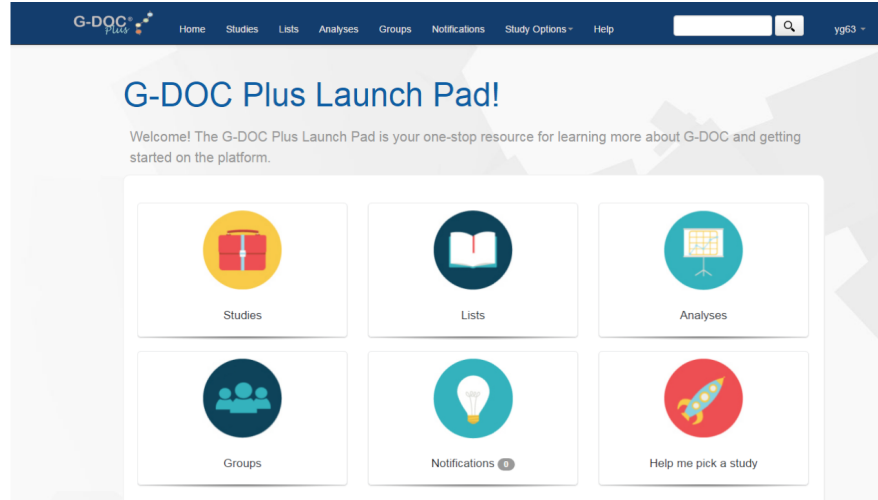


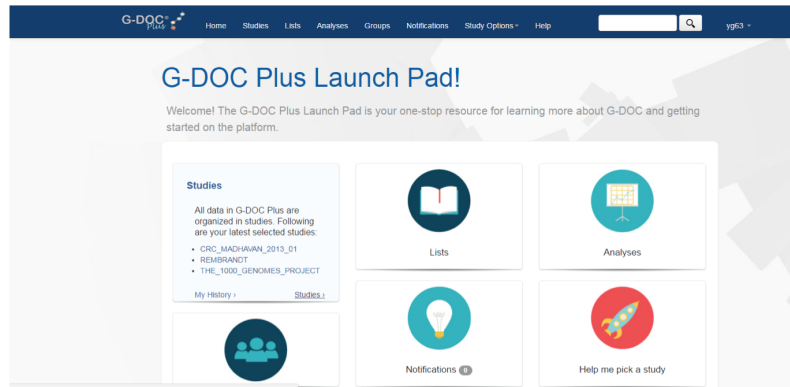
G-DOC Exercise

1. Go to G-DOC at <http://gdoc.georgetown.edu/>. Please register for an account if you have not already done so.

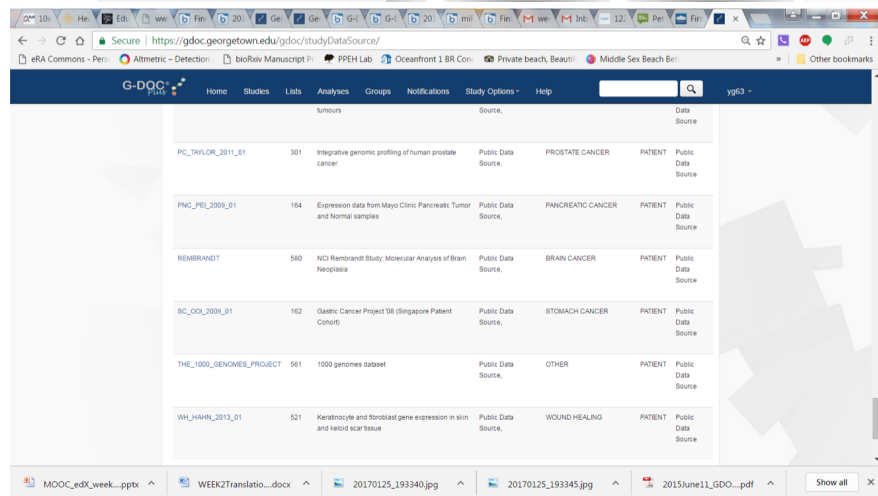
2. Once you have registered successfully and signed in, click on the "Studies" button.



