

G-DOC *Plus* demo Translational research use case

using the Rembrandt dataset

Innovation Center for Biomedical Informatics Georgetown University Medical Center

Georgetown | Lombardi

Case study

• Perform multi-omics analysis

• Example query:

Compared patients with Astrocytoma (low grade glioma) with those with Gliobastoma (GBM, high grade glioma) in the NCI REMBRANDT study.

Overview

- Register
- Login
- Navigation
- How to create patient groups
- Group comparison using gene expression data
- Group comparison using copy number data
- Clinical KM plot

G-DOC Plus front page

Can get info on:

- Disease types
- Total number of studies for each disease type



News

[read]

GUMC News: Triple Negative Breast Cancer in

Amarantus Options Blood-based Alzheimer's

Biomarkers from Georgetown - 1/15/2015

iPAD Application Makes Boring Data Collection History - 12/3/2012 [read]

Biomedical Computational Review: Personalized Cancer Treatment - Seeking Cures Through Computation - 1/2/2012 [read]

OncLive: Georgetown Lombardi Comprehensive Cancer Center: Innovation

9/1/2011 [read]

Steps Towards Individualized Treatment

African-American Women has Distinct Difference - 4/22/2015 [read]

Log In

register now | forgot password



Understanding Data in G-DOC Plus

It all begins with a study ...

All data in G-DOC Plus derives from studies on topics such as breast cancer, wound healing, or even 1,000 Genomes. Each study may contain clinical and/or biospecimen data. Below is an overview of studies by topic.

* private studies, ones which are uploaded and marked private, are not counted here



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First time user ? Register



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New	s
October	02, 2014: ICBI Symposium 2014
[read]	
May 02,	2014: Featured in Frontiers' Top 10
May 02, 2013 Mo	2014: Featured in Frontiers' Top 10 ist viewed Genetics Research articles

Login

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October	02, 2014: ICBI Symposium 2014
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way uz,	
2013 Mc	st viewed Genetics Research articles



Home

0

G-DOC Plus Launch Pad!

Welcome! The G-DOC Plus Launch Pad is your one-stop resource for learning more about G-DOC and getting started on the platform.



Home

0

What's your area of interest?

Groups

G-DOC Plus has three overlapping entry points for the user based on their interests. Choose your area of interest to launch the workflow.



Select disease/data of interest



Choose between patient and cell line data



Select study



Study selected. Let's now create some groups



Explore Clinical Data and Create Groups

Current Study: REMBRANDT change study?

Subject Search

Filter [reset tip:	advanced search
----------------------	-----------------

Demographics

- 🔄 Age range 🔞
- 🗌 Gender 🔞
- 🔄 Race 🔞

Sample details

Anti convulsant status
 Copy number data
 Gene expression data

view all (2 more ...)

Clinical evaluation

Disease evaluation by MRI

Neurologic exam score

Performance Status Score:

Karnofsky 😡

Outcome

Event indicator for overall survival

0

🗆 Overall survival in months 😡

Current Split Attribute Type of disease	•
Type of disease	All Subjects
OLIGODENDROGLIOMA	86
ASTROCYTOMA	170
UNKNOWN	68
UNCLASSIFIED	1
NON TUMOR	31
GBM	261
MIXED	13
Total	630

This page allows you to explore the clinical data. This is an online shopping type of experience. Feel free to check and uncheck the boxes on the left – this will update the patient numbers in the table.

e.g. In this example you can see that among there are 86 Oligodendroglioma patients, 170 Astro and 261 GBM patients

Let's save the Astro and GBM patients

Explore Clinical Data and Create Groups

Current Study: REMBRANDT

change study?

	Subject Search	
Filter [reset tips advanced search] Demographics	Current Split Attribute	
Age range 😡	Type of disease	All Subjects
☐ Gender (6) ☐ Race (6)	OLIGODENDROGLIOMA	86
	ASTROCYTOMA	170
Sample details	UNKNOWN	68 View Detailed Report
Copy number data	UNCLASSIFIED	1 Save ids as list
Gene expression data	NON TUMOR	31
view all (2 more)	GBM	261

To save a list of patients, click on the hyperlinked number, and select "Save ids as list". Repeat this procedure to create as many number of patient groups as needed.

E.g.: Click on "170" to save Astro patient list. Click on "261" to save GBM patient list

Note: "View detailed report" shows a detailed clinical report of those selected patients.

Enter a name for the list, and click "Save"

udy: REMBRANDT

change study?

