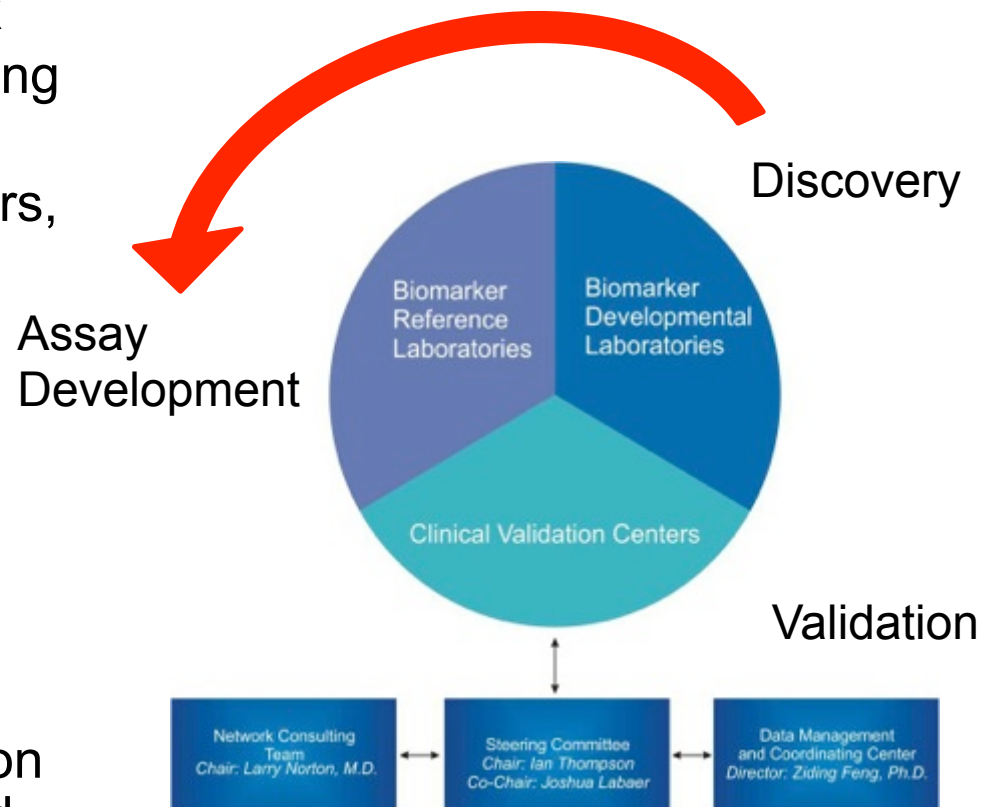


Visualization Techniques

EDRN – Early Detection Research Network



- Early Detection Research Network (EDRN) is a network of 40+ institutions all performing research geared towards the discovery of cancer biomarkers, which are early indicators of onset of disease
- NCI/NIH funded program
 - Started in ~2000
 - NCI's flagship program
- Informatics efforts cited as a model for biomarker research
- Cross-disciplinary collaboration (FHCRC, JPL, Dartmouth and NCI)

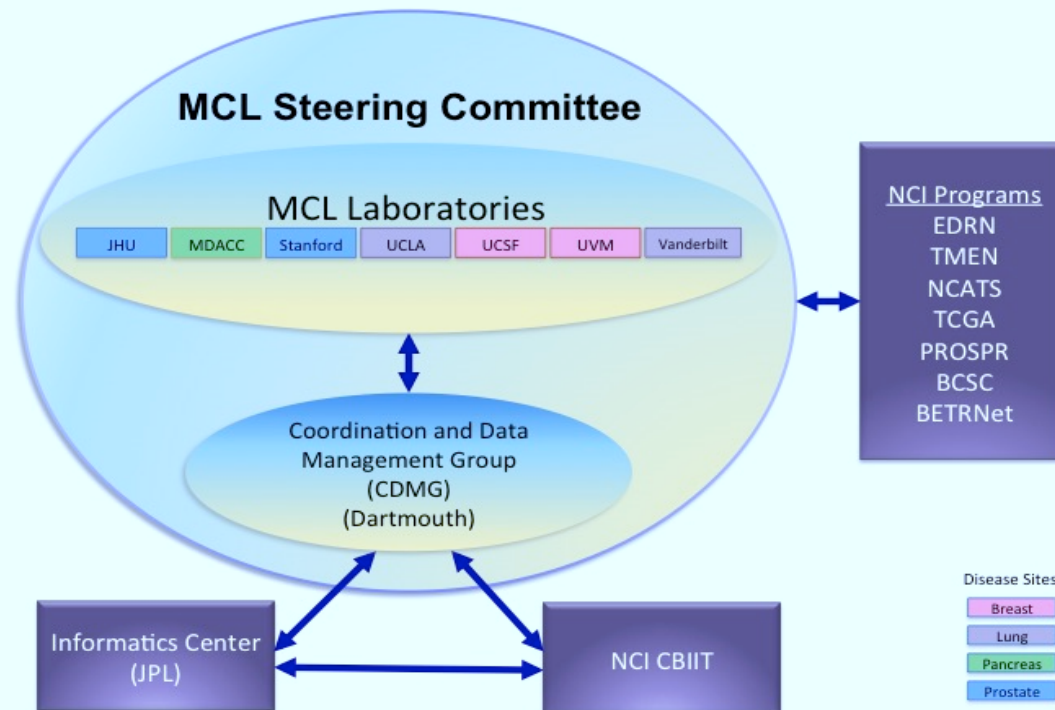


EDRN Organizational Structure

MCL - Consortium for the Characterization of Screen Detected Lesions



Organizational Structure of the MCL Consortium



MCL Consortium Working Groups

Methodology

Genomics and Genotyping

Imaging

Pathology

Data, Informatics and Resource Sharing

To conduct a comprehensive molecular and cellular characterization of tumor tissue, cell, and microenvironment components to distinguish screen-detected early lesions from interval and symptom-detected cancers. (Funded 2015)