3. Click on the link "Studies."



4. The Studies list is organized by names in alphabetical order. Scroll down to "REMBRANDT" and click on the name.



5. On the Study page, click on "Select Study."

G-DOC Plus Home Studies Lists Analyses Groups Notifications Study Options Help

Studies

REMBRANDT Details

[Select Study](#)

Study Name REMBRANDT (id 560)

Study Abstract

This is the NCI Rembrandt Study: Molecular Analysis of Brain Neoplasia.
 Note: There are differences between the Rembrandt and the G-DOC platforms due to the way the two systems are built. The differences are listed "here".

Primary brain tumors are the fourth leading cause of cancer mortality in adults under the age of 54 years and the leading cause of cancer mortality in children in the United States. Therapy for the most common type of primary brain tumors, gliomas, remains suboptimal. The development of new and more effective treatments will likely require a better understanding of the biology of these tumors. Here, we show that use of the high-density 100K single-nucleotide polymorphism arrays in a large number of primary tumor samples allows for a much higher resolution survey of the glioma genome than has been previously reported in any tumor type. We not only confirmed alterations in genomic areas previously reported to be affected in gliomas, but we also refined the location of those sites and uncovered multiple, previously unknown regions that are affected by copy number alterations (amplifications, homozygous and heterozygous deletions) as well as allelic imbalances (loss of heterozygosity/gene conversions). The wealth of genomic data produced may allow for the development of a more rational molecular classification of gliomas and serve as an important starting point in the search for new molecular therapeutic targets.

This dataset was generated through the Glioma Molecular Diagnostic Initiative from 874 glioma specimens comprising 566 gene expression arrays (Affymetrix U133 Plus 2), 834 copy number arrays (two Affymetrix 50K SNP arrays), and 13,472 clinical phenotype data points.

6. Based on selected study, a list of tools appears on the next page that can be used to explore data in this particular study. Under the Search column, select "Explore Clinical Data and Create Groups."

By selecting the event indicator for overall survival, you are selecting those patients from the study who have been reported as having died at a certain point within the duration of the study.

G-DOC Plus Home Studies Lists Analyses Groups Notifications Study Options Help

Study Selected!

You have picked the study: REMBRANDT*

[Change my study](#) [Help me pick another study](#)

*NCI Rembrandt Study: Molecular Analysis of Brain Neoplasia

Based upon the study you picked, here is a list of tools you can use:

Search	Analyze
<ul style="list-style-type: none"> Genome Browser Compound/Drug Targets Findings Explore Clinical Data and Create Groups Gene Expression Data 	<ul style="list-style-type: none"> Group Comparison Chromosomal Instability Index KM Clinical Plot KM Gene Expression Plots Classification HeatMap Viewer

7. When on "Explore Clinical Data and Create Groups," check the Current Split Attribute window, and make sure that "Event indicator for overall survival" is selected. Check the table in the middle of the screen, then point and click at hyperlinked number in the upper row in the table.

G-DOC Plus Home Studies Lists Analyses Groups Notifications Study Options Help

Explore Clinical Data and Create Groups

Current Study: REMBRANDT [change study?](#)

Filter [reset] [tips] [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

Subject Search

Current Split Attribute [?](#)

Event indicator for overall survival

Event indicator for overall survival	All Subjects
EVENT	479
CENSORING	93
Total	572

8. Click on Number in the table in a row "EVENT" and select option "Save as ID List."

G-DQC Plus Home Studies Lists Analyses Groups Notifications Study Options Help

Explore Clinical Data and Create Groups

Current Study: REMBRANDT [change study?](#)

Filter [reset] [tips] [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

Subject Search

Current Split Attribute: Event indicator for overall survival

Event indicator for overall survival	All Subjects
EVENT	47
CENSORING	93
Total	572

[View Detailed Report](#)
[Save ids as list](#)

9. Type in a name for this list of IDs: rembr_event and click on "Save." After confirmation message is shown, click on "close."

G-DQC Plus Home Studies Lists Analyses Groups Notifications Study Options Help

Explore Clinical Data and Create Groups

Current Study: REMBRANDT [change study?](#)

Subject Search

Save your list

rembr_event created successfully

List Type: clinical, patient

List Name: rembr_event

[Cancel](#) [Save](#) [close](#)

10. Repeat saving of the IDs list one more time for a second group, "CENSORING."

By selecting and saving a group of patient IDs in a category "censoring," you are selecting those patients who did not die during the course of the study.

