

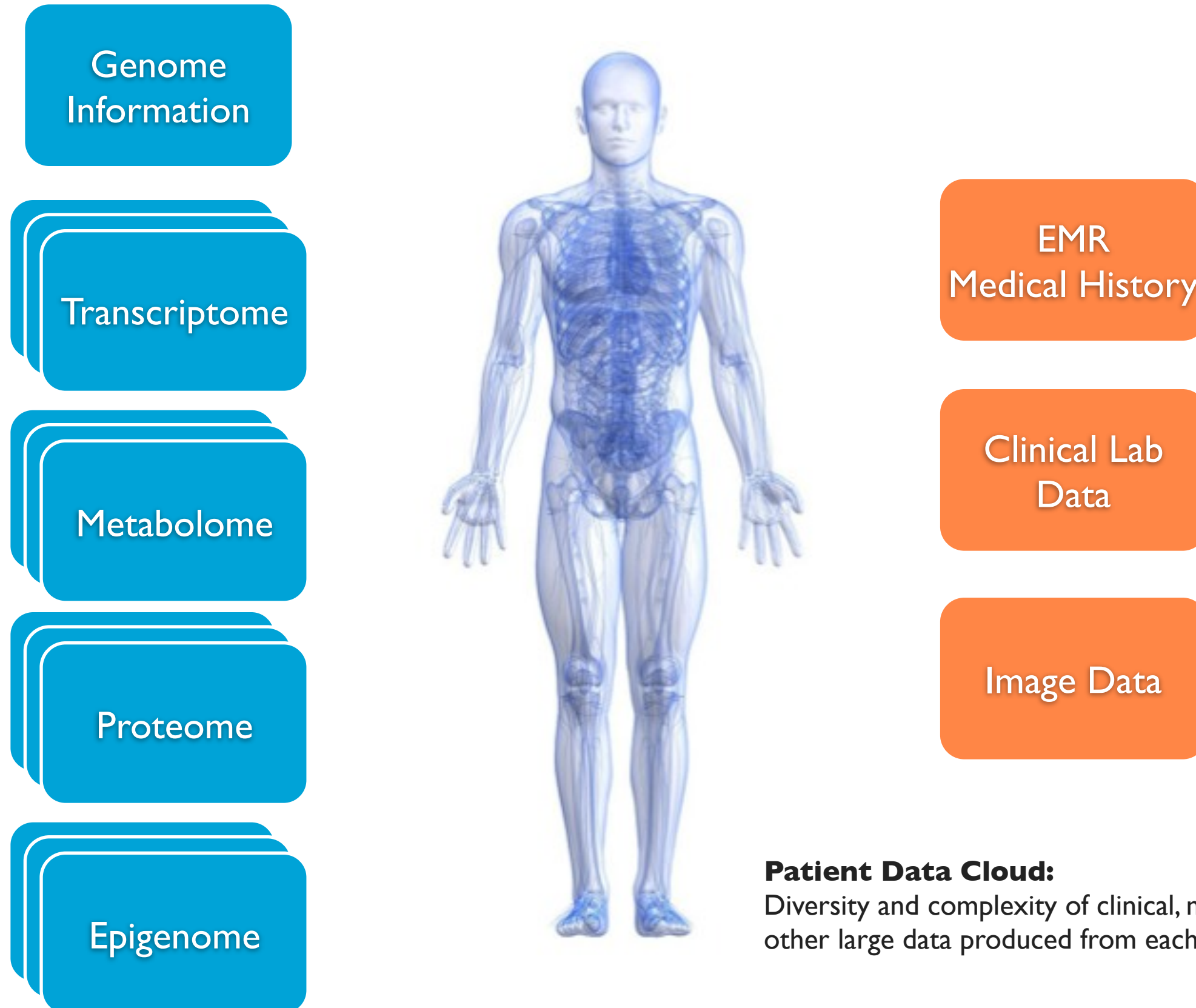


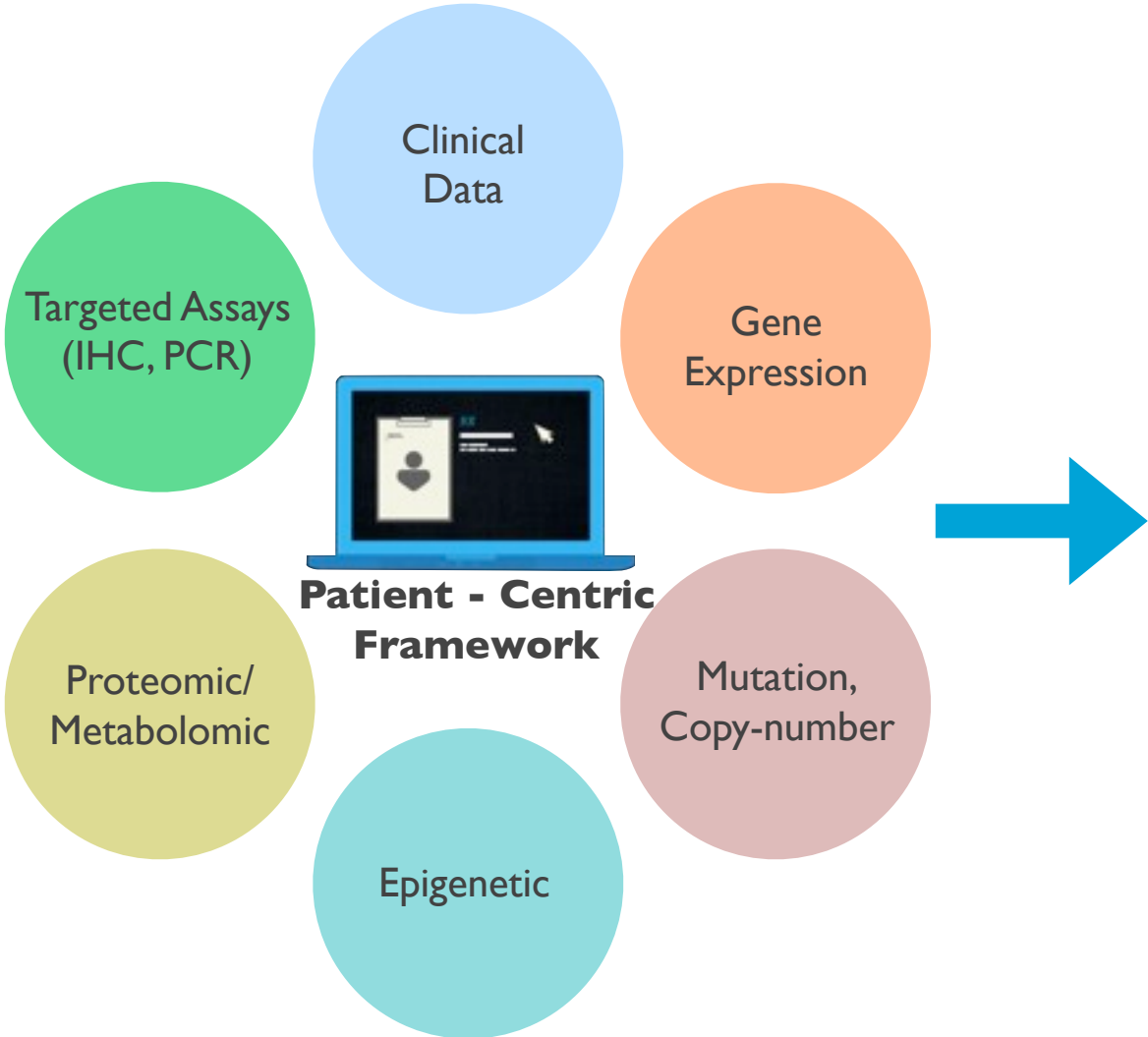
NEXTBIO™



Patient-centered approaches and modern drug R&D

Ilya Kupersmidt
Cofounder, VP Products, NextBio





PATIENT REGISTRY

PATIENT DATA

REPORTS

Patient ID

Barisha-0007

Age

35

Sex

Female

Patient Condition

Diabetes mellitus type II

Available reports for this patient

Genetic Predisposition

Therapeutic Guidance

Ongoing Monitoring

Genome Browser

Meta Analysis

PATIENT SUMMARY

MOLECULAR DATA

FAMILY INFO

Patient's Molecular Data Summary

RNA Expression

30,000

Genes

DNA Methylation

1,432

Regions Identified

Protein Expression

340

Regions Identified

Metabolites

285

Metabolites Identified

Patient's Clinical Details

Diagnosis

Diabetes mellitus type II

Sample

Blood

Clinical record

At diagnosis

At follow-up: 2 weeks

Physical attributes

Gender

Female

Female

Ethnicity

Caucasian

Caucasian

Age

35 years

35 years

Year of initial diagnosis

2006

2006

Height

5.7ft

5.7ft

Clinical attributes

Weight

225 lbm

222 lbm