Key Informatics Accomplishments in Life Sciences



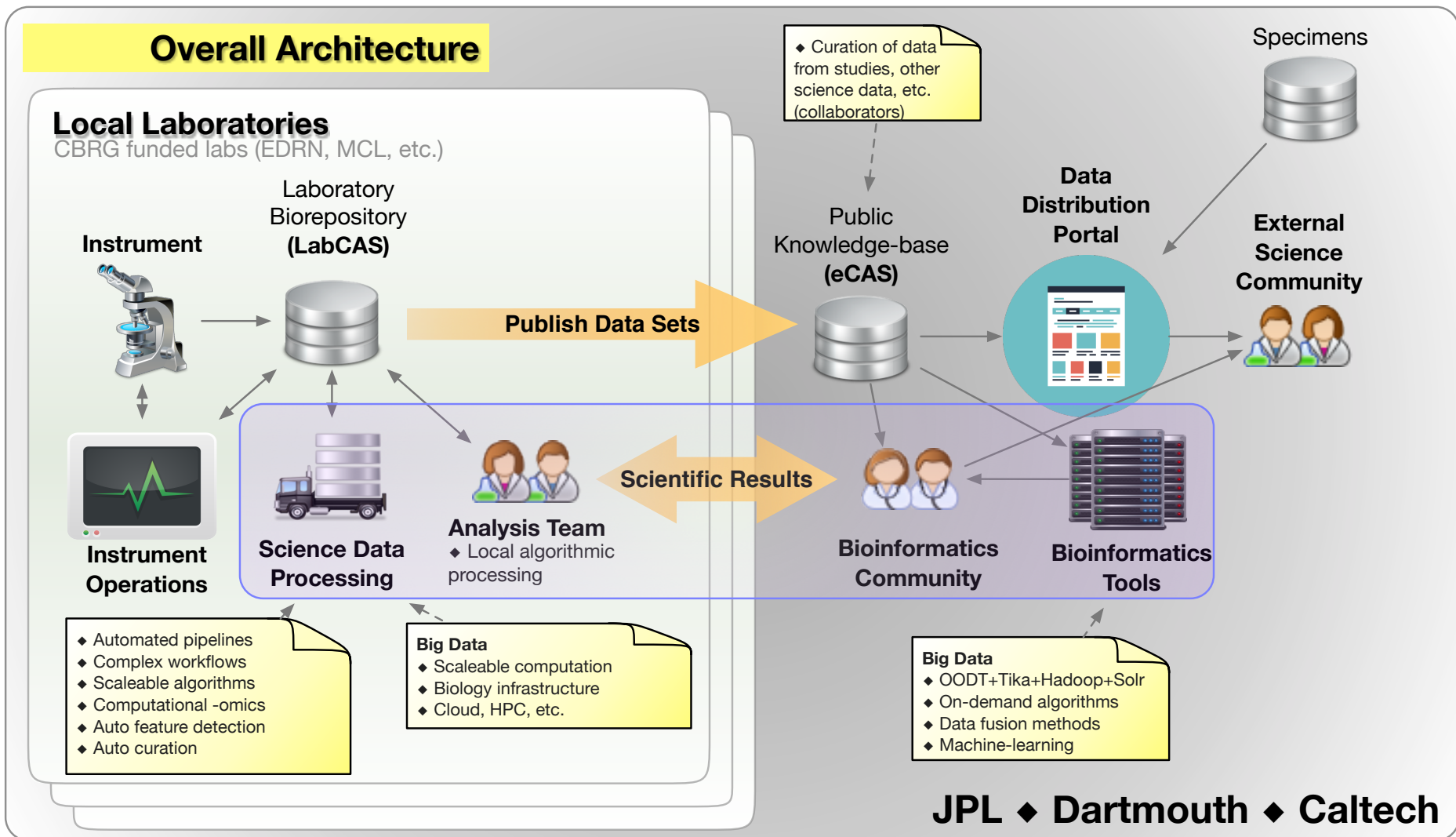
- Implemented a national, biomarker knowledge system re-using advanced informatics technology developed for planetary data science
- Pioneered the concept of providing access to information about biospecimens across EDRN at a national level (2001)
- Developed a repository for capturing scientific data sets; captured 90 data sets; integrated with the Canary Foundation infrastructure.
- Developed a biomarker database for capturing and annotating EDRN biomarkers; high-quality curation on more than 900 biomarkers
- Developed a public portal that provides dissemination of EDRN information as well as scientific data and results; over 2400 unique visitors a month
- Developing new tools for the Laboratories to support the processing, capture, curation and sharing of data before publications
- Received NASA Award in 2011 for the “innovative use of NASA software technologies to support cancer research” due to significant reuse of capability
- Began leveraging the architecture across multiple NCI programs

