

The CGDS-R library

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1 Introduction

This package provides a basic set of R functions for querying the Cancer Genomic Data Server (CGDS) hosted by the Computational Biology Center (cBio) at the Memorial Sloan-Kettering Cancer Center (MSKCC). This service is a part of the cBio Cancer Genomics Portal, <http://www.cbioportal.org/>.

In summary, the library can issue the following types of queries:

- `getCancerStudies()` : What cancer studies are hosted on the server? For example, TCGA glioblastoma or TCGA ovarian cancer.
- `getGeneticProfiles()` : What genetic profile types are available for cancer study X? For example, mRNA expression or copy number alterations.
- `getCaseLists()` : what case sets are available for cancer study X? For example, all samples or only samples corresponding to a given cancer subtype.

- `getProfileData()`: Retrieve slices of genomic data. For example, a client can retrieve all mutation data for PTEN and EGFR in TCGA glioblastoma.
- `getClinicalData()`: Retrieve clinical data (e.g. patient survival time and age) for a given cancer study and list of cases.

Each of these functions will be briefly described in the following sections. The last part of this document includes some concrete examples of how to access and plot the data.

The purpose of this document is to give the reader a quick overview of the `cgdsr` package. Please refer to the corresponding R manual pages for a more detailed explanation of arguments and output for each function.

2 The CGDS R interface

2.1 `CGDS()` : Create a CGDS connection object

Initially, we will establish a connection to the public CGDS server hosted by Memorial Sloan-Kettering Cancer Center. The function for creating a CGDS connection object requires the URL of the CGDS server service, in this case <http://www.cbioportal.org/public-portal/>, as an argument.

```
> library(cgdsr)
> # Create CGDS object
> mycgds = CGDS("http://www.cbioportal.org/public-portal/")
```

The variable `mycgds` is now a CGDS connection object pointing at the URL for the public CGDS server. This connection object must be included as an argument to all subsequent interface calls. Optionally, we can now perform a set of simple tests of the data returned from the CGDS connection object using the `test` function:

```
> # Test the CGDS endpoint URL using a few simple API tests
> test(mycgds)
```

```
getCancerStudies... OK
getCaseLists (1/2) ... OK
getCaseLists (2/2) ... OK
getGeneticProfiles (1/2) ... OK
getGeneticProfiles (2/2) ... OK
getClinicalData (1/1) ... OK
getProfileData (1/6) ... OK
getProfileData (2/6) ... OK
getProfileData (3/6) ... OK
getProfileData (4/6) ... OK
getProfileData (5/6) ... OK
getProfileData (6/6) ... OK
```

2.2 `getCancerStudies()` : Retrieve a set of available cancer studies

Having created a CGDS connection object, we can now retrieve a data frame with available cancer studies using the `getCancerStudies` function:

```
> # Get list of cancer studies at server
> getCancerStudies(mycgds)[,c(1,2)]
```

	cancer_study_id
1	laml_tcga_pub
2	acyc_mskcc
3	acc_tcga
4	blca_mskcc_solit_2014
5	blca_mskcc_solit_2012
6	blca_bgi
7	blca_tcga_pub
8	blca_tcga
9	lgg_tcga
10	brca_bccrc
11	brca_broad
12	brca_sanger
13	brca_tcga_pub
14	brca_tcga
15	cellline_ccle_broad
16	cesc_tcga
17	chol_nccs_2013
18	chol_nus_2012
19	coadread_genentech
20	coadread_tcga_pub
21	coadread_tcga
22	coadread_mskcc
23	esca_broad
24	esca_tcga
25	escc_icgc
26	gbm_tcga_pub2013
27	gbm_tcga_pub
28	gbm_tcga
29	hnscc_broad
30	hnscc_jhu
31	hnscc_tcga
32	hnscc_tcga_pub
33	kich_tcga_pub
34	kirc_bgi
35	kirc_tcga_pub
36	kirc_tcga
37	kirp_tcga
38	lihc_amc_prv
39	lihc_riken
40	lihc_tcga
41	luad_broad