Body mass index

33.9

33.9

Waist to hip ratio

0.85

0.85

Waist

38 in

38 in

Concurrent disease

Polycystic ovary syndrome

Polycystic ovary syndrome

Prior conditions

Not available

Not available

VO2 max

Below average (39mL/kg/min)

Below average (39mL/kg/min)

Systolic blood pressure

155 mmHg

150 mmHg

Diastolic blood pressure

105 mmHg

101 mmHg

Plasma metabolites

Total Cholesterol

240 mg/dL

185mg/dL

Triglycerides

450 mg/dL

365 mg/dL

Low density lipoprotein

135mg/dL

105 mg/dL

High density lipoprotein

65 mg/dL

55 mg/dL

Very low density lipoprotein

50 mg/dL

44 mg/dL

PATIENT REGISTRY



PATIENT DATA



REPORTS

Patient ID

TCGA-02-0037



Age

74

Sex

FEMALE

Patient Condition

Glioblastoma multiforme of brain

Available reports



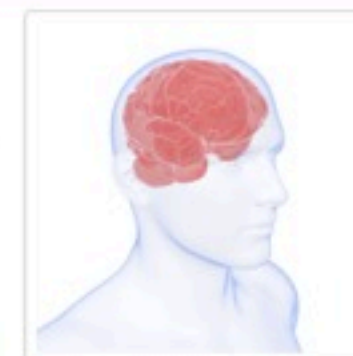
Tumor
Biomarkers



Therapeutic
Guidance



Genome
Browser



CLINICAL DATA

MOLECULAR DATA

FAMILY INFO

Summary of Molecular Data

Patient's tumor sample was compared to normal tissue in order to identify tumor-specific molecular changes

