BioMart and GMOD working towards a closer integration?

Arek Kasprzyk
Ontario Institute for Cancer Research
16th January 2009
BioMart in a nutshell

• open source data management system
  □ Large scale datasets
  □ Data federation
  □ Query optimization
  □ supports MySQL, Oracle and Postgres

• www.biobase.org
BioMart Work Flow

- Data transformation
- GUI configuration
- Web GUI, web service, API, DAS server
Publicly Available Marts

- Ensembl
- HapMap
- High Throughput Gene Targeting Group
- Dictybase
- Wormbase
- Gramene
- Europhenome
- Rat Genome Database
- EU Rat Mart
- ArrayExpress Data Warehouse
- Eurexpress
- DroSpeGe
- GermOnLine
- PRIDE
- PepSeeker
- VectorBase
- Pancreatic Expression Database
- Reactome
- Paramecium DB

www.biomart.org
Software with BioMart Plugin

- Bioclipse
- Bioconductor
- Cystoscape
- Galaxy
- Taverna
- WetLab

Single point of access
Single interface
Coming up …

• Uniprot
• HGNC
• Integr8
• IntAct
• Ensembl genomes
• EMMA
• I-DCC
• CREATE
• MGI
• Cancer Mart
  • Mouse Informatics Portal
  • International Cancer Genome Consortium (ICGC) Portal
## Ontario Institute for Cancer Research

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<th>Innovation Platforms</th>
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<td>Ontario Cancer Cohort</td>
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<td>Cancer Targets</td>
<td>Cancer Stem Cells</td>
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<td>Bio-repositories and Pathology</td>
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<td>Selective Agents (Terry Fox Research Institute - Ontario Node)</td>
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<td>Informatics and Biocomputing</td>
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<tr>
<td></td>
<td></td>
<td>Data Coordination Center (DCC)</td>
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</table>

### Translation Programs
- Patents to Products
- High Impact Clinical Trials
- Cancer Care and Services (including Health Promotion)
International Cancer Genome Consortium

Goals

• Catalogue genomic abnormalities in tumors in 50 different cancer types and/or subtypes of clinical and societal importance across the globe

• Generate complementary catalogues of transcriptomic and epigenomic datasets from the same tumors

• Make the data available to the entire research community as rapidly as possible and with minimal restrictions to accelerate research into the causes and control of cancer

50 different tumor types and/or subtypes

500 samples per tumor

25,000 Human Genome Projects!
Data Types

For each specimen
- pathology
- clinical history
- sequence variants
- structural variants
- copy number variants
- gene expression
- splice variants
- epigenetic variants

Annotations
- gene ontologies
- pathways
- protein-protein interactions
- transcription factors
- other public and licensed annotation

Diverse data types
- images
- clinical notes and tests
- genomic data
# Current Members of ICGC

<table>
<thead>
<tr>
<th>Country</th>
<th>Funding Organization</th>
<th>Tumor Type</th>
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<tbody>
<tr>
<td>Australia</td>
<td>National Health and Medical Research Council Announcement</td>
<td>Imminent</td>
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<tr>
<td>Canada</td>
<td>Ontario Institute for Cancer Research</td>
<td>Pancreas</td>
</tr>
<tr>
<td>China</td>
<td>Chinese Cancer Genome Consortium</td>
<td>Stomach</td>
</tr>
<tr>
<td>France</td>
<td>Institut National du Cancer</td>
<td>Liver (alcohol-related)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Breast (HER2-positive)</td>
</tr>
<tr>
<td>India</td>
<td>Department of Biotechnology, Ministry of Science &amp; Technology</td>
<td>Oral Cavity</td>
</tr>
<tr>
<td>Japan</td>
<td>RIKEN, National Cancer Center and National Institute of Biomedical Innovation</td>
<td>Liver (virus-related)</td>
</tr>
<tr>
<td>Spain</td>
<td>Spanish Ministry of Science and Innovation</td>
<td>Chroniclymphocytic leukemia</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>The Wellcome Trust; Wellcome Trust Sanger Institute</td>
<td>Breast (several subtypes)</td>
</tr>
</tbody>
</table>
ICGC Data Coordination Centre