Cancer Biomarker Bioinformatics Workshop



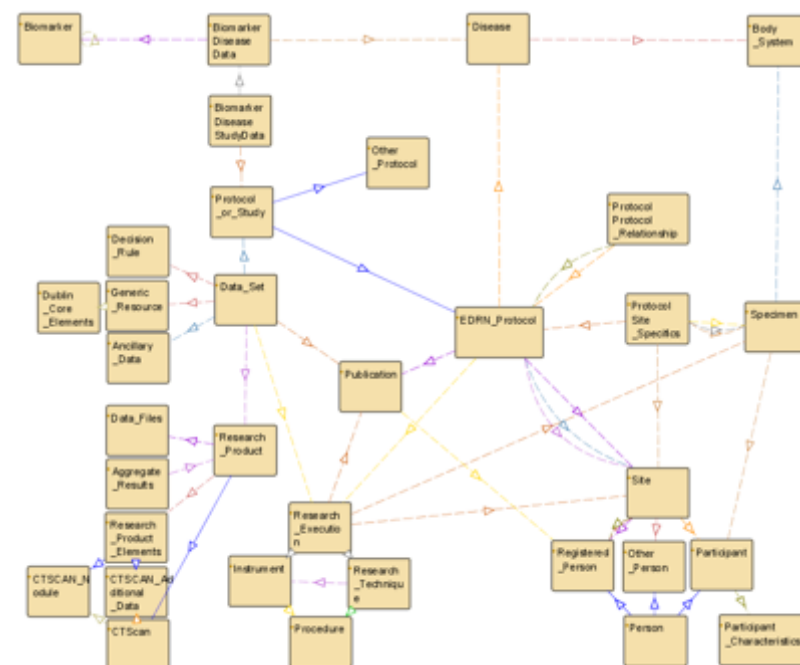
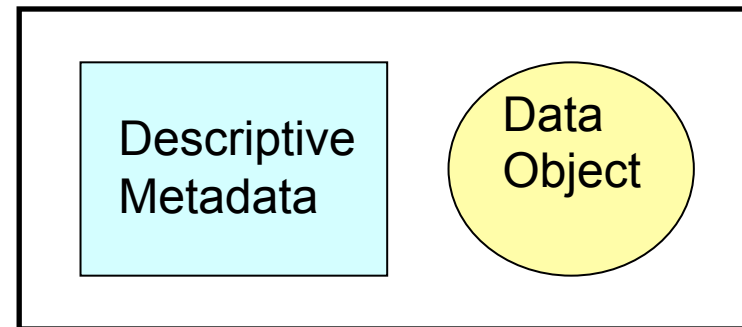
- The NCI and NASA Jet Propulsion Laboratory held a workshop in May 2013 at Caltech to address informatics and data-driven research in cancer biomarkers
 - <http://edrn.nci.nih.gov/cancer-bioinformatics-workshop/cancer-biomarker-bioinformatics-workshop-report-may-2013>
 - A major outcome focused on data usability, reproducibility of results, methods and algorithms to systematize data analysis, and scalable computing infrastructures.
- Key Recommendations
 - Systematic approaches to the generation, capture, management of data to enable reproducibility
 - Increased emphasis on data curation to promote data reuse
 - Automation of data process/analytics software pipelines
 - Data integration and fusion of data from multiple platforms, studies
 - Scalable data infrastructures and repositories
 - Use of big data tools and bioinformatics techniques to scale data analysis
 - Increased training of scientists in the use of computational tools/methods

Data and Computational Flow



Common Data Elements and Information Models

- CDEs provide a common set of data semantics to capture and share data
 - EDRN CDEs
 - MCL CDEs
- Work with CBIIT to reuse standard elements in caDSR for consistency across NCI
- All archived data are captured as information objects (same as planetary)
 - Metadata described using CDEs
 - Data captured and stored in a data repository



Biomarker Ontology Information Model

LabCAS: Laboratory Catalog and Archive Service



- Provides investigators with a secure, reliable means to capture their **pre-publication** research datasets
- Provides integrated data processing
- Enables investigators and collaborative groups/projects to share data in a secure manner as early as possible
- Scales to support data intensive projects
- Facilitates repeatable data processing pipelines

LabCAS is a new capability under development

The screenshot shows the LabCAS website interface. At the top, there is a red header with the National Cancer Institute logo and the text "National Cancer Institute" on the left, and "U.S. National Institutes of Health | www.cancer.gov" on the right. Below the header, the main content area features the "Early Detection Research Network" logo and the tagline "Biomarkers: The Key to Early Detection" on the left, and "DCP Division of Cancer Prevention" on the right. A "Log In" link is also visible. The central part of the page is a large image of green, rod-shaped bacteria, with the text "LabCAS Laboratory Catalog and Archive Service" overlaid. At the bottom, there are two columns of text: "What is LabCAS" and "More Information".