42 luad_tcga_pub
 43 luad_tcga
 44 luad_tsp
 45 lusc_tcga_pub
 46 lusc_tcga
 47 dlbc_tcga
 48 mpnst_mskcc
 49 mbl_broad
 50 mbl_icgc
 51 mbl_pcg
 52 skcm_broad_dfarber
 53 mm_broad
 54 cellline_nci60
 55 npc_nusingapore
 56 ov_tcga_pub
 57 ov_tcga
 58 paad_icgc
 59 paad_tcga
 60 thca_tcga_pub
 61 pcpg_tcga
 62 prad_broad_2013
 63 prad_broad
 64 prad_mskcc
 65 prad_tcga
 66 prad_mskcc_2014
 67 prad_mskcc_chenyl_organoids_2014
 68 prad_mich
 69 sarc_mskcc
 70 sarc_tcga
 71 skcm_broad
 72 skcm_tcga
 73 skcm_yale
 74 scco_mskcc
 75 sclc_clcg
 76 sclc_jhu
 77 stad_pfizer_uhongkong
 78 stad_tcga_pub
 79 stad_tcga
 80 stad_utokyo
 81 stad_uhongkong
 82 thca_tcga
 83 ucs_tcga
 84 ucec_tcga
 85 ucec_tcga_pub

	name
1	Acute Myeloid Leukemia (TCGA, NEJM 2013)
2	Adenoid Cystic Carcinoma (MSKCC, Nature Genetics 2013)
3	Adrenocortical Carcinoma (TCGA, Provisional)
4	Bladder Cancer (MSKCC, Eur Urol 2014)
5	Bladder Cancer (MSKCC, JCO 2013)