Somatic Mutations

25

SNPs

RNA Expression

17,787

Genes

DNA Copy-number

170

Regions

DNA Methylation

26,486

Regions

Patient's Clinical Details

Tumor type
Histological diagnosis

Primary tumor

Glioblastoma multiforme of the brain

Physical attributes

Gender

Female

Race

Caucasian

Ethnicity

Not Hispanic or Latino

Age

74

Year of initial diagnosis

2004

Clinical attributes

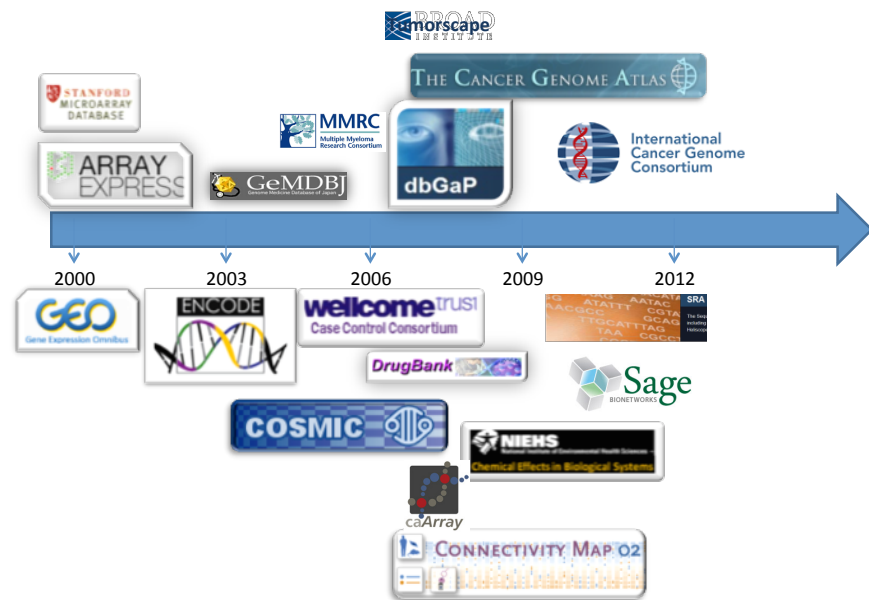
Prior diagnosis

No

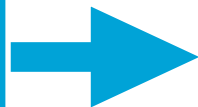
Overall survival

0.3 years

Technology generating exponential data



Internal Data



NEXTBIO™ PATIENT CENTRIC *beta*

DASHBOARD | IMPORT DATA | KNOWLEDGEBASE | SETTINGS | Ilya Kupersmidt

PATIENT REGISTRY | **PATIENT DATA** | **REPORTS**

Patient ID
TCGA-02-0037

Patient Condition
Brain cancer

Age: 74
Sex: Female

Available reports for this patient:
Tumor Biomarkers | Therapeutic Guidance | Genome Browser

APPROVED THERAPIES | **OFF LABEL THERAPIES**

Genome Filter Setup | 30 results out of 30 | Summary report | Filter Report by Gene or SNP

Drugs Specific to Patient Biomarkers

30 Patient Biomarkers
52 Total Biomarkers

| Report | Biomarker | Gene(s) | Biomarker Type | Therapy | Disease Indication | Validation Status | Clinical Interpretation |
|---------------------|-----------|---------|----------------|--------------------|---------------------------|---------------------|---|
| ISG20-Expressed | ISG20 | ISG20 | RNA Expression | Denileukin difitox | Cutaneous T Cell Lymphoma | FDA approved | Response to denileukin difitox therapy |
| ESR1-Underexpressed | ESR1 | ESR1 | RNA Expression | Exemestane | Breast Cancer | FDA approved | Response to hormone-suppression therapy |
| ESR1-Underexpressed | ESR1 | ESR1 | RNA Expression | Anastrozole | Breast Cancer | FDA approved | Response to hormone-suppression therapy |
| ESR1-Underexpressed | ESR1 | ESR1 | RNA Expression | Tamoxifen | Breast Cancer | FDA approved | Response to hormone-suppression therapy |
| ESR1-Underexpressed | ESR1 | ESR1 | RNA Expression | Fulvestrant | Breast Cancer | FDA approved | Response to hormone-suppression therapy |
| rs28934578 | TP53 | TP53 | Variant | Cisplatin | Adenocarcinoma Of Lung | CLIA test available | - |
| rs28934578 | TP53 | TP53 | Variant | Paclitaxel | Breast Cancer | CLIA test available | - |