Subject Search



Now we want to compare the Astrocytoma patients with GBM patients

Go to Study Options -> Group comparison

G-DOC Home Studies Lists	Analyses Groups Notifica	tions	Study Options Help	
Explore Clinic Current Study: REMBRANDT change st	al Data ar	٦d	Study Selected REMBRANDT SEARCH Genome Browser Compound/Drug Targets)S
Filter [reset tips advanced search] Demographics	Subject Search Current Split Attribute Type of disease	-	Findings Explore Clinical Data and Create Groups Gene Expression Data	s
☐ Gender @ ☐ Race @	OLIGODENDROGLIOMA ASTROCYTOMA	86 170	Group Comparison Chromosomal Instability Index KM Clinical Plot	
Anti convulsant status @ Copy number data @ Gene expression data @	UNKNOWN UNCLASSIFIED NON TUMOR	68 1 31	KM Gene Expression Plots Classification HeatMap Viewer	
view all (2 more)	GBM MIXED	261 13		

Select the two groups

Select a baseline group and a comparison group(s	s) 🕦	
Select baseline group: astro	•	
Select comparison group: gbm	•	
p-value:		
Fold Change:	Soloct bacoling group	(loss scrowed up
Statistical Method: T-Test: Two Sample Test	group), comparison g for the comparison a	roup, and settings nalysis.
Multiple Comparison Adjustment:	Click "Submit analysis	<i>"</i>
False Discovery Rate(FDR): Be -		
Data-Type: GENE EXPRESSION		
Dataset: mas5 normalization		

Compare two groups using gene expression data

STEP 1



Notifications

Below are your latest running analyses. Once completed, click on the Analysis name to see detailed results.

GROUP_COMPARISON (2:05 1/22/2015)

Complete



Once you click "submit analysis", you will be re-directed to the "Notifications" page. Once the status is "Complete", click on "Group comparison"

Results of group comparison

Analysis Results	0		
Statistical Method	TTest		
Adjustment	FDR		These are the results of the group
Fold Change	2		comparison — shows list of 1015
Pvalue	0.0001		
Study	REMBRANDT		Differentially expressed genes (DEGs)
Data File	REMBRANDT.Rda		
Baseline Group	astro		
Groups	gbm		You can sort this table based on any o
List Name:			the columns.
		Save Selected ↓	
View HeatMap for	selected reporters		In this example, they are sorted based on fold change

Ana	lysis Results									0
0	Reporter ID	Gene Symbol	p-value	Fold Change 🌲	Mean Baseline (lo	Mean Group (logi	Std Baseline	Std Group	Target Data	
	1562264_at	LOC339685	2.448 x 10 ⁻¹³	-5.752	8.047	5.523	3.003	2.886		
	213375_s_at	N4BP2L1	0.000×10^{0}	-5.434	11.476	9.034	1.790	1.882		
	221252_s_at	GSG1	0.000×10^{0}	-5.374	9.526	7.101	2.335	2.644		
	219045_at	RHOF	0.000×10^{0}	-5.169	6.937	4.568	2.263	1.941		
	237015_at		0.000×10^{0}	-5.067	7.301	4.960	2.002	1.778		
	1561123_at		8.654 x 10 ⁻¹²	-5.035	8.759	6.427	2.609	3.103		
	208806_at	CHD3	0.000×10^{0}	-4.969	10.344	8.031	2.097	1.860		
	236316_at	FAM3C	0.000×10^{0}	-4.571	5.137	2.944	2.361	1.802		
	221365_at	MLNR	1.383×10^{-13}	-4.386	10.003	7.870	2.430	2.467		
	1560758_at		0.000×10^{0}	-4.197	7.502	5.432	2.125	1.657		
	228079_at	C3orf58	1.533×10^{-14}	-4.168	7.455	5.396	2.638	1.982		
\square	233949 s at	MYH7R	0.000 × 10 ⁰	-4.080	6.954	4 926	2 457	1 890		

Discussion

- One of the most down-regulated gene RHOF
 - 5 fold under-expressed in the GBM group compared to the Astrocytoma group.
 - From literature: RHOF is down regulated in GBM patients through the over expression of their activators
- MLNR : also 4 fold under expressed in GBM

 Literature: Similar changes in expression in MLNR
 were found in low-grade gliomas of Chinese
 - patients

Save gene and reporter list

lysis Results		0
tistical Method	TTest	
Adjustment	FDR	
Fold Change	2	
Pvalue	0.0001	
Study	REMBRANDT	
Data File	REMBRANDT.Rda	
Baseline Group	astro	
Groups	gbm	
List Name		
List Name		
Astro	VsGBM.Rep)
w HeatMap fr	r selected reporte	rs