6 Bladder Urothelial Carcinoma (BGI, Nature Genetics 2013)
7 Bladder Urothelial Carcinoma (TCGA, Nature 2014)
8 Bladder Urothelial Carcinoma (TCGA, Provisional)
9 Brain Lower Grade Glioma (TCGA, Provisional)
10 Breast Invasive Carcinoma (British Columbia, Nature 2012)
11 Breast Invasive Carcinoma (Broad, Nature 2012)
12 Breast Invasive Carcinoma (Sanger, Nature 2012)
13 Breast Invasive Carcinoma (TCGA, Nature 2012)
14 Breast Invasive Carcinoma (TCGA, Provisional)
15 Cancer Cell Line Encyclopedia (Novartis/Broad, Nature 2012)
16 Cervical Squamous Cell Carcinoma and Endocervical Adenocarcinoma (TCGA, Provisional)
17 Cholangiocarcinoma (National Cancer Centre of Singapore, Nature Genetics 2013)
18 Cholangiocarcinoma (National University of Singapore, Nature Genetics 2012)
19 Colorectal Adenocarcinoma (Genentech, Nature 2012)
20 Colorectal Adenocarcinoma (TCGA, Nature 2012)
21 Colorectal Adenocarcinoma (TCGA, Provisional)
22 Colorectal Adenocarcinoma Triplets (MSKCC, Genome Biology 2014)
23 Esophageal Adenocarcinoma (Broad, Nature Genetics 2013)
24 Esophageal Carcinoma (TCGA, Provisional)
25 Esophageal Squamous Cell Carcinoma (ICGC, Nature 2014)
26 Glioblastoma (TCGA, Cell 2013)
27 Glioblastoma (TCGA, Nature 2008)
28 Glioblastoma Multiforme (TCGA, Provisional)
29 Head and Neck Squamous Cell Carcinoma (Broad, Science 2011)
30 Head and Neck Squamous Cell Carcinoma (Johns Hopkins, Science 2011)
31 Head and Neck Squamous Cell Carcinoma (TCGA, Provisional)
32 Head and Neck Squamous Cell Carcinoma (TCGA, in revision)
33 Kidney Chromophobe (TCGA, Cancer Cell 2014)
34 Kidney Renal Clear Cell Carcinoma (BGI, Nature Genetics 2012)
35 Kidney Renal Clear Cell Carcinoma (TCGA, Nature 2013)
36 Kidney Renal Clear Cell Carcinoma (TCGA, Provisional)
37 Kidney Renal Papillary Cell Carcinoma (TCGA, Provisional)
38 Liver Hepatocellular Carcinoma (AMC, Hepatology 2014)
39 Liver Hepatocellular Carcinoma (RIKEN, Nature Genetics 2012)
40 Liver Hepatocellular Carcinoma (TCGA, Provisional)
41 Lung Adenocarcinoma (Broad, Cell 2012)
42 Lung Adenocarcinoma (TCGA, Nature 2014)
43 Lung Adenocarcinoma (TCGA, Provisional)
44 Lung Adenocarcinoma (TSP, Nature 2008)
45 Lung Squamous Cell Carcinoma (TCGA, Nature 2012)
46 Lung Squamous Cell Carcinoma (TCGA, Provisional)
47 Lymphoid Neoplasm Diffuse Large B-cell Lymphoma (TCGA, Provisional)
48 Malignant Peripheral Nerve Sheath Tumor (MSKCC, Nature Genetics 2014)
49 Medulloblastoma (Broad, Nature 2012)
50 Medulloblastoma (ICGC, Nature 2012)
51 Medulloblastoma (PCGP, Nature 2012)
52 Melanoma (Broad/Dana Farber, Nature 2012)
53 Multiple Myeloma (Broad, Cancer Cell 2014)
54 NCI-60 Cell Lines (NCI, Cancer Res. 2012)
55 Nasopharyngeal Carcinoma (Singapore, Nature Genetics 2014)

```

56         Ovarian Serous Cystadenocarcinoma (TCGA, Nature 2011)
57         Ovarian Serous Cystadenocarcinoma (TCGA, Provisional)
58         Pancreatic Adenocarcinoma (ICGC, Nature 2012)
59         Pancreatic Adenocarcinoma (TCGA, Provisional)
60         Papillary Thyroid Carcinoma (TCGA, Cell 2014)
61         Pheochromocytoma and Paraganglioma (TCGA, Provisional)
62         Prostate Adenocarcinoma (Broad/Cornell, Cell 2013)
63         Prostate Adenocarcinoma (Broad/Cornell, Nature Genetics 2012)
64         Prostate Adenocarcinoma (MSKCC, Cancer Cell 2010)
65         Prostate Adenocarcinoma (TCGA, Provisional)
66         Prostate Adenocarcinoma CNA study (MSKCC, PNAS 2014)
67         Prostate Adenocarcinoma Organoids (MSKCC, Cell 2014)
68         Prostate Adenocarcinoma, Metastatic (Michigan, Nature 2012)
69         Sarcoma (MSKCC/Broad, Nature Genetics 2010)
70         Sarcoma (TCGA, Provisional)
71         Skin Cutaneous Melanoma (Broad, Cell 2012)
72         Skin Cutaneous Melanoma (TCGA, Provisional)
73         Skin Cutaneous Melanoma (Yale, Nature Genetics 2012)
74         Small Cell Carcinoma of the Ovary (MSKCC, Nature Genetics 2014)
75         Small Cell Lung Cancer (CLCGP, Nature Genetics 2012)
76         Small Cell Lung Cancer (Johns Hopkins, Nature Genetics 2012)
77         Stomach Adenocarcinoma (Pfizer and UHK, Nature Genetics 2014)
78         Stomach Adenocarcinoma (TCGA, Nature 2014)
79         Stomach Adenocarcinoma (TCGA, Provisional)
80         Stomach Adenocarcinoma (U Tokyo, Nature Genetics 2014)
81         Stomach Adenocarcinoma (UHK, Nature Genetics 2011)
82         Thyroid Carcinoma (TCGA, Provisional)
83         Uterine Carcinosarcoma (TCGA, Provisional)
84         Uterine Corpus Endometrial Carcinoma (TCGA, Provisional)
85         Uterine Corpus Endometrioid Carcinoma (TCGA, Nature 2013)

```

Here we are only showing the first two columns, the cancer study ID and short name, of the result data frame. There is also a third column, a longer description of the cancer study. The cancer study ID must be used in subsequent interface calls to retrieve case lists and genetic data profiles (see below).