Mission
• implement project-wide standards for data completeness, quality and protection of confidentiality
• manage the collection and distribution of ICGC data
• manage an ICGC portal that provides researchers with project-wide data search and retrieval services

Challenges

Data
□ quantity
□ content
□ format
□ location
□ diversity

Database & Software
□ design
□ implementation
□ resources
□ time scale
□ synchronization with data
Multiple Querying Interfaces

Analysis & Visualization tools

ICGC DCC Portal

Conceptual Data Architecture – Federated Model

OICR

ICGC Member

ICGC Member

Federated Public Databases

- DNA Sequences (Sanger, UK)
- Pancreatic Expression (UK)
- Reactome (CSHL, US)
Controlled access data

Data Protection Office

OpenID

DCC?

Authorization Db

DCC Data Mart
Versioning of Data

Time

Release date for ICGC Build 1

Release date for ICGC Build 2

Site 1

- V.1
- V.2
- V.3

Available versions: 1 2 3

BioMart

FTP

Site 2

- V.a
- V.b
- V.c
- V.d
- V.e

Available versions: a b c d e

FTP

Portal

ICGC Build 1

ICGC Build 2

Available versions: 1 a 3 e
Demo: functionality

Biomarker discovery

In pancreatic tumor, which genes have copy number gain and up-regulated expression?

a. Retrieve DNA sequences 100bp upstream to these genes
b. Compare these fold changes with Pancreatic Expression Database

OICR (Canada) 
Sanger (UK) 
Pancreatic Expression (UK) 
Bethesda (US)
New GUI example

Mouse Informatics Project

Explore MIP

Genes

Phenotypes

Expression

Function

Pathways

Strains / SNPs

Orthology

FAQs

How do I...

.. search for genes? FAQ

.. find mutations for phenotypes or diseases? FAQ

.. find expression data? FAQ

.. view a structural genomic map? FAQ

News

………… Read more…

……. Read more…

…… ...

Contributing Projects:
Mouse Genome Database (MGD), Gene Expression Database (GXD), Mouse Tumor Biology (MTB), Gene Ontology (GO), MouseCyc

More MIP news

MIP Statistics

last database update
10/21/2006

Web browser compatibility

Citing These Resources
Funding Information
Warranty, Disclaimer & Copyright Notice
Send questions and comments to User Support.
Visualization: Gene List Analysis & Clinical Significance

**Query**
- Cancer types
- Gene annotation
- Chromosomal rearrangement (CR)
- Copy number variation (CNV)
- Single nucleotide polymorphism (SNP)
- Epigenetic modification (EM)
- Alternative splicing (AS)
- Transcript expression
- High throughput screen (HTS)

**Gene List**

**Visualization**
- Gene list analysis
- Clinical Significance
  - Event-free survival
  - Response therapy
  - Map genes onto genome
  - Map genes onto GO
  - Map genes onto Pathways
Map Genes onto Genome
Visualization: Gene List Analysis & Clinical Significance

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Gene List

Visualization
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  - Map genes onto genome
  - Map genes onto GO
  - Map genes onto Pathways
- Clinical Significance
  - Event-free survival
  - Response therapy
Map Genes onto GO

- Biological process (32)
  - Molecular Function (24)
  - Cellular component (18)
  - Developmental process (15)
    - Cell killing (17)
      - Stem cell maintenance (7)
      - Positive regulation of developmental process (8)
      - Leukocyte mediated cytotoxicity (5)
      - regulation of cell killing (12)
Visualization: Gene List Analysis & Clinical Significance

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**Gene List**

**Visualization**
- Gene list analysis:
  - Map genes onto genome
  - Map genes onto GO
  - Map genes onto Pathways
- Clinical Significance:
  - Event-free survival
  - Response therapy
Map Genes onto Pathways