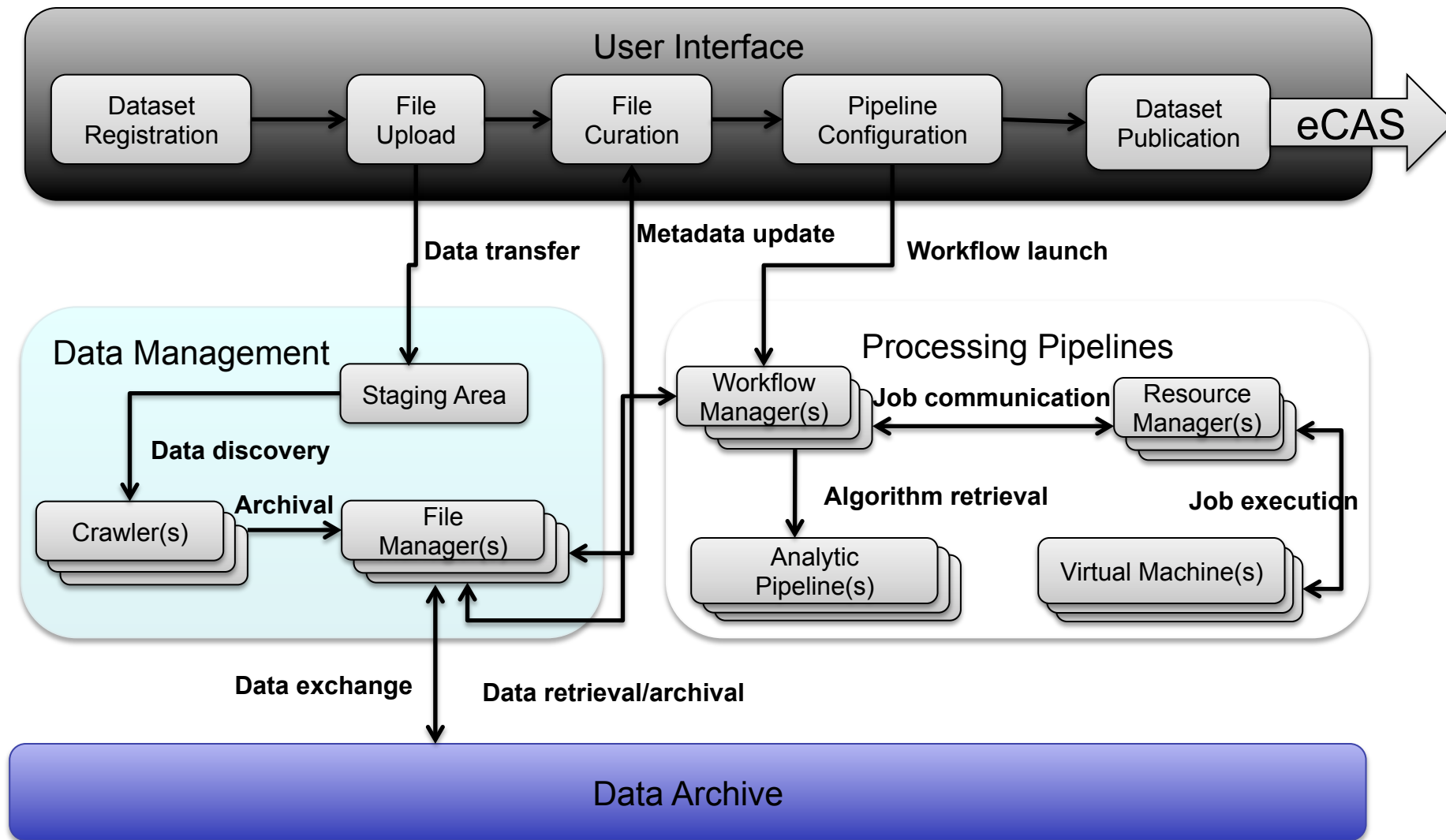
What is LabCAS

EDRN LabCAS is a better way to catalog and archive laboratory data files in a way that facilitates later retrieval and dissemination among collaborators.

More Information

LabCAS is currently under active development. For more information, please send an email to: edrn-proteome@jpl.nasa.gov.

Data Capture , Processing and Ingestion



eCAS: Capture and Sharing of Public Data Sets



- **EDRN has a warehouse of public biomarker data**
 - Uses the CDEs to populate a catalog describing the data sets
 - Supports public release/access to the data
 - Supports peer review of the data by collaborative groups prior to public release
 - Integrated with the rest of the knowledge system
 - Supports reproducibility studies
- **Provides a long term and central capture of biomarker study results for the broad community**
- **Being extended to MCL**

The image displays two screenshots of the EDRN website. The top screenshot shows the EDRN homepage with the "Science Data Warehouse" logo and a list of datasets under "Datasets By Protocol". The bottom screenshot shows a detailed dataset page for "Autoantibody Biomarkers" with the following information:

Dataset Metadata:

- Protocol Name: Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques
- Protocol ID: 138
- Dataset Abstract: We have implemented a high throughput platform for quantitative analysis of serum autoantibodies, which we have applied to lung cancer for discovery of novel antigens and for validation in pre-diagnostic sera of autoantibodies to antigens previously defined based on analysis of sera collected at the time of diagnosis. RESULTS: We present evidence for the occurrence in lung cancer sera of autoantibodies to annexin I, 14-3-3 theta, and a novel lung cancer antigen, LAMR1, which precede onset of symptoms and diagnosis.
- Dataset Name: Autoantibody Biomarkers
- Principal Investigator: Samir Hanash

1-7 of 7 Products Associated With This Dataset:

- (by Batch)ANXA1(FR-00-84).pdf
- (by Batch)14-3-3.pdf
- CARET_lung_cancer.xls
- (by Batch)01-1.pdf
- (by Batch)LAMR1.pdf
- (by Batch)FCPS-1.pdf
- annexin+lamr1+14-3-3.pdf

ANXA1(FR-00-84)

Sample Size	p-value
1st 2626	p-value = 0.005
2nd 2727	p-value = 0.034
3rd 3202	p-value = 0.042
all 8595	p-value = 0.001

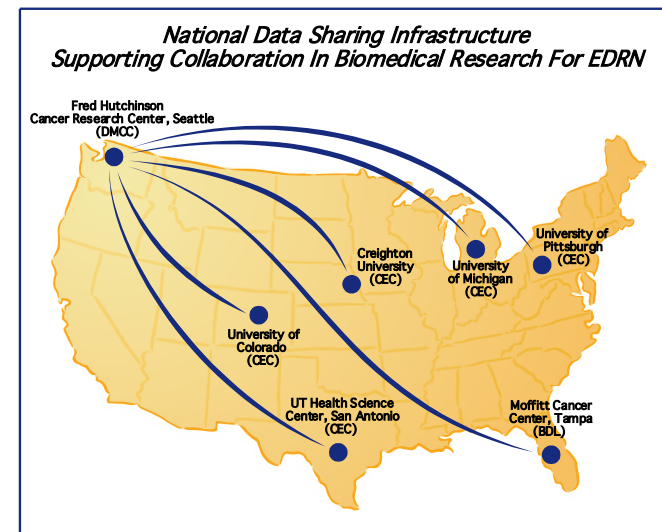
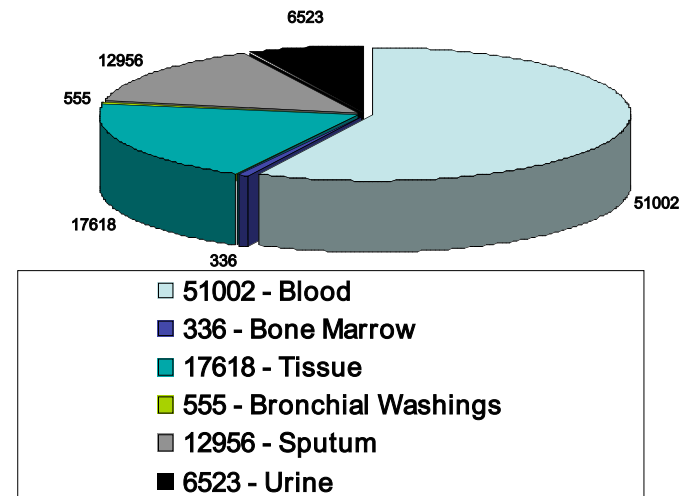
Below the p-values are four ROC curves corresponding to the sample sizes above, showing the True Positive Fraction versus the False Positive Fraction. The AUC values for the curves are: 0.713, 0.719, 0.647, and 0.711.