G-DQC Plus Home Studies Lists Analyses Groups Notifications Study Options Help

Explore Clinical Data and Create Groups

Current Study: REMBRANDT [change study?](#)

Filter [reset] [tips] [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

Subject Search

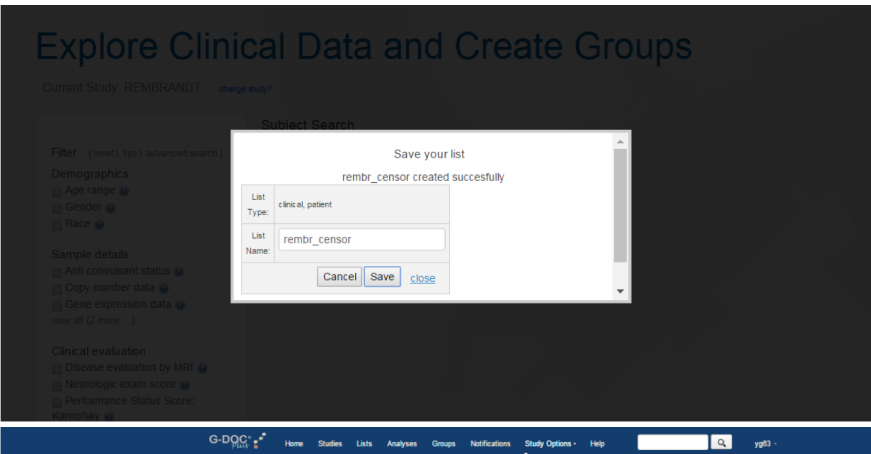
Current Split Attribute: Event indicator for overall survival

Event indicator for overall survival	All Subjects
EVENT	479
CENSORING	93
Total	572

11. Type in a name for this list of IDs: "rembr_censor" and click on "Save." After confirmation message is shown, click on "close."

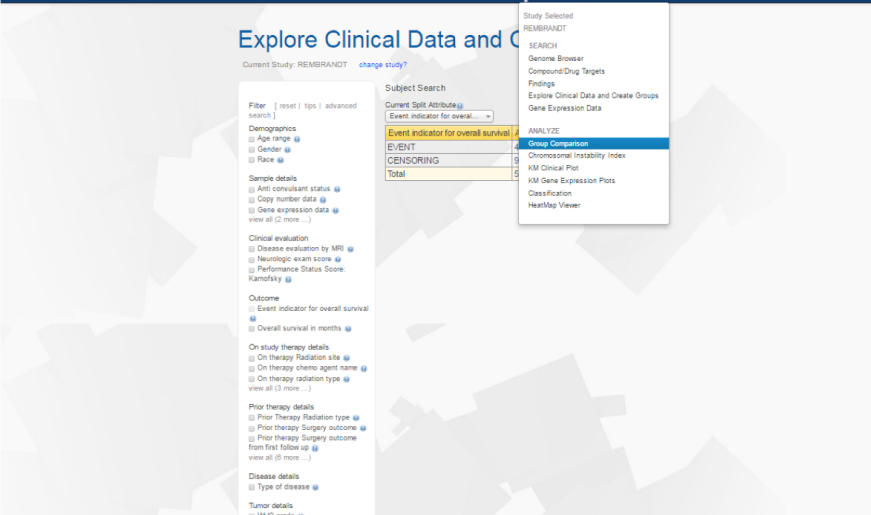
Note: by creating these two groups, you have selected two cohorts of patients for comparison, and the G-DQC system will automatically pull the molecular profiling data for each of those patients from the

database and will have them ready for comparative analysis and exploration in the next few steps.