2.3 `getGeneticProfiles()` : Retrieve genetic data profiles for a specific cancer study

This function queries the CGDS API and returns the available genetic profiles, e.g. mutation or copy number profiles, stored about a specific cancer study. Below we list the current genetic profiles for the TCGA glioblastoma cancer study:

```

> getGeneticProfiles(mycgds, 'gbm_tcga')[,c(1:2)]

      genetic_profile_id
1      gbm_tcga_gistic
2      gbm_tcga_mrna_U133
3      gbm_tcga_mrna_U133_Zscores

```

```

4         gbm_tcga_mrna_median_Zscores
5         gbm_tcga_rna_seq_v2_mrna
6 gbm_tcga_rna_seq_v2_mrna_median_Zscores
7         gbm_tcga_log2CNA
8         gbm_tcga_methylation_hm27
9         gbm_tcga_methylation_hm450
10        gbm_tcga_mutations
11        gbm_tcga_RPPA_protein_level
12        gbm_tcga_mrna
        genetic_profile_name
1 Putative copy-number alterations from GISTIC
2 mRNA expression (U133 microarray only)
3 mRNA Expression z-Scores (U133 microarray only)
4 mRNA Expression z-Scores (microarray)
5 mRNA expression (RNA Seq V2 RSEM)
6 mRNA Expression z-Scores (RNA Seq V2 RSEM)
7 Log2 copy-number values
8 Methylation (HM27)
9 Methylation (HM450)
10 Mutations
11 protein/phosphoprotein level (RPPA)
12 mRNA expression (microarray)

```

Here we are only listing the first two columns, genetic profile ID and short name, of the resulting data frame. Please refer to the R manual pages for a more extended specification of the arguments and output.

2.4 `getCaseLists()` : Retrieve case lists for a specific cancer study

This function queries the CGDS API and returns available case lists for a specific cancer study. For example, within a particular study, only some cases may have sequence data, and another subset of cases may have been sequenced and treated with a specific therapeutic protocol. Multiple case lists may be associated with each cancer study, and this method enables you to retrieve meta-data regarding all of these case lists. Below we list the current case lists for the TCGA glioblastoma cancer study:

```
> getCaseLists(mycgds, 'gbm_tcga')[,c(1:2)]
```

	case_list_id	case_list_name
1	gbm_tcga_3way_complete	All Complete Tumors
2	gbm_tcga_all	All Tumors
3	gbm_tcga_sequenced	Sequenced Tumors
4	gbm_tcga_cna	Tumors CNA
5	gbm_tcga_log2CNA	Tumors log2 copy-number
6	gbm_tcga_methylation_hm27	Tumors with methylation data (HM27)
7	gbm_tcga_methylation_hm450	Tumors with methylation data (HM450)
8	gbm_tcga_rna_seq_v2_mrna	Tumors with mRNA data (RNA Seq V2)
9	gbm_tcga_mrna_U133	Tumors with mRNA data (U133 microarray only)

10	gbm_tcga_rppa	Tumors with RPPA data
11	gbm_tcga_cnaseq	Tumors with sequencing and CNA data

Here we are only listing the first two columns, case list ID and short name, of the resulting data frame. Please refer to the R manual pages for a more extended specification of the arguments and output.