30 Results

Technology generating exponential data



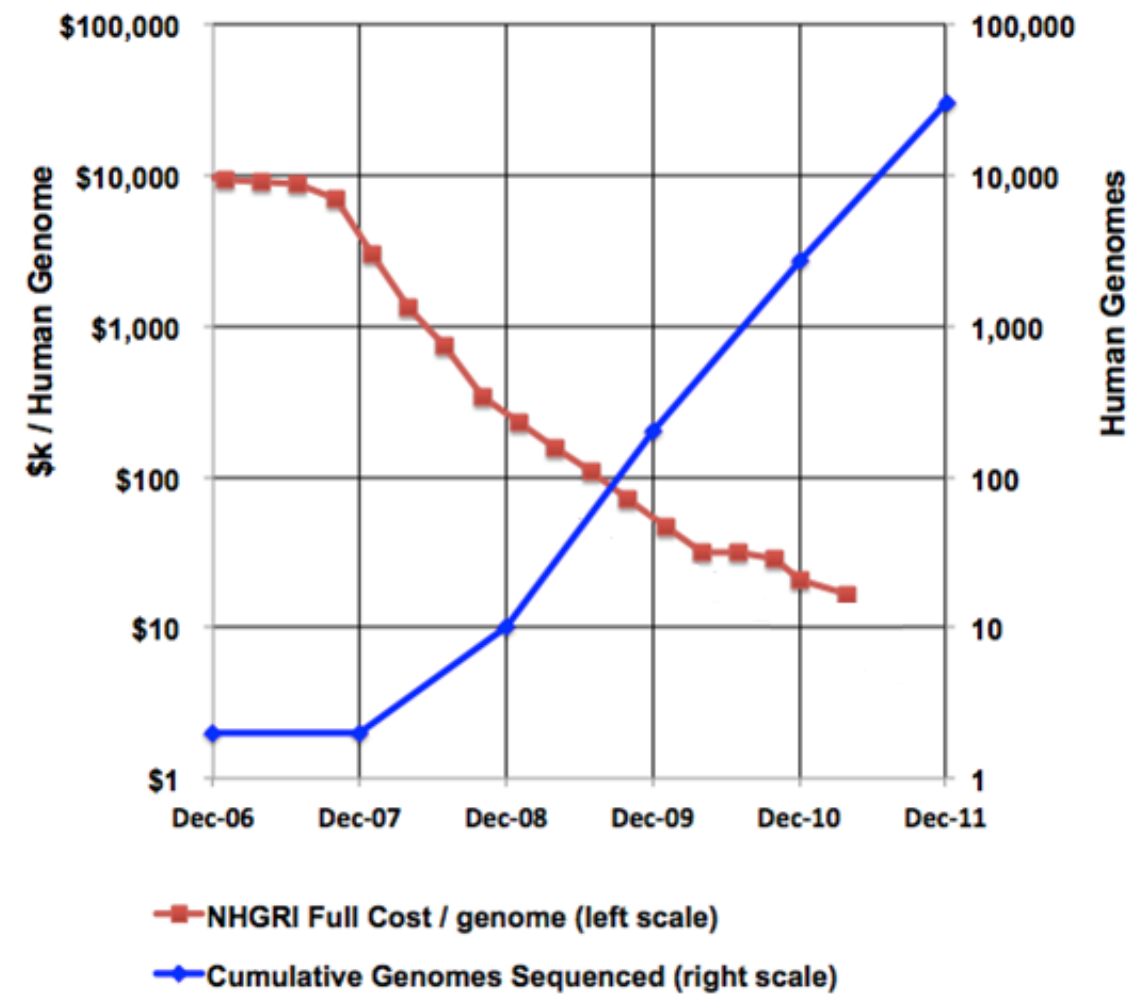
illumina



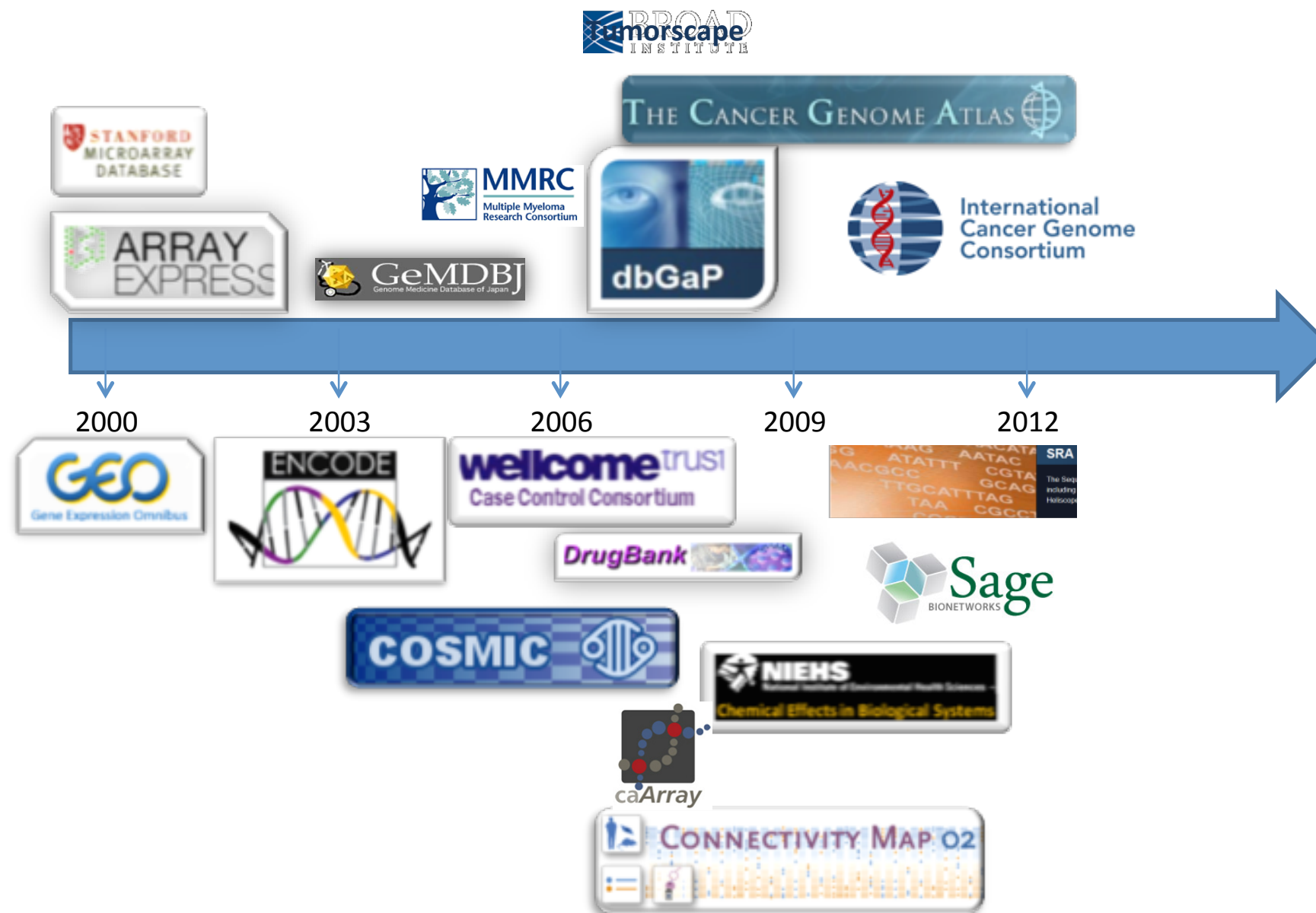
life technologies ion torrent



Oxford NANOPORE Technologies



Public Patient DataSources



- Better targets, assessed in real clinical samples
- Understanding disease by surveying data from large populations
- Biomarkers allowing better patient selection
- Adaptive clinical trials allowing integration of new research knowledge
- Personalized, safer and more effective therapies