1. Select all results

Analysis Results

Std Group Reporter ID Gene Symbol p-value Fold Change ÷ Mean Baseline (lo Mean Group (logi Std Baseline ✓ 1562264_at LOC339685 2.448 x 10-13 -5.752 2.886 8.047 5.523 3.003 213375_s_at N4BP2L1 0.000×10^{0} -5.434 11.476 9.034 1.790 1.882 221252_s_at GSG1 0.000×10^{0} -5.374 9.526 7.101 2.335 2.644 ✓ 219045_at 0.000×10^{0} -5.1696.937 4.568 2.263 1.941 RHOF 237015_at 0.000×10^{0} -5.067 7.301 4.960 2.002 1.778 8.654 x 10-12 -5.035 8.759 6.427 2.609 3.103 1561123_at 208806_at CHD3 0.000×10^{0} -4.969 10.344 8.031 2.097 1.860 FAM3C 0.000×10^{0} -4.571 5.137 2.944 2.361 1.802 236316_at 1.383 x 10⁻¹³ ✓ 221365_at MLNR -4.386 10.003 7.870 2.430 2.467 1560758_at 0.000×10^{0} -4.197 7.502 5.432 2.125 1.657 ✓ 228079_at C3orf58 1.533 x 10-14 -4.1687.455 5.396 2.638 1.982 2.457 1.890 233949_s_at MYH7B 0.000×10^{0} -4.0806.954 4.926

Study options -> Classification

OC° 🐔 Home	Studies Lists	Analyses Groups	Notifications	Study Options - Help	Q	kb47
Analysis Results				Study Selected REMBRANDT		
Statistical Method Adjustment Fold Change Pvalue Study Data File Baseline Group	TTest FDR 2 0.0001 REMBRANDT REMBRANDT.Rda astro			SEARCH Genome Browser Compound/Drug Targets Findings Explore Clinical Data and Create Groups Gene Expression Data		
Groups List Name:	gbm selected reporters	Save Selected 1 Reporters Gene Symbols		ANALYZE Group Comparison Chromosomal Instability Index KM Clinical Plot KM Gene Expression Plots Classification HeatMap Viewer		

1	Analysis Results									0	
		Reporter ID	Gene Symbol	p-value 🗘	Fold Change	Mean Baseline (lo	Mean Group (logi	Std Baseline	Std Group	Target Data	
		1554491_a_at	SERPINC1	0.000 × 10 ⁰	11.664	6.373	9.917	3.599	3.634		
		1555409_a_at	BAGE2	0.000 × 10 ⁰	11.033	9.236	12.700	2.535	1.862		1
		1568931_at		0.000×10^{0}	9.091	10.129	13.314	2.520	1.877		1
		1568930_at	EFCAB1	0.000×10^{0}	8.427	10.350	13.425	2.416	1.820		1
		1563637_at	LOC729652	0.000×10^{0}	8.276	6.496	9.545	2.064	2.250		ĩ
		1558869_at		0.000×10^{0}	8.176	6.467	9.498	2.441	2.280		
	_			0.000 4.00	0.000				0.000		

Perform PCA



PCA results

PCA Results Current Study: REMBRANDT

Principal Component Analysis Color items by: Group ٠ PC1 vs. PC3 PC2 vs. PC3 PC1 vs. PC2 Selected subject IDs 40 30 20 10 0 -10 -20 -30 -40 Options... Ŧ -50 20 40 -80 -20 0 60 80 .40 No Data astro gbm

Classification analysis showing decent separation (but some overlap present)

STEP 2

Compare two groups using copy number data

Group comparison on copy number data

Perform Group Comparison Analysis

Select baseline group (less screwed up group), comparison group, and settings for the comparison analysis.

Click "Submit analysis"

Current Study: REMBRANDT change study?
Select a baseline group and a comparison group(s)
Select a baseline group and a companison group(s)
Select baseline group: astro
Select comparison group: gbm
p-value:
.05
Fold Change:
Statistical Method:
T-Test: Two Sample Test
Multiple Comparison Adjustment:
None
Dataset:
Cytobands-level Chromosom:

Results of group comparison

Analysis Results	0	
Statistical Method	d TTest	
Adjustment	NONE	
Fold Change	1	
Pvalue	.05	
Study	REMBRANDT	
Data File	REMBRANDT_CIN_CYTOBANDS_XBA.Rda	
Baseline Group	astro	
Groups	gbm	Showing differentially changed
List Name:		cytobands. Top results
	Save Selected ↓	- 8q arm
		- 7p
View HeatMap	o for selected reporters	- 10a