- Intrinsic pathway for apoptosis (26)
  - Activation of BH3-only proteins (5)
  - Permeabilization of mitochondria (3)
  - Release of apoptotic factors from mitochondria (18)

- Signaling by Wnt (10)

- Signaling by TGFβ (23)

- Apoptosis (43)
Visualization: Gene List Analysis & Clinical Significance

Query
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Gene List

Visualization

Gene list analysis
- Map genes onto genome
- Map genes onto GO
- Map genes onto Pathways

Clinical Significance
- Response to therapy
- Event – free survival
Stratify Patients’ Response to Therapy by Gene Signature

<table>
<thead>
<tr>
<th>Response to Therapy</th>
<th>Number of Patients</th>
</tr>
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<tbody>
<tr>
<td>none</td>
<td>with gene signature X: 3</td>
</tr>
<tr>
<td>partial</td>
<td>with gene signature X: 2</td>
</tr>
<tr>
<td>complete</td>
<td>with gene signature X: 1</td>
</tr>
</tbody>
</table>
Visualization: Gene List Analysis & Clinical Significance

**Query**
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**Gene List**

**Visualization**

**Gene list analysis**
- Map genes onto genome
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- Map genes onto Pathways

**Clinical Significance**
- Response to therapy
- Event – free survival
Stratify Patients’ Survival by Gene Signature

Number of patients

Survival (years from diagnosis)

with gene signature X
without gene signature X
The plan - 0.8

• Full portal support
• New configuration system
  □ Multiple GUI framework
  □ Analysis and Visualization
  □ Multi-tier secure data access
• Better federation support
• Better integration with third party tools
Part II

BioMart GMOD integration
Configuring BioMart Server

XML configuration

Mart

Dataset

Attribute

Filter
**MartView (Web GUI)**

### Dataset
- 741 out of 37435 Genes
- Homo sapiens genes (NCBI36)

### Filters
- Chromosome: 1
- Band Start: p36.33
- Band End: p35.2

### Attributes
- Ensembl Gene ID
- Ensembl Transcript ID
- Chromosome Name
- Band

### Dataset
- MSD protein structures

### Filters
- Experiment type: NMR

### Attributes
- PDB ID(s)
- Release Date
- Experiment Type

### Table
<table>
<thead>
<tr>
<th>Ensembl Gene ID</th>
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<td>1k4</td>
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<td></td>
<td>NMR</td>
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</tbody>
</table>

**biomart version 0.7**
my $initializer = BioMart::Initializer->new('registryFile'=>$confFile);
my $registry = $initializer->getRegistry;
my $query = BioMart::Query->new('registry'=>$registry,'virtualSchemaName'=>"central_server_1");

$query->setDataset("hsapiens_gene_ensembl");
    $query->addFilter("band_start", ["p36.33"]);
    $query->addFilter("chromosome_name", ["1"]);
    $query->addFilter("band_end", ["p35.2"]);
    $query->addAttribute("ensembl_gene_id");
    $query->addAttribute("ensembl_transcript_id");
    $query->addAttribute("chromosome_name");
    $query->addAttribute("band");

$query->setDataset("msd");
    $query->addFilter("experiment_type", ["NMR"]);
    $query->addAttribute("pdb_id");
    $query->addAttribute("release_date");
    $query->addAttribute("experiment_type");

my $query_runner = BioMart::QueryRunner->new();
$query_runner->execute($query);
$query_runner->printResults();
<Query virtualSchemaName = "default" formatter = "TSV" datasetConfigVersion = "0.5" >