2.5 `getProfileData()` : Retrieve genomic profile data for genes and genetic profiles

The function queries the CGDS API and returns data based on gene(s), genetic profile(s), and a case list. The function only allows specifying a list of genes and a single genetic profile, or oppositely a single gene and a list of genetic profiles. Importantly, the format of the output data frame depends on if a single or a list of genes was specified in the arguments. Below we are retrieving mRNA expression and copy number alteration genetic profiles for the NF1 gene in all samples of the TCGA glioblastoma cancer study:

```
> getProfileData(mycgds, "NF1", c("gbm_tcga_gistic", "gbm_tcga_mrna"), "gbm_tcga_all")[c(1:
```

	gbm_tcga_gistic	gbm_tcga_mrna
TCGA.02.0001.01	-1	NA
TCGA.02.0003.01	0	NA
TCGA.02.0006.01	0	NA
TCGA.02.0007.01	0	NA
TCGA.02.0009.01	0	NA

We are here only showing the first five rows of the data frame. In the next example, we are retrieving mRNA expression data for the MDM2 and MDM4 genes:

```
> getProfileData(mycgds, c("MDM2", "MDM4"), "gbm_tcga_mrna", "gbm_tcga_all")[c(1:5),]
```

	MDM2	MDM4
TCGA.02.0001.01	NA	NA
TCGA.02.0003.01	NA	NA
TCGA.02.0006.01	NA	NA
TCGA.02.0007.01	NA	NA
TCGA.02.0009.01	NA	NA

We are again only showing the first five rows of the data frame.

2.6 `getClinicalData()` : Retrieve clinical data for a list of cases

The function queries the CGDS API and returns available clinical data (e.g. patient survival time and age) for a given case list. Results are returned in a data frame with a row for each case and a column for each clinical attribute. The available clinical attributes are:

- `overall_survival_months`: Overall survival, in months.

- `overall_survival_status`: Overall survival status, usually indicated as "LIVING" or "DECEASED".
- `disease_free_survival_months`: Disease free survival, in months.
- `disease_free_survival_status`: Disease free survival status, usually indicated as "DiseaseFree" or "Recurred/Progressed".
- `age_at_diagnosis`: Age at diagnosis.

Below we retrieve clinical data for the TCGA ovarian cancer dataset (only first five cases/rows are shown):

```
> getClinicalData(mycgds, "ova_all")[c(1:5),]

data frame with 0 columns and 5 rows
```

3 Examples

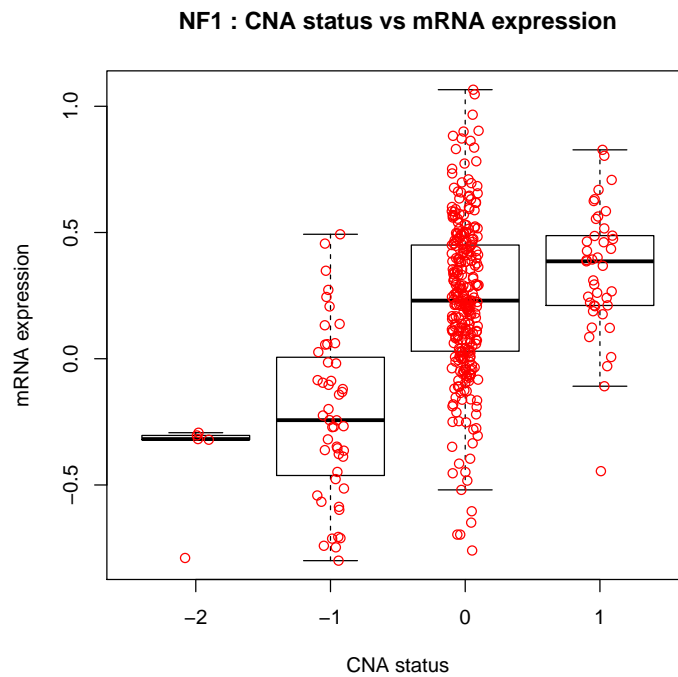
3.1 Example 1: Association of NF1 copy number alteration and mRNA expression in glioblastoma