Credit: Sam Hanash (Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques)

Virtual, Distributed Specimen System



H. Lee Moffitt Cancer Center
University of Texas, San Antonio
Creighton University
University of Colorado
University of Pittsburgh
University of Michigan/Dartmouth College
(Great Lakes New England Consortium)
Brigham and Womens Hospital
MD Anderson
New York University
UCSD
Center for Disease Control
Johns Hopkins
Duke University
Fred Hutchinson Cancer Research Center
Fox Chase Cancer Research Center



JNCI  **CANCER SPECTRUM**

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Go To: [Home](#) > [JNCI](#) > [Archive](#) > [Vol. 95, No. 3](#) > Tenenbaum, pp. 186-187.

JNCI

*Journal of the
National
Cancer
Institute*

Journal of the National Cancer Institute, Vol. 95, No. 3, 186-187, February 5, 2003
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NEWS

Serving Up Specimens: NASA-NCI Project Links Databases Across the Country

David Tenenbaum

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 - [Cancer Statistics](#)
 - [PDQ Summaries/Trials](#)
 - [PDQ Physical/Diag. References](#)

Enrichment with Biological Database References and Information



National Cancer Institute U.S. National Institutes of Health

Early Detection Research Network

Biomarkers: the key to early detection

DCP Division of Cancer Prevention

Home About EDNRN Biomarkers Protocols Science Data Specimens Publications Resources Committees

Secure Site Public, Patients, Advocates Funding Opportunities Sites Members Committees Biomarker Informatics Standards Division of Cancer Prevention Cancer Biomarkers Research Group Bookshelf

You are here: [Home](#) → Biomarkers

Biomarkers

Cancer biomarkers currently being evaluated by the EDNRN. The EDNRN is involved in researching hundreds of biomarkers. The following is a partial list of biomarkers and associated results that are currently available for access and viewing. The bioinformatics team at EDNRN is currently working with EDNRN collaborative groups to capture, curate, review, and post the results as it is available. EDNRN also provides secure access to additional biomarker information not available to the public that is currently under review by EDNRN research groups. If you have access to this information, please ensure that you are logged in. If you are unsure or would like access, please [contact the operator](#) for more information.

Contents

Title	Type	Organ(s)
14-3-3 theta	Protein	Lung
4DELf	Proteomic	Colon
AAT	Protein	Liver
AFP	Protein	Liver
AFP-L3	Protein	Liver
AFPIC	Protein	Liver
AGRN	Protein	Ovary
AKAP12	Genomic	Esophagus
AMACR	Protein	Prostate
AMBP	Protein	Ovary

Search Site [] Search

Announcement 01/13/2011

The 22nd EDNRN Steering Committee Meeting is scheduled from Tuesday-Thursday, March 8-10, 2011, in Los Angeles, CA. Information about this event, such as meeting registration, agendas, and hotel accommodations can be found [here](#).

Announcement 11/20/2010

The American College of Radiology Imaging Network (ACRIN) is pleased to announce the availability of the National Lung Screening Trial (NLST) ACRIN Biorepository for research opportunities. Click [for more information](#).

Facilitates capture and sharing of 'omics annotations

Provides connection to the following:

- Protocol
- Scientific Data
- Publications
- Additional Biomarker Resources

14-3-3 theta — EDNRN Public Portal

National Cancer Institute U.S. National Institutes of Health

Early Detection Research Network

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14-3-3 theta

Search Site [] Search

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Basics Organs Studies Publications Resources

Aliases:
This biomarker is also known as:
14-3-3 protein T-cell, Protein H51, 14-3-3 protein theta, Iyocine 2-monooxygenase/histidine 5-monooxygenase activation protein, theta pol, YW440, 14-3-3 protein tau.

ATTRIBUTES:
CA State: Accepted
Type: Protein
Short Name:

Description:
14-3-3 theta belongs to the 14-3-3 family of proteins which mediate signal transduction by binding to phosphoserine-containing proteins. This highly conserved protein family is found in both plants and mammals, and this protein is 99% identical to the mouse and rat orthologs. The 14-3-3 proteins have a wide range of ligands, are involved in a variety of biological pathways, and are known to be overexpressed in some human lung cancers, suggesting that they may play a role in tumorigenesis. 14-3-3 theta is an adapter protein implicated in the regulation of a large spectrum of both general and specialized signaling pathway. It binds to a large number of partners, usually by recognition of a phosphoserine or phosphothreonine motif. Binding generally results in the modulation of the activity of the binding partner. 14-3-3 theta antigens have been found to be targets of autoantibodies in subjects newly diagnosed with lung cancer.

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Portal: Dissemination and Access to Knowledge System Data



- Gateway to information
- Information managed both within and outside the knowledge system
- Initial starting point for community to access research data
- Google-like search to access the wealth of data
- Multi-level Security protects pre-publication and sensitive data

<http://cancer.gov/edrn>
<http://mcl.jpl.nasa.gov>



Navigating the Knowledge System: Data Semantically Linked

Early Detection Research Network
Research and development of biomarkers and technologies for the clinical application of early cancer detection strategies

14-3-3 theta

Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques

PURPOSE: We have implemented a high throughput platform for quantitative analysis of serum autoantibodies which we have applied to lung cancer for discovery of novel antigens, and for validation in pre-diagnostic sera of autoantibodies to antigens previously defined based on analysis of sera collected at the time of diagnosis. **MATERIALS AND METHODS:** Proteins from human lung adenocarcinoma cell line A549 lysates were subjected to extensive fractionation. The resulting 1824

Biomarker Annotations

Early Detection Research Network

Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques

Description: We have implemented a high throughput platform for quantitative analysis of serum autoantibodies which we have applied to lung cancer for discovery of novel antigens, and for validation in pre-diagnostic sera of autoantibodies to antigens previously defined based on analysis of sera collected at the time of diagnosis. **MATERIALS AND METHODS:** Proteins from human lung adenocarcinoma cell line A549 lysates were subjected to extensive fractionation. The resulting 1824 factors were spotted in duplicate on nitrocellulose coated slides. The microarrays produced were used in a blinded validation study to determine whether annexin I, PDPS, and 14-3-3 theta antigens previously found to be targets of autoantibodies in newly diagnosed subjects with lung cancer are associated with autoantibodies in sera collected at the pre-symptomatic stage and to determine whether additional antigens may be identified in pre-diagnostic sera. Individual sera collected from 85

Protocols

Early Detection Research Network

Science Data

Captured scientific data results from biomarker studies

The EDNRN is involved in researching hundreds of biomarkers. The following is a partial list of associated results from biomarker research that are currently available for access and viewing. The bioinformatics team at EDNRN is currently working with EDNRN collaborative groups to capture, curate, review and post additional data as it is available. EDNRN also provides secure access to additional biomarker information not available to the public that is currently under review by EDNRN research groups. If you have access to this information, please ensure that you are logged in, if you are unsure or would like access, please contact the operator for more information.