<Dataset name = "hsapiens_gene_ensembl" interface = "default" >
   <Filter name = "band_start" value = "p36.33"/>
   <Filter name = "chromosome_name" value = "1"/>
   <Filter name = "band_end" value = "p35.2"/>
   <Attribute name = "ensembl_gene_id" />
   <Attribute name = "ensembl_transcript_id" />
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   <Attribute name = "band" />
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<Dataset name = "msd" interface = "default" >
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</Query>
MartService (SOAP)

```xml
<soapenv:Envelope xmlns:soapenv="http://schemas.xmlsoap.org/soap/envelope/"
xmlns:mar="http://www.biomart.org:80/MartServiceSoap">
  <soapenv:Header/>
  <soapenv:Body>
    <mar:Query>
      <virtualSchemaName>default</virtualSchemaName>
      <header>0</header>
      <count>0</count>
      <uniqueRows>0</uniqueRows>
      <Dataset>
        <name>hsapiens_gene_ensembl</name>
        <Filter><name>chromosome_name</name><value>1</value></Filter>
        <Filter><name>band_start</name><value>p36.33</value></Filter>
        <Filter><name>band_end</name><value>p35.2</value></Filter>
        <Attribute><name>ensembl_gene_id</name></Attribute>
        <Attribute><name>ensembl_transcript_id</name></Attribute>
        <Attribute><name>chromosome_name</name></Attribute>
        <Attribute><name>band</name></Attribute>
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      <Dataset>
        <name>msd</name>
        <Filter><name>experiment_type</name><value>NMR</value></Filter>
        <Attribute><name>pdb_id</name></Attribute>
        <Attribute><name>release_date</name></Attribute>
        <Attribute><name>experiment_type</name></Attribute>
      </Dataset>
    </mar:Query>
  </soapenv:Body>
</soapenv:Envelope>
```
URL-based access

- Pre-defined queries (links shown in webpage)
- Bookmark / referencing
- An example:
  http://www.biomart.org/biomart/martview?VIRTUALSCHEMANAME=default&ATTRIBUTES=
  default.feature_page.ensembl_transcript_id|hsapiens_gene_ensembl.default.feature_page.ch
 romosome_name|hsapiens_gene_ensembl.default.feature_page.band|msd.default.feature_p
  age.pdb_id|msd.default.feature_page.release_date|msd.default.feature_page.experiment_typ
  e&FILTERS=hsapiens_gene_ensembl.default.filters.band_start."p36.33"|hsapiens_gene_ens
  embl.default.filters.chromosome_name."1"|hsapiens_gene_ensembl.default.filters.band_end.
  "p35.2"|msd.default.filters.experiment_type."NMR"&VISIBLEPANEL=resultspanel
# Major GMOD components

<table>
<thead>
<tr>
<th>Community Annotation</th>
<th>Gene Expression Visualization</th>
<th>Ontology Visualization</th>
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<td>Apollo</td>
<td>Caryoscope</td>
<td>Go Graphic Viewer</td>
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<tr>
<td>Wiki</td>
<td>GeneXplorer</td>
<td></td>
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<td>Table Editor</td>
<td>Java TreeView</td>
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<thead>
<tr>
<th>Comparative Genome Visualization</th>
<th>Genome Annotation</th>
<th>Workflow Management</th>
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<tbody>
<tr>
<td>CMap</td>
<td>Apollo</td>
<td>Ergatis</td>
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<tr>
<td>GBrowse syn</td>
<td>MAKER</td>
<td></td>
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<tr>
<td>SynView</td>
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<tr>
<td>SynBrowse</td>
<td></td>
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<td>Sybil</td>
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<th>Genome Visualization &amp; Editing</th>
<th>Middleware</th>
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<tbody>
<tr>
<td>Chado</td>
<td>Apollo</td>
<td>Modware</td>
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<td>Flash GVviewer</td>
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<td>GBrowse</td>
<td>Chado::AutoDBI</td>
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<td>GMODWeb</td>
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<td></td>
<td>Restriction Graphic Viewer</td>
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<tr>
<th>Database tools</th>
<th>Literature Tools</th>
<th>Tool Integration</th>
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<tr>
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<td>BioMart</td>
<td>Textpresso</td>
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<td>Genome grid</td>
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<td>GMODTools</td>
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<td>LuceGene</td>
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<tr>
<td>XORT</td>
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<td>InterMine</td>
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<thead>
<tr>
<th>Molecular Pathway Visualization</th>
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<th>Sequence Alignment</th>
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<tbody>
<tr>
<td>Pathway Tools</td>
<td></td>
<td>Blast Graphic</td>
</tr>
</tbody>
</table>

(gmod.org/wiki/Overview)
GMOD and BioMart

Chado

GMOD visualization, analysis tools:
- GBrowse
- CMap
- Galaxy
- etc.