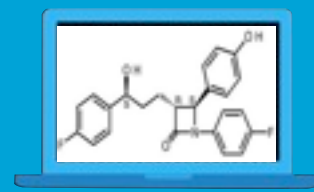
NextBio Research



Disease Signatures



Animal Models



Drug Signatures

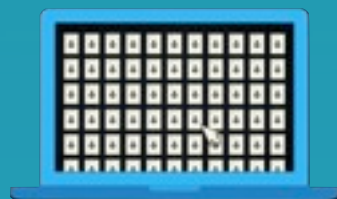


Targets & Pathways

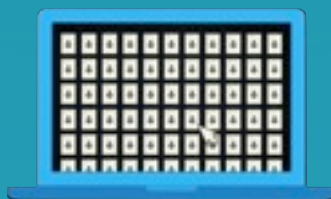
COHORT-LEVEL
Transcriptomics
Genomics
Proteomics
Metabolomics



NextBio Clinical



Patients



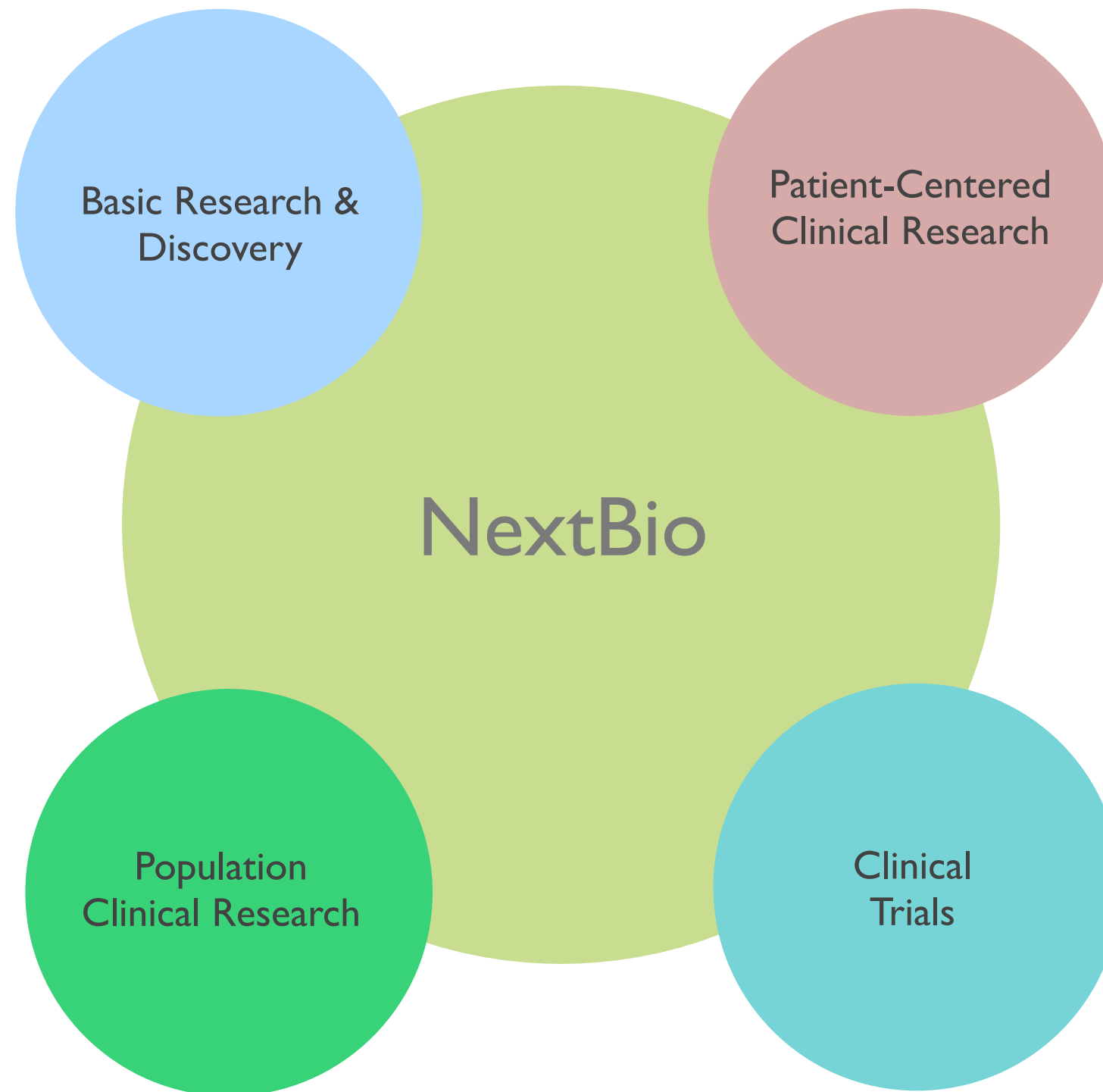
Cell Lines



Biomarkers

SUBJECT-LEVEL
Transcriptomics
Genomics
Proteomics
Metabolomics
Clinical

NextBio TM Platform



Applications

| | | | | |
|-------|-------|-------|-------|-------|
| A C C | C G C | C T T | A T A | G G A |
| A T T | C T C | G C A | A G A | C G C |
| C T C | C A C | A C T | G T A | G G A |
| A A T | C G C | C G C | T T A | G G A |
| A G T | C G C | C C C | A T A | T G A |
| A T T | C A C | C C C | A T A | G G C |
| A C T | C G T | C T A | A C C | G G A |