Title	PI(s)	Organ	Protocol	Collaborative Group
Autoantibody Biomarkers	Hanash, Samir	Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques	Lung and Upper Aerodigestive	
Barnett's Esophagus Methylation Profile	Meltzer, Stephen			GI and Other Associated

Biomarker Data Results

Early Detection Research Network

Search results for **lung biomarker**

334 Specimens at Centers for Disease Control
334 matching specimens at Centers for Disease Control. last modified Aug 09, 2010 01:04 PM — Reference: 100%

14-3-3 theta
14-3-3 theta belongs to the 14-3-3 family of proteins which mediate signal transduction by binding to phosphoserine-containing proteins. This highly conserved... last modified Jul 22, 2010 07:10 PM — Reference: 58%

Specimens

Early Detection Research Network

Welcome to EDNRN

The Early Detection Research Network (EDNRN) is an initiative of the National Cancer Institute (NCI), linking together dozens of institutions to help accelerate the translation of biomarker information into clinical applications and to evaluate new ways of testing cancer in its earliest stages and for cancer risk.

Getting Started...

- Scientific Components
- Collaborative Opportunities How to Join EDNRN
- For Public, Patients, Advocates
- For Researchers

Linked through Public Portal

Early Detection Research Network

Autoantibody Biomarkers

Dataset Metadata:

Protocol Name: Validation of Protein Markers for Lung Cancer Using CARET Sera and Proteomics Techniques

Protocol ID: 138

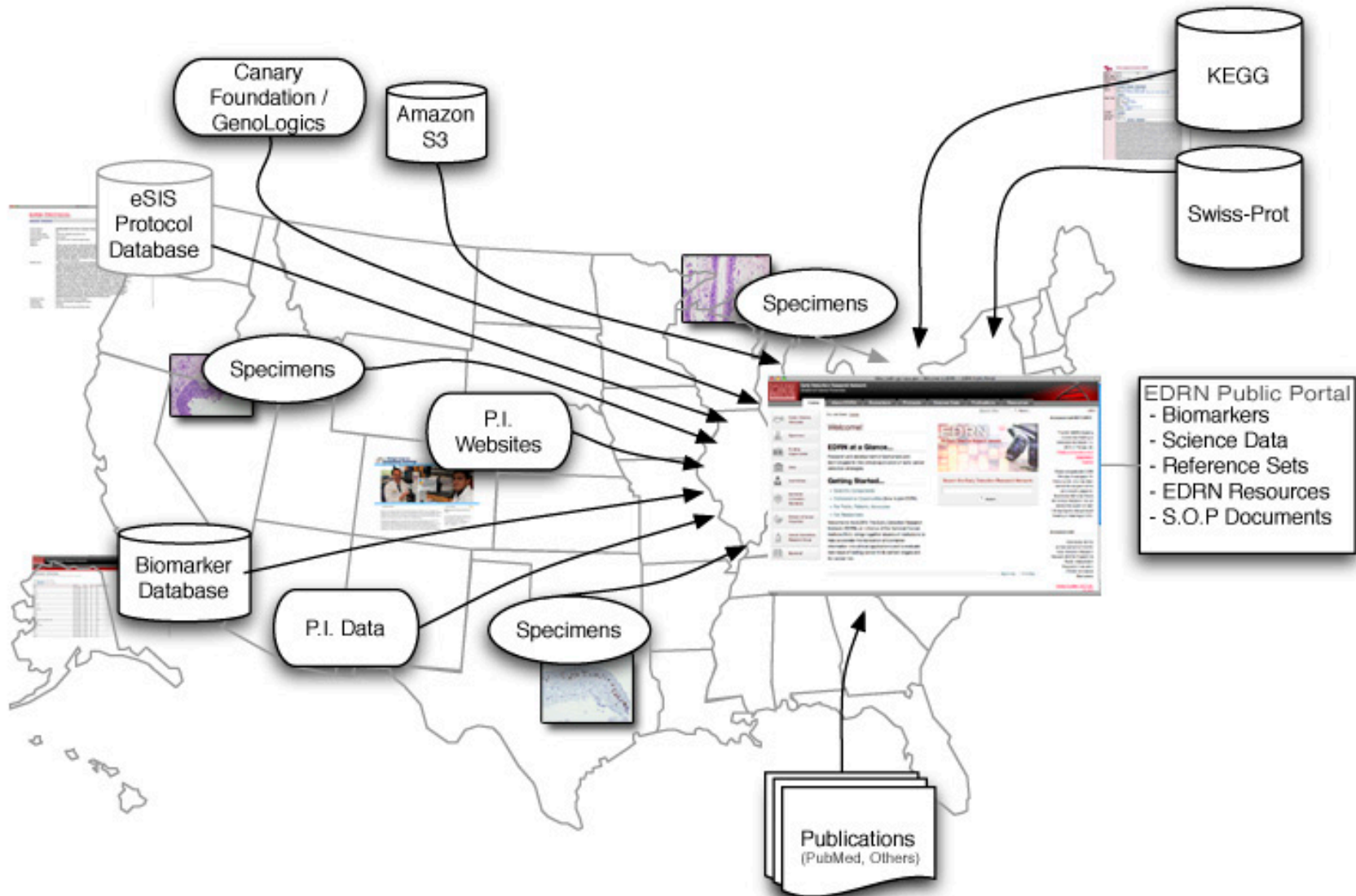
Dataset Abstract: We have implemented a high throughput platform for quantitative analysis of serum autoantibodies, which we have applied to lung cancer for discovery of novel antigens and for validation in pre-diagnostic sera of autoantibodies to antigens previously defined based on analysis of sera collected at the time of diagnosis. **RESULTS:** We present evidence for the occurrence in lung cancer sera of autoantibodies to annexin I, 14-3-3 theta, and a novel lung cancer antigen, LAMR1, which precede onset of symptoms and diagnosis.