Ana	alysis Results								0
	Reporter ID	Cytoband	p-value	Fold Change 🌲	Mean Baseline (lo	Mean Group (log	Std Baseline	Std Group	
	8q24.13	8q24.13	5.372 x 10 ⁻⁵	-1.612	1.147	0.458	1.337	0.697	
	8q24.22	8q24.22	5.946 x 10 ⁻⁵	-1.606	0.906	0.222	1.390	0.661	
	8q23.3	8q23.3	6.877×10^{-4}	-1.580	1.193	0.533	1.513	0.813	
	8q24.21	8q24.21	1.320×10^{-4}	-1.542	1.005	0.380	1.255	0.686	
	8q24.12	8q24.12	1.141×10^{-4}	-1.507	0.839	0.247	1.287	0.574	
	8q23.1	8q23.1	6.497 x 10 ⁻³	-1.405	1.208	0.717	1.258	0.841	
	8q22.3	8q22.3	1.649 x 10 ⁻³	-1.371	0.805	0.350	1.118	0.612	
	8q22.1	8q22.1	9.246 x 10 ⁻³	-1.361	0.928	0.484	1.180	0.801	
	8q24.23	8q24.23	9.751×10^{-4}	-1.343	0.580	0.155	1.028	0.527	
	8q23.2	8q23.2	7.976 x 10 ⁻³	-1.307	0.938	0.552	1.024	0.674	
	8q24.11	8q24.11	3.261×10^{-4}	-1.294	0.471	0.099	0.862	0.396	

Chromosome instability index (CIN)

Study options -> Chromosome instability index

G-DOC of the	ome Studies	Lists Ana	alyses Groups	Notifications	Study Options -	Help	Q
Analysis F Current Stu Analysis Results Statistical Method Adjustment Fold Change Pvalue Study Data File Baseline Group Groups List Na	Results dy: REMBRAND TTest NONE 1 .05 REMBRANDT REMBRANDT_CIN_C astro gbm)T YTOBANDS_XBA.R	ada ave Selected ↓		Study Selected REMBRANDT SEARCH Genome Browser Compound/Drug T Findings Explore Clinical Da Gene Expression D ANALYZE Group Comparison Chromosomal Inst KM Clinical Plot KM Gene Expressi Classification HeatMap Viewer	Targets ata and Create Groups Data n rability Index ion Plots	

View HeatMap for selected reporters

Perform CIN analysis

Chromosomal Instability Index	
Current Study: REMBRANDT change study?	
Select a baseline group and a comparison group(s)	
Select baseline group: astro	
Submit Analysis	

Notifications

Below are your latest running analyses. Once completed, click on the Analysis name to see detailed results.

CIN (4:14 12/11/2015) PCA (3:21 12/11/2015)

Complete

Complete

CIN heat map

Click on CHROMOSOME number to see CYTOBAND heat map



Discussion

- Conclusion from group comparison results and CIN heatmaps
 - high level of chromosomal instability chromosome
 8q arm
 - Aberrations in the 8q arm in Astrocytoma patients are known in literature
 - Also lists 7p and 10q regions
 - 7p and 10q regions are known to be highly amplified in GBM patients

STEP 3

Compare two groups using clinical data (Survival analysis)

How to do a clinical KM plot

From either the home page, or the current page you are in, go to Study options - > KM Clinical plot





kb472 -

Create Clinical KM Plot

Lists

Analyses

Current Study: REMBRANDT change study?



- Select patient group(s) of interest using the "add" button
- Select endpoint -
- Click "plot" -

Clinical KM plot results



Conclusion

- G-DOC *Plus* enables users to
 - generate new hypotheses from existing data
 - perform such in silico meta-analysis of disparate studies.
- There is added value in obtaining new insights into the etiology, diagnosis, treatment, and prevention of diseases from re-analyzing published datasets

General tips

- G-DOC *Plus* works best is you don't use the **back** button in the web browser repeatedly.
- Once you select a study, most tools will be easily available from the the top menu bar inside G-DOC *Plus*.

Clearing cache

- If the G-DOC web page does not respond after several seconds, try:
 - refreshing the page.
 - Log out and log back in, and try again
 - If the above two do not work, its possible that your web browser cache may need to be cleared
 - For Google chrome, go to Settings -> Show Advanced Settings -> Under "Privacy", select Clear Browsing data
 - For Mozilla Firefox, go to Preferences -> Advanced -> Network -> Under "Cached Web Content" -> Clear now

	Auvanced
Clear browsing data	General Tabs Search Content Applications Privacy Security Sync Advanced
Obliterate the following items from: the past day Browsing history Download history Cookies and other site and plug-in data Cached images and files Passwords Autofill form data	General Data Choices Network Update Certificates Connection Configure how Firefox connects to the Internet Settings Cached Web Content Settings () Settings () Your web content cache is currently using 0 bytes of disk space Clear Now Override automatic cache management Limit cache to 350 () MB of space
 Hosted app data Content licenses Learn more Cancel Clear browsing data 	Offline Web Content and User Data Your application cache is currently using 0 bytes of disk space Clear Now Image: Tell me when a website asks to store data for offline use Exceptions The following websites are allowed to store data for offline use: Image: Clear Now
Saved content settings and search engines will not be cleared and may reflect your browsing habits. Google chrome	Remove Mozilla Firefox ?

 We are working hard to improve G-DOC *Plus.* Please feel free to email your questions and comments (no homework questions please) to us at :<u>gdoc-help@georgetown.edu</u>