Discovery, Translational Research

- Target and mechanism assessment in clinical samples
- Molecular-based disease classification
- Biomarker discovery and assessment in cell lines and patient populations

Clinical

- Incorporating of latest biomarker knowledge in ongoing and future trials
- Informed patient selection - biomarkers and epidemiology
- Retrospective and perspective analysis of clinical trial data
- Aggregation of ongoing patient data for future studies

Live Application Examples

| | | | | |
|-------|-------|-------|-------|-------|
| A C C | C G C | C T T | A T A | G G A |
| A T T | C T C | G C A | A G A | C G C |
| C T C | C A C | A C T | G T A | G G A |
| A A T | C G C | C G C | T T A | G G A |
| A G T | C G C | C C C | A T A | T G A |
| A T T | C A C | C C C | A T A | G G C |
| A C T | C G T | C T A | A C C | G G A |

Patient-Centered Use Cases

- Target discovery and validation in clinical samples
- Using cell lines to identify biomarkers of drug response
- Patient selection for clinical trial optimization
- Patient monitoring - disease risk, prognosis, therapeutic response



How Do We Make It Work?

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | C | C | C | G | C | C | T | T | A | T | A | G | G | A |
| A | T | T | C | T | C | G | C | A | A | G | A | C | G | C |
| C | T | C | C | A | C | A | C | T | G | T | A | G | G | A |
| A | A | T | C | G | C | C | G | C | T | T | A | G | G | A |
| A | G | T | C | G | C | C | C | C | A | T | A | T | G | A |
| A | T | T | C | A | C | C | C | C | A | T | A | G | G | C |
| A | C | T | C | G | T | C | T | A | A | C | C | G | G | A |

How do we make it work?

Standardizing Patient Data


Common Language for Clinical Information

Precomputing Data Correlations

Data In The Cloud

Standardizing Patient DATA


Patient ID
TCGA-13-1405





Age
49
Sex
Female

Patient Condition
Ovarian cancer

Available reports


Molecular Classification


Prognosis


Therapeutic Guidance

CLINICAL DATA

MOLECULAR DATA

FAMILY INFO

Summary of Molecular Data

Patient's tumor sample was compared to normal tissue in order to identify tumor-specific molecular changes

RNA expression
17,786 Genes

DNA copy-number
247 Regions

DNA methylation
26,486 Regions

Somatic mutations
38 SNPs

Somatic Mutations Inspector

Download to Excel

Genome Browser

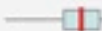







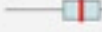

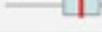

Genome Filter Setup

Filtered Variants

38


38 SNPs

Find Mutation by Gene or SNP

| SNP | Sequence Region | Mapping | Gene | NB Computed AA Change | NB Computed Mutation Class | Reference Allele | Tumor Allele1 | Tumor Allele2 |
|-----|------------------------------|--|--------------|-----------------------|----------------------------|------------------|---------------|---------------|
| | chr19: 50808770 |  | EML2 | | Splice site disru... | C | C | T |
| | chr1: 145593003 .. 145593004 |  | ACP6 | | Frameshift indels | - | - | A |
| | chr1: 89295139 |  | GBP1 | Q381. | Nonsense | G | G | A |
| | chr17: 7518988 |  | TP53 | R196. | Nonsense | G | G | A |
| | chr1: 100122272 |  | AGL | E773K | Missense | G | G | A |
| | chr1: 102042416 |  | OLFM3 | L448R | Missense | A | A | C |
| | chr1: 157002280 |  | OR6N1 | A273S | Missense | C | C | A |
| | chr2: 53934071 |  | GPR75 | D443Y | Missense | C | C | A |
| | chr3: 89342190 |  | EPHA3 | T215M | Missense | C | C | T |
| | chr4: 104257209 |  | CENPE | M2472I | Missense | C | C | T |
| | chr4: 53926373 |  | SCFD2 | P165S | Missense | G | G | A |
| | chr6: 32143602 |  | TNXB | G2192C | Missense | C | C | A |

Standardizing Patient DATA


Patient ID
TCGA-13-1405





Age
49
Sex
Female

Patient Condition
Ovarian cancer

Available reports


Molecular Classification


Prognosis


Therapeutic Guidance

CLINICAL DATA

MOLECULAR DATA

FAMILY INFO

Summary of Molecular Data

Patient's tumor sample was compared to normal tissue in order to identify tumor-specific molecular changes

RNA expression
17,786 Genes

DNA copy-number
247 Regions

DNA methylation
26,486 Regions

Somatic mutations
38 SNPs

RNA Expression Inspector

Download to Excel

Genome Browser

17,813 Genes

Find Mutation by Gene or SNP

| Symbol | Imported ID | Control Cy5/cy3 Ratio | Fold Change | P-Value | Patient Cy5/cy3 Ratio |
|----------|-------------|-----------------------|-------------|---------|-----------------------|
| CRISP3 | CRISP3 | 93.6 | -429.0 | 1.4E-5 | 0.218 |
| AGR3 | AGR3 | 37.8 | -130.0 | 4.3E-6 | 0.292 |
| C11orf88 | FLJ46266 | 90.1 | -119.0 | 2.7E-7 | 0.758 |
| SNTN | FLJ44379 | 95 | -116.0 | 8.0E-6 | 0.817 |
| LDLRAD1 | LDLRAD1 | 31.8 | -110.0 | 7.2E-7 | 0.288 |
| TTC29 | TTC29 | 90.3 | -109.0 | 9.0E-7 | 0.832 |
| FAM81B | FAM81B | 124.7 | -90.7 | 9.7E-7 | 1.37 |
| DNAH9 | DNAH9 | 53.5 | -88.3 | 4.2E-6 | 0.606 |
| S100A2 | S100A2 | 0.156 | 84.8 | 0.0005 | 13.3 |
| COL11A1 | COL11A1 | 0.743 | 70.3 | 0.0014 | 52.2 |
| KCNMB2 | KCNMB2 | 43.7 | -65.7 | 0.0011 | 0.665 |
| CDKN2A | CDKN2A | 0.184 | 63.4 | 6.3E-5 | 11.7 |