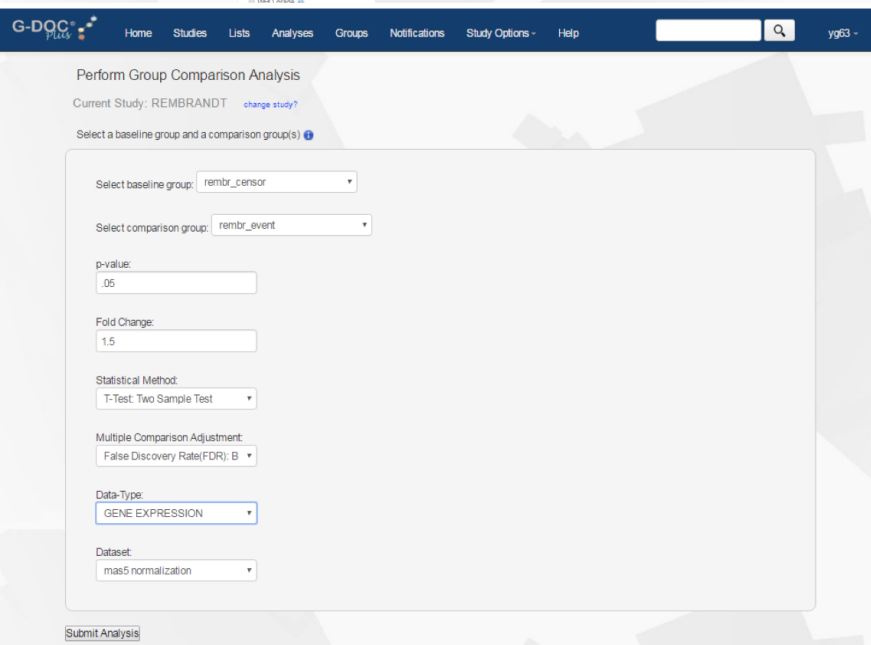
12. Select "Group Comparison" from the main menu.

A group comparison allows you to compare average trends in gene expression across all known genes between two groups of cancer patients to find out what the average molecular differences in level of activity of all the known genes are that might have contributed to overall survival of cancer patients.



13. Select "rembr_censor" as a baseline group from dropdown list. Then select "rembr_event" as a comparison group. Keep the settings for p-value and fold change, as well as for statistical method. Select False discovery rate option for Multiple comparison adjustment, then select Gene expression for Data Type, and finally click on "Submit Analysis."

A program will now compare two sets of gene expression matrices and determine those genes that are showing significantly different levels of activity (expression) in the comparison group (deceased) as opposed to the baseline group (alive).



14. Check the analysis results table. Find the total number of differentially expressed genes (listed on the lower right corner of the table). Then find the gene

symbol for the gene at the top of the table (which has the lowest p-value).

The resulting table contains a short list of only those genes that on average are significantly more activated (up-regulated) or inhibited (down-regulated) in one group of patients (deceased) when compared to a baseline group (alive).

G-DQC+
Plus

HomeStudiesListsAnalysesGroupsNotificationsStudy Options - Help

yg03 -

Analysis Results

Current Study: REMBRANDT

Analysis Results

Statistical Method

TTest

Adjustment

FDR

Fold Change

1.5

Pvalue

.05

Study

REMBRANDT

Data File

REMBRANDT.Rda

Baseline Group

rembr_censor

Groups

rembr_event

List Name:

Save Selected

View HeatMap for selected reporters

Analysis Results

Reporter ID	Gene Symbol	p-value	Fold Change	Mean Baseline	Mean Group	Std Baseline	Std Group	Target Data
211368_s_at	CASP1	2.064×10^{-9}	-2.126	5.786	4.697	1.592	1.254	
208634_s_at	MACF1	2.063×10^{-9}	1.744	10.455	11.258	1.365	1.012	
223854_at	PCDH810	2.063×10^{-9}	-1.647	7.876	7.157	0.924	0.969	
226894_at	SLC35A3	1.579×10^{-9}	-2.041	6.745	5.716	1.261	1.525	
1561140_at		1.971×10^{-9}	2.230	5.571	6.728	1.973	1.650	
1554277_s_at	FANCM	3.038×10^{-9}	1.781	9.143	9.975	1.312	1.250	
239623_at	FLJ44606	4.518×10^{-9}	1.511	6.737	7.333	1.269	0.841	
1554132_s_at	KIAA1128	4.863×10^{-9}	-1.658	11.473	10.743	1.070	1.153	
1554743_s_at	PMS1	5.513×10^{-9}	1.606	9.938	10.622	1.308	1.029	
241604_at	ATP11A	5.941×10^{-9}	1.936	5.127	4.174	2.054	1.385	
232413_at		1.110×10^{-9}	1.808	3.787	4.641	1.669	1.347	
1560104_at		1.110×10^{-9}	1.611	7.387	8.075	1.284	1.099	
1560432_at	CLRN1OS	1.110×10^{-9}	1.523	7.320	7.926	1.083	0.981	
1561998_at		1.112×10^{-9}	-1.646	6.714	5.994	1.002	1.216	