1-7 of 2 Products Associated With This Dataset:

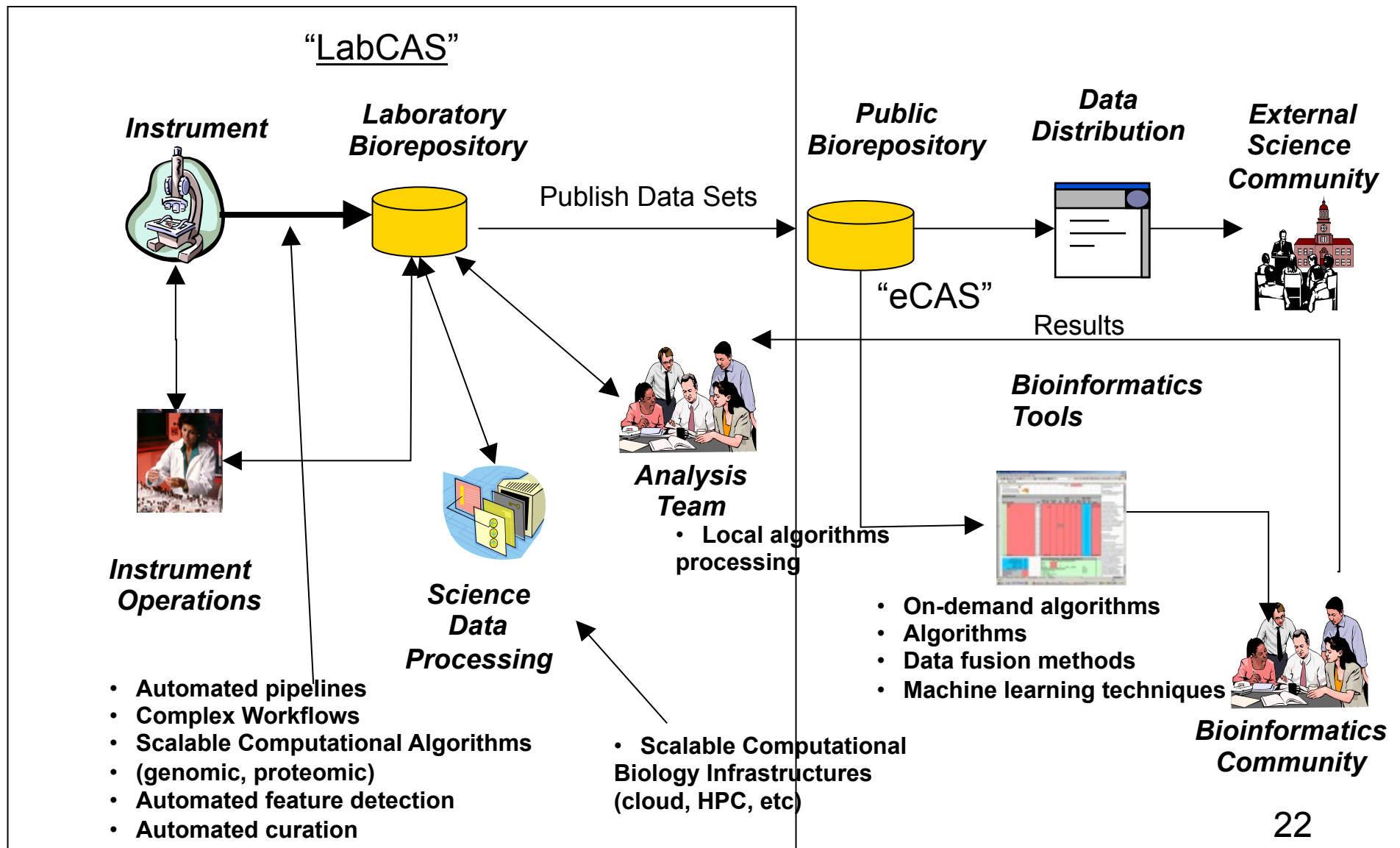
- By: BatchANXA1PR_00_840.pdf
- By: Batch14-3-3.pdf
- By: BatchLung cancer.xls
- By: BatchLDM1-1.pdf
- By: BatchLAMR1.pdf
- By: BatchNP25_5.pdf
- By: BatchNP25_14-3-3.pdf
- By: annexinIamr14-3-3.pdf

Access to download data

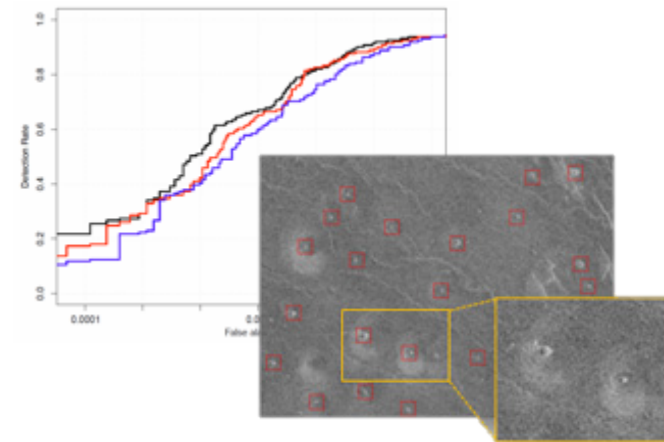
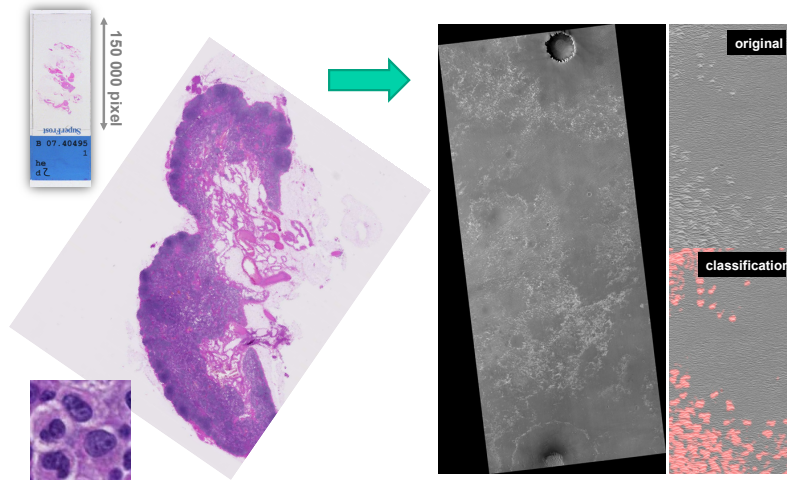
A Virtual, National Integration Biomarkers Knowledge System