How do we make it work?

Developing Dynamically Expanding Ontologies

[NEXTBIO RESEARCH](#)
[CORPORATE HOME](#)
[CLINICAL](#)

Browse & Search

Alpha Search

History

Admin Pages

chronic |

phenotype> Chronic pain (SNOMED_CT)

phenotype> Chronic eczema (SNOMED_CT)

phenotype> Chronic anemia (SNOMED_CT)

phenotype> Chronic tremor (SNOMED_CT)

phenotype> Chronic colitis (SNOMED_CT)

phenotype> Chronic uveitis (SNOMED_CT)

phenotype> Chronic disease (SNOMED_CT)

phenotype> Chronic pulpitis (SNOMED_CT)

phenotype> Chronic cystitis (SNOMED_CT)

phenotype> Chronic vulvitis (SNOMED_CT)

Search

Please select a tag from this list.

Browse Ontology

NEXTBIO_CORE

TISSUE (21)

BIODESIGN (10)

BIOGROUP (9)

BIOSOURCE (15)

COMPOUND (15)

GENEMODE (12)

PHENOTYPE (2)

SNOMED_CT (2) [phenotype]

Clinical finding (13) [phenotype]

Clinical history and observation findings (39) [phenotype]

Clinical stage finding (4) [phenotype]

Disease (88) [phenotype]

AIDS-associated disorder (34) [phenotype]

Acute disease (50) [phenotype]

Biphasic disease [phenotype]

Calculus finding (24) [phenotype]

Chromosomal disorder (10) [phenotype]

Chronic disease (35) [phenotype]

Acute-on-chronic glaucoma [phenotype]

Chronic anemia (3) [phenotype]

Chronic anterior uveitis (1) [phenotype]

Chronic central serous chorioretinopathy (1) [phenotype]

Chronic digestive system disorder (56) [phenotype]

Chronic disease of breast (4) [phenotype]

Chronic disease of cardiovascular system (23) [phenotype]

Chronic disease of ear (7) [phenotype]

Chronic disease of genitourinary system (29) [phenotype]

Chronic disease of immune function (13) [phenotype]

Chronic disease of immune structure (2) [phenotype]

Chronic disease of lymphatic vessels (2) [phenotype]

Chronic disease of musculoskeletal system (8) [phenotype]

Chronic disease of ocular adnexa (7) [phenotype]

Chronic disease of respiratory system (39) [phenotype]

Ontology node "Chronic anemia"

Edit

Name:

Chronic anemia

Disable

Synonyms:

Chronic anemia (disorder)

Chronic anaemia

Enable Branch

Disable Branch

Add Child

Curated Studies

Paths:

PHENOTYPE / Clinical finding / Disease

Chronic disease / Chronic anemia

Finding of cellular component of blood / Red blood cell disorder / Anemia / Chronic anemia

History:

No history is available.

NextBio Confidential 2012

- ⊕ GENEMODE (12)
- ⊖ PHENOTYPE (2)
 - ⊖ SNOMED_CT (2) [phenotype]
 - ⊖ ● Clinical finding (13) [phenotype]
 - ⊕ ● Clinical history and observation findings (39) [phenotype]
 - ⊕ ● Clinical stage finding (4) [phenotype]
 - ⊖ ● Disease (88) [phenotype]
 - ⊕ ● AIDS-associated disorder (34) [phenotype]
 - ⊕ ● Acute disease (50) [phenotype]
 - Biphasic disease [phenotype]
 - ⊕ ● Calculus finding (24) [phenotype]
 - ⊕ ● Chromosomal disorder (10) [phenotype]
 - ⊖ ● Chronic disease (35) [phenotype]
 - Acute-on-chronic glaucoma [phenotype]
 - ⊕ ● Chronic anemia (3) [phenotype]
 - ⊕ ● Chronic anterior uveitis (1) [phenotype]
 - ⊕ ● Chronic central serous chorioretinopathy (1) [phenotype]
 - ⊕ ● Chronic digestive system disorder (56) [phenotype]
 - ⊕ ● Chronic disease of breast (4) [phenotype]
 - ⊕ ● Chronic disease of cardiovascular system (23) [phenotype]
 - ⊕ ● Chronic disease of ear (7) [phenotype]
 - ⊕ ● Chronic disease of genitourinary system (29) [phenotype]
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 - ⊕ ● Chronic disease of immune structure (2) [phenotype]
 - ⊕ ● Chronic disease of lymphatic vessels (2) [phenotype]
 - ⊕ ● Chronic disease of musculoskeletal system (8) [phenotype]
 - ⊕ ● Chronic disease of ocular adnexa (7) [phenotype]
 - ⊕ ● Chronic disease of respiratory system (39) [phenotype]

Ontology node "Chronic anemia"

Edit

Name:

Chronic anemia

Disable

Synonyms:

- Chronic anemia (disorder)
- Chronic anaemia

Enable Branch

Disable Branch

Add Child

Curated Studies

Paths:

PHENOTYPE / Clinical finding / Disease

- Chronic disease / Chronic anemia
- Finding of cellular component of blood / Red blood cell disorder / Anemia / Chronic anemia

History:

No history is available.