BioMart

Interfaces (API, web, web service) provided by BioMart
Possible interactions between BioMart server and other GMOD components

Data Provider

BioMart

Data Input Helper

Ontology Visualization:
- Go Graphic Viewer

Genome Visualization Tools:
- GBrowse
- CMap
- GBrowse_syn
- SynView
- SynBrowse
- Sybil

Expression Visualization Tools:
- Caryoscope
- GeneXplorer
- Java TreeView

Tool Integration:
- Galaxy

Data Consumers
BioMart in addition to Chado as a data source

GMOD annotation tools:
- Apollo

Data Loaders:
- GFF to Chado
- GMODTools
- XORT
- Modware

GMOD visualization, analysis tools:
- GBrowse
- CMap
- Galaxy
- etc.

Interfaces (API, web, web service) provided by BioMart
BioMart Data sources -> GMOD

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GMOD/BioMart integration: architecture overview

BioMart Server

Configurations

Web Service

Perl API

For each client, an application-specific adaptor is needed to communicate with BioMart server.

Client applications written in Perl:
- GBrowse
- CMap
- etc.

Client applications written in other languages:
- Java TreeView
- Galaxy
- etc.
GMOD/BioMart integration: examples

BioMart Server

Configurations (including application-specific settings)
- GBrowser
- DAS
- CMap
- ...

Web Service
Perl API

BioMart Server side

GBrowser
DAS client
CMap
Others

Client side

Universal code communicating with BioMart
Application-aware code

BioMart-aware code for submitting query to a BioMart Server
GBrowse-aware code for preparing query and retrieving data
DAS-aware code for preparing query and retrieving data
CMap-aware code for preparing query and retrieving data

Via: Web Service
Via: Perl API
Via: BioMart Web Service
Via: Web Service
Via: Perl API
Via: Web Service
Via: Perl API
Via: Web Service
Via: Perl API
Server side application-specific configuration example

Configurations (including application-specific settings)

- GBrowse
- DAS
- CMap
- ...

```
<Importable
    filters="chromosome_name,start,end"
    internalName="ensembl_das_chr"
    linkName="ensembl_das_chr"
    name="ensembl_das_chr"
    type="dasChr" />

<Exportable
    attributes="ensembl_gene_id,start_position,end_position,strand,
                ensembl_transcript_id,transcript_start,transcript_end,
                ensembl_exon_id,exon_chrom_start,exon_chrom_end"
    internalName="ensembl_das_chr"
    linkName="ensembl_das_chr"
    name="ensembl_das_chr"
    pointer="true"
    type="dasChr" />
```

Importable defines the filter(s) of the query
Exportable defines the attribute(s) of the query
BioMart in addition to Chado as a data source

GMOD annotation tools:
- Apollo

Data Loaders:
- GFF to Chado
- GMODTools
- XORT
- Modware

Chado

GMOD visualization, analysis tools:
- GBrowse
- CMap
- Galaxy
- etc.

Interfaces (API, web, web service) provided by BioMart

Data source

BioMart
**BioMart Adaptor**

<table>
<thead>
<tr>
<th>Via: Web Service</th>
<th>Via: Perl API</th>
</tr>
</thead>
<tbody>
<tr>
<td>BioMart-aware code for submitting query to a BioMart Server</td>
<td>Third party app aware code for preparing query and retrieving data</td>
</tr>
</tbody>
</table>

**Hackathon?**
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