As a simple example, we will generate a plot of the association between copy number alteration (CNA) status and mRNA expression change for the NF1 tumor suppressor gene in glioblastoma. This plot is very similar to Figure 2b in the TCGA research network paper on glioblastoma (McLendon et al. 2008). The mRNA expression of NF1 has been median adjusted on the gene level (by globally subtracting the median expression level of NF1 across all samples).

```
> df = getProfileData(mycgds, "NF1", c("gbm_tcga_gistic", "gbm_tcga_mrna"), "gbm_tcga_all")
> head(df)
```

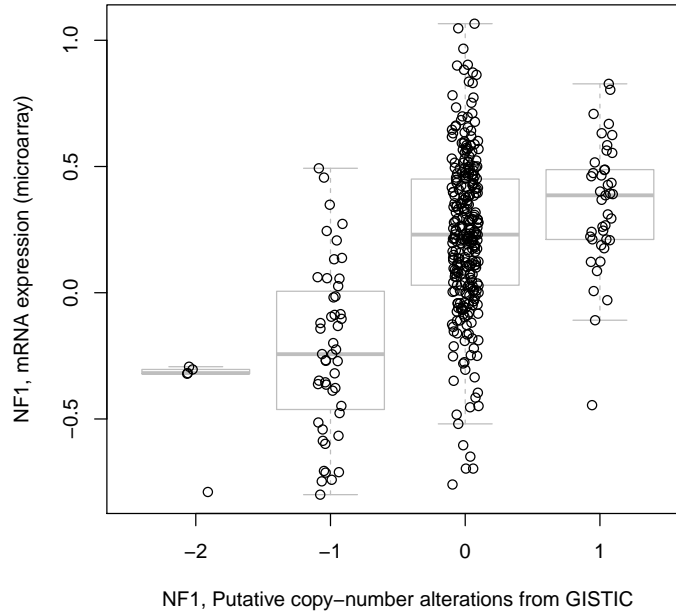
	gbm_tcga_gistic	gbm_tcga_mrna
TCGA.02.0001.01	-1	NA
TCGA.02.0003.01	0	NA
TCGA.02.0006.01	0	NA
TCGA.02.0007.01	0	NA
TCGA.02.0009.01	0	NA
TCGA.02.0010.01	0	NA

```
> boxplot(df[,2] ~ df[,1], main="NF1 : CNA status vs mRNA expression", xlab="CNA status",
> stripchart(df[,2] ~ df[,1], vertical=T, add=T, method="jitter",pch=1,col='red')
```



Alternatively, the generic `cgdsr plot()` function can be used to generate a similar plot:

```
> plot(mycgds, "gbm_tcga", "NF1", c("gbm_tcga_gistic", "gbm_tcga_mrna"), "gbm_tcga_all", sk
[1] TRUE
```



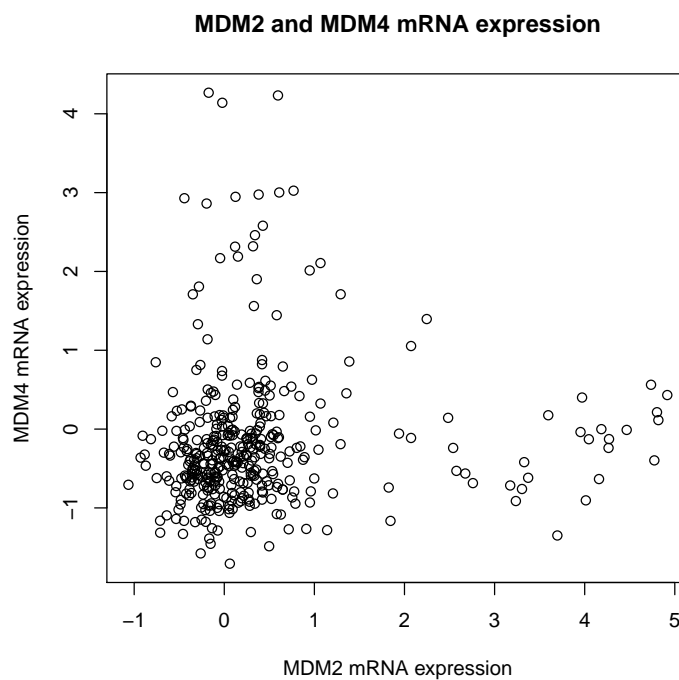
3.2 Example 2: MDM2 and MDM4 mRNA expression levels in glioblastoma