How do we make it work?

Patient Data Needs to be Indexed and Correlated

In The Cloud

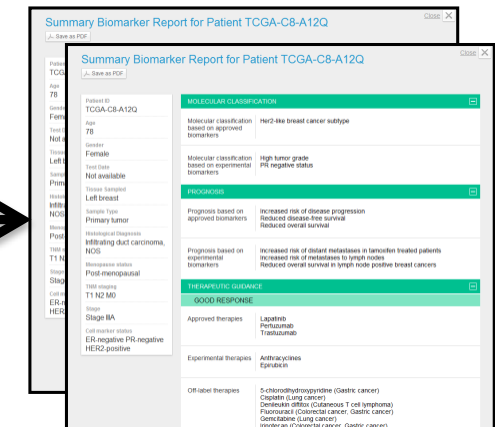
Scalable Service Oriented Architecture

HIPAA
Health Insurance Portability
and Accountability Act

- Single Instance Multiple Tenant SaaS Architecture
- Rapid Agile Development
- Reusable Services

Alignment
Comparison to
Reference

Correlation to
All Genomic Data



Scale with
Commodity Hardware

Comparison to
Genomic Coordinates

Generate Reports
Generate Searchable Index

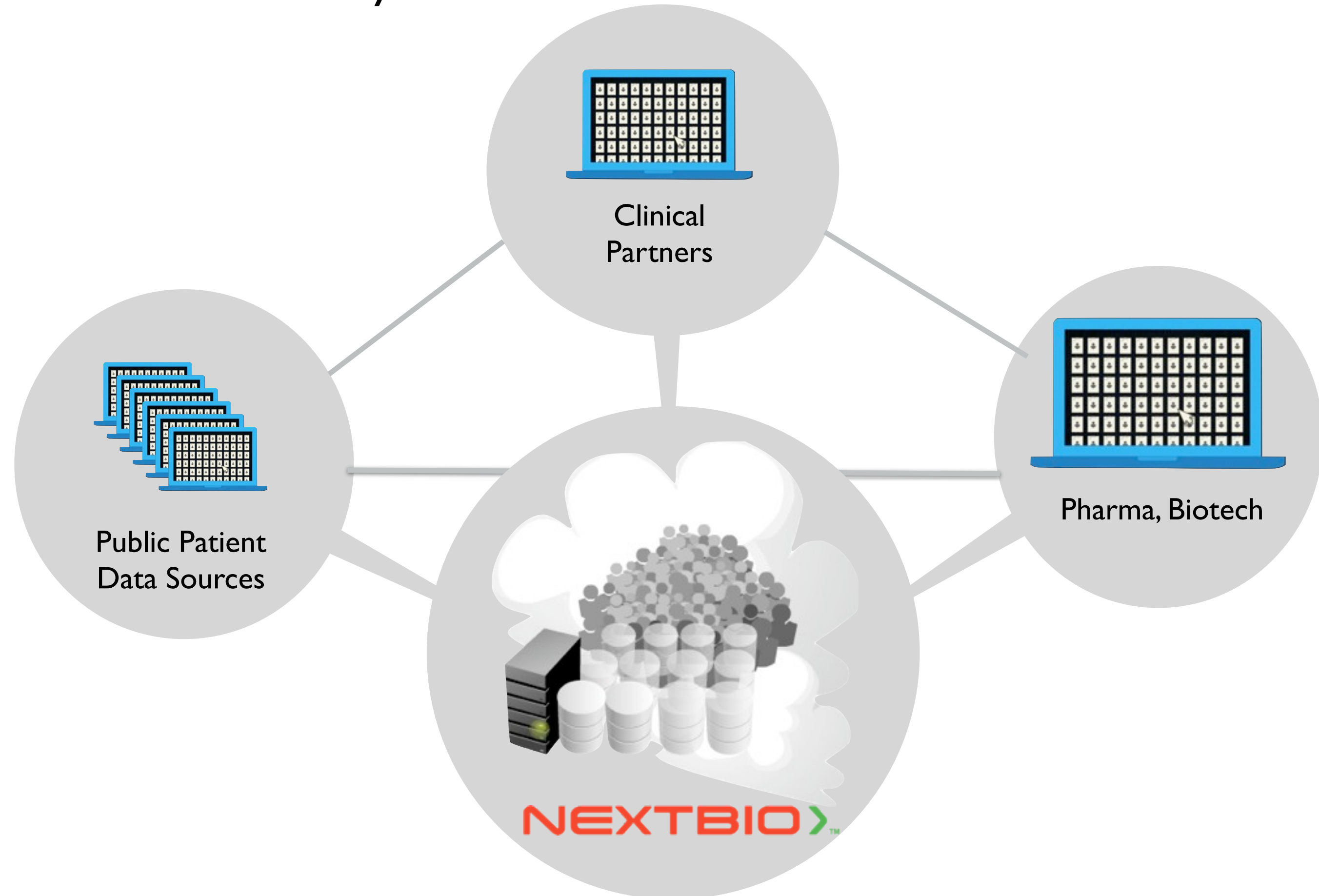


Principles

- Leverage Open-Source
- Single instance multiple tenant
- Services oriented architecture
- Stateless services
- Partitioned for scale
- Scale with commodity hardware
- No downtime philosophy
- Agile development



Patient Data Ecosystem



Thank You