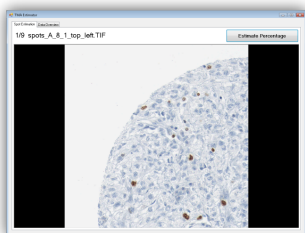
Moving towards data-driven discovery for cancer biomarkers



Application of Machine Learning Techniques

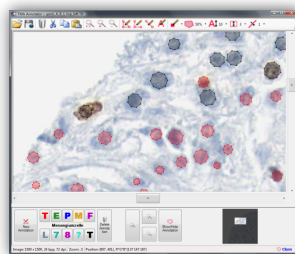


TMA Estimator



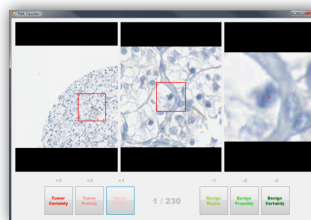
Estimate the Staining on a whole spot

TMA Annotator



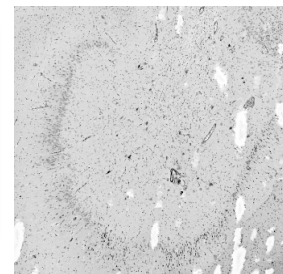
Detect nuclei on a whole spot

TMA Classifier

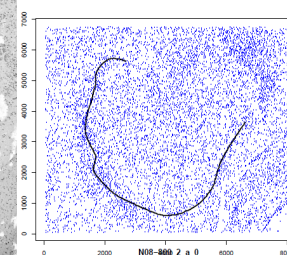


Classify single nuclei into tumor, non-tumor and stained, not-stained

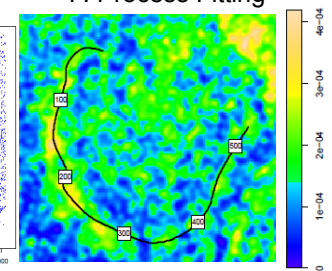
Original Image



Discriminative
Object Detection



Generative
P. Process Fitting

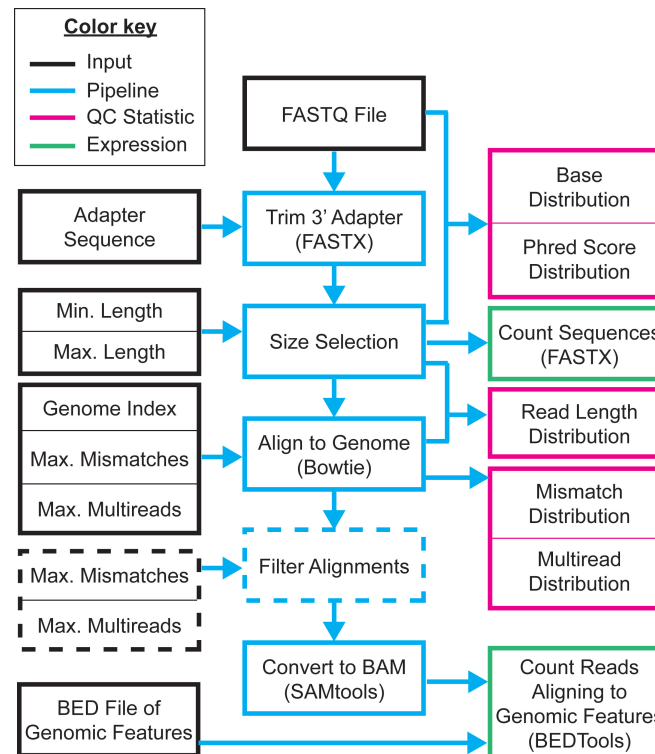


Feature/Object Detection

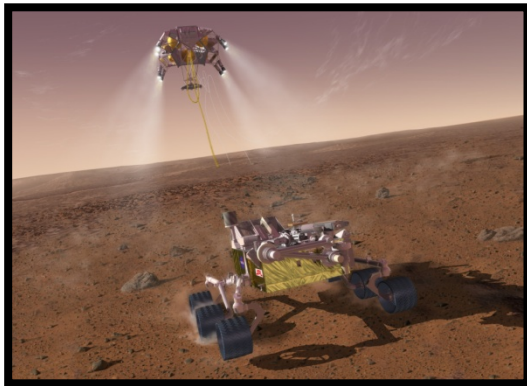
Automated Classification

Potential Collaboration Areas

- Reproducibility experiments
- Analytic Data Pipelines/Computational Methods
- Bioinformatics Tool Integration
- Data Integration
- Data Capture, Curation and Sharing
- Image Archiving and Visualization
- Linking of Distributed Capabilities
- Ontologies, Common Data Elements, etc.



Courtesy of Josh Campbell and Teresa Wang



Reproduced from *Wired* magazine



The JPL Informatics Center would like to collaborate with the ITCR Program to explore how data, tools, and methods can be shared to expand the knowledge system and support the EDRN and MCL Programs and other NCI research.



http://twitter.com/edrn_ic

[http://www.facebook.com/
group.php?gid=56938589930](http://www.facebook.com/group.php?gid=56938589930)