Export results

Page 1 of 4

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View 1 - 50 of 191

15. Explore the biological function of a gene in the top row of the table. (Click on gene symbol and click on GeneCards option from drop-down list.)

G-DQC+
Plus

HomeStudiesListsAnalysesGroupsNotificationsStudy Options - Help

yg03 -

Adjustment

FDR

Fold Change

1.5

Pvalue

.05

Study

REMBRANDT

Data File

REMBRANDT.Rda

Baseline Group

rembr_censor

Groups

rembr_event

List Name:

Save Selected

View HeatMap for selected reporters

Analysis Results

Reporter ID	Gene Symbol	p-value	Fold Change	Mean Baseline	Mean Group	Std Baseline	Std Group	Target Data
211368_s_at	CASP1	2.064×10^{-9}	-2.126	5.786	4.697	1.592	1.254	
208634_s_at	MACF1	2.063×10^{-9}	1.744	10.455	11.258	1.365	1.012	
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1561140_at		1.971×10^{-9}	2.230	5.571	6.728	1.973	1.650	
1554277_s_at	FANCM	3.038×10^{-9}	1.781	9.143	9.975	1.312	1.250	
239623_at	FLJ44606	4.518×10^{-9}	1.511	6.737	7.333	1.269	0.841	
1554132_s_at	KIAA1128	4.863×10^{-9}	-1.658	11.473	10.743	1.070	1.153	
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1560432_at	CLRN1OS	1.110×10^{-9}	1.523	7.320	7.926	1.083	0.981	
1561998_at		1.112×10^{-9}	-1.646	6.714	5.994	1.002	1.216	

Export results

Page 1 of 4

50

View 1 - 50 of 191

16. Explore annotation and function of top significant gene in GeneCards.

GeneCards Suite

GeneCards

MetaCards

LifeMap Discovery

PathCards

TBox

VarEffect

GeneAnalytics

GeneALaCart

GenesLikeMe

Free for academic non-profit institutions. Other users need a Commercial license

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CASP1 Gene (Protein Coding) ★

GCID: GC11M105025

GIFS: 74

Genes Participants

Jump to section

Aliases

Disorders

Domains

Drugs

Expression

Function

Genomics

Localization

Orthologs

Paralogs

Pathways

Products

Proteins

Publications

Sources

Summaries

Transcripts

Variants

MEDILLIPSON

Proteins & Enzymes

Antibodies

Assays & Kits

GenScript

Genes

Peptides

Proteins

CRISPR

ORIGEN

Proteins

Antibodies

Assays

Genes

shRNA

Primers

CRISPR

Vigen

Genes

(adenoviral)

siRNA

Genes

(lentiviral)

miRNA

shRNA

(AAV)

Aliases for CASP1 Gene

Aliases for CASP1 Gene

Caspase 1^{2 3 5}

Caspase 1, Apoptosis-Related Cysteine Peptidase (Interleukin 1, Beta, Convertase)^{2 3}

Interleukin 1, Beta, Convertase^{2 3}

IL-1 Beta-Convertase^{3 4}

EC 3.4.22.36^{4 61}

Caspase-1^{2 3}

IL-1B-Convertase³

Interleukin-1 Beta-Convertase⁴

CASP1 Nirs Variant 1³

IL1B-Convertase³

EC 3.4.22⁶¹

CASP-1⁴

IL-1B-Convertase³

Interleukin-1 Beta-Convertase⁴

Interleukin-1-B Converting Enzyme³

Interleukin-1 Beta Convertase⁴