In this example, we evaluate the relationship of MDM2 and MDM4 expression levels in glioblastoma. mRNA expression levels of MDM2 and MDM4 have been median adjusted on the gene level (by globally subtracting the median expression level of the individual gene across all samples).

```
> df = getProfileData(mycgds, c("MDM2", "MDM4"), "gbm_tcga_mrna", "gbm_tcga_all")
> head(df)
```

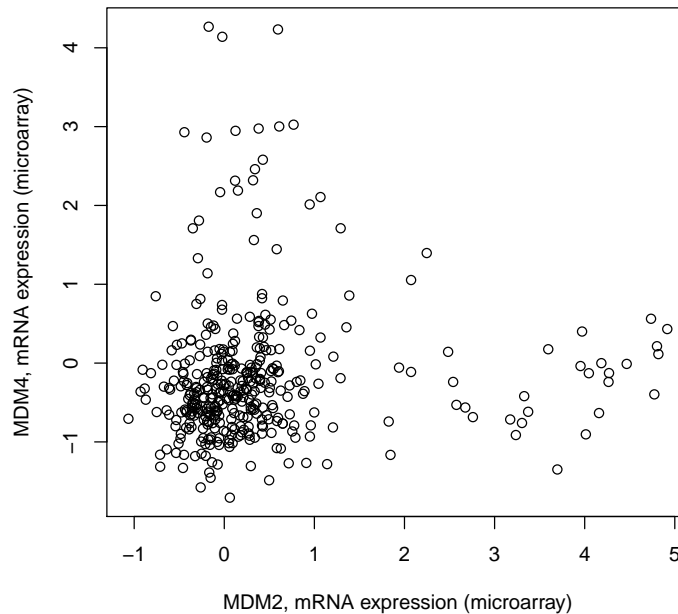
	MDM2	MDM4
TCGA.02.0001.01	NA	NA
TCGA.02.0003.01	NA	NA
TCGA.02.0006.01	NA	NA
TCGA.02.0007.01	NA	NA
TCGA.02.0009.01	NA	NA
TCGA.02.0010.01	NA	NA

```
> plot(df, main="MDM2 and MDM4 mRNA expression", xlab="MDM2 mRNA expression", ylab="MDM4 m
```



Alternatively, the generic `cgdsr plot()` function can be used to generate a similar plot:

```
> plot(mycgds, "gbm_tcga", c("MDM2","MDM4"), "gbm_tcga_mrna" ,"gbm_tcga_all")  
[1] TRUE
```



3.3 Example 3: Comparing expression of PTEN in primary and metastatic prostate cancer tumors

In this example we plot the mRNA expression levels of PTEN in primary and metastatic prostate cancer tumors.

```
> df.pri = getProfileData(mycgds, "PTEN", "prad_mskcc_mrna", "prad_mskcc_primary")
> head(df.pri)
```

	PTEN
PCA0001	9.467183
PCA0002	9.041528
PCA0003	8.511305
PCA0004	NA
PCA0005	9.413217
PCA0006	NA

```
> df.met = getProfileData(mycgds, "PTEN", "prad_mskcc_mrna", "prad_mskcc_mets")
> head(df.met)
```

	PTEN
PCA0182	7.486938
PCA0183	NA
PCA0184	7.578755
PCA0185	NA
PCA0186	NA
PCA0187	8.756132

```
> boxplot(list(t(df.pri),t(df.met)), main="PTEN expression in primary and metastatic tumor  
> stripchart(list(t(df.pri),t(df.met)), vertical=T, add=T, method="jitter",pch=1,col='red')
```

