

The R package *trioClasses* for definition of the class *SNPTrioExperiment*, an extension of *SummarizedExperiment*, for use in trio based analyses of genetic data.

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1 Packages

```
> library("trioClasses")
```

2 Sample Data

```
> data("sample")
> se <- SummarizedExperiment(assays = SimpleList(geno = t(sm)),
  colData = col.DF, rowData = gr)
```

2.1 Pedigree

```
> ped <- PedClass(ped.DF)
```

2.2 SNPTrioExperiment

```
> ste <- SNPTrioExperiment(se, pedigree = ped)
```

```
> ste
```

```
class: SNPTrioExperiment
dim: 511 968
exptData(0):
assays(1): geno
rownames(511): chr14:54383433 chr14:54383470 ...
  chr14:54444385 chr14:54444750
rowData metadata column names(0):
colnames(968): H_ME-CSc175_1-CSc175_1_a.1
  H_ME-CSc175_2-CSc175_2 ... H_ME-DS11418_2-DS11418_2
  H_ME-DS11418_3-DS11418_3
colData names(28): vcfid jb_famid ... id ped
pedigree(4139): famid id fid mid sex dx
```

3 Methods

3.1 ScanTrio

Run ScanTrio for windows of size 1 kB centered at each rare variant.

```
> ste.rare <- ste[MAF(ste) <= 0.01]
> ScanTrio(object = ste.rare, window = relist.sgy(rowData(ste.rare) +
  1000/2), block = range(gr))
```

	trans	trans.out	trans.block
[1,]	2	140	142
[2,]	2	140	142
[3,]	2	140	142
[4,]	2	140	142
[5,]	4	138	142
[6,]	4	138	142
[7,]	4	138	142
[8,]	4	138	142
[9,]	4	138	142
[10,]	4	138	142
[11,]	4	138	142
[12,]	4	138	142
[13,]	4	138	142
[14,]	4	138	142
[15,]	0	142	142
[16,]	0	142	142
[17,]	4	138	142
[18,]	4	138	142
[19,]	4	138	142
[20,]	4	138	142
[21,]	4	138	142
[22,]	1	141	142
[23,]	1	141	142
[24,]	0	142	142
[25,]	0	142	142
[26,]	1	141	142
[27,]	3	139	142
[28,]	3	139	142
[29,]	4	138	142
[30,]	4	138	142
[31,]	3	139	142
[32,]	3	139	142
[33,]	2	140	142
[34,]	2	140	142
[35,]	2	140	142
[36,]	1	141	142
[37,]	1	141	142
[38,]	4	138	142
[39,]	4	138	142
[40,]	4	138	142
[41,]	4	138	142

[42,]	4	138	142
[43,]	4	138	142
[44,]	4	138	142
[45,]	4	138	142
[46,]	4	138	142
[47,]	3	139	142
[48,]	0	142	142
[49,]	0	142	142
[50,]	3	139	142
[51,]	3	139	142
[52,]	3	139	142
[53,]	3	139	142
[54,]	3	139	142
[55,]	1	141	142
[56,]	1	141	142
[57,]	2	140	142
[58,]	2	140	142
[59,]	2	140	142
[60,]	2	140	142
[61,]	1	141	142
[62,]	1	141	142
[63,]	1	141	142
[64,]	1	141	142
[65,]	2	140	142
[66,]	2	140	142
[67,]	2	140	142
[68,]	2	140	142
[69,]	2	140	142
[70,]	3	139	142
[71,]	3	139	142
[72,]	2	140	142
[73,]	2	140	142
[74,]	2	140	142
[75,]	2	140	142
[76,]	0	142	142
[77,]	0	142	142
[78,]	0	142	142
[79,]	0	142	142
[80,]	4	138	142
[81,]	4	138	142
[82,]	4	138	142
[83,]	4	138	142
[84,]	4	138	142
[85,]	4	138	142
[86,]	0	142	142
[87,]	0	142	142
[88,]	0	142	142
[89,]	0	142	142
[90,]	0	142	142
[91,]	0	142	142
[92,]	1	141	142

[93,]	5	137	142
[94,]	5	137	142
[95,]	5	137	142
[96,]	5	137	142
[97,]	5	137	142
[98,]	3	139	142
[99,]	2	140	142
[100,]	2	140	142
[101,]	6	136	142
[102,]	6	136	142
[103,]	6	136	142
[104,]	6	136	142
[105,]	9	133	142
[106,]	8	134	142
[107,]	8	134	142
[108,]	4	138	142
[109,]	4	138	142
[110,]	4	138	142
[111,]	4	138	142
[112,]	3	139	142
[113,]	1	141	142
[114,]	1	141	142
[115,]	1	141	142
[116,]	1	141	142
[117,]	1	141	142
[118,]	2	140	142
[119,]	3	139	142
[120,]	3	139	142
[121,]	5	137	142
[122,]	5	137	142
[123,]	5	137	142
[124,]	7	135	142
[125,]	7	135	142
[126,]	6	136	142
[127,]	6	136	142
[128,]	5	137	142
[129,]	5	137	142
[130,]	5	137	142
[131,]	0	142	142
[132,]	0	142	142
[133,]	0	142	142
[134,]	0	142	142
[135,]	0	142	142
[136,]	0	142	142
[137,]	0	142	142
[138,]	0	142	142
[139,]	0	142	142
[140,]	0	142	142
[141,]	0	142	142
[142,]	1	141	142
[143,]	1	141	142

[144,]	1	141	142
[145,]	1	141	142
[146,]	3	139	142
[147,]	5	137	142
[148,]	5	137	142
[149,]	5	137	142
[150,]	5	137	142
[151,]	5	137	142
[152,]	7	135	142
[153,]	4	138	142
[154,]	2	140	142
[155,]	2	140	142
[156,]	2	140	142
[157,]	2	140	142
[158,]	1	141	142
[159,]	2	140	142
[160,]	1	141	142
[161,]	1	141	142
[162,]	1	141	142
[163,]	1	141	142
[164,]	1	141	142
[165,]	1	141	142
[166,]	1	141	142
[167,]	1	141	142
[168,]	0	142	142
[169,]	1	141	142
[170,]	1	141	142
[171,]	3	139	142
[172,]	3	139	142
[173,]	3	139	142
[174,]	3	139	142
[175,]	5	137	142
[176,]	4	138	142
[177,]	4	138	142
[178,]	4	138	142
[179,]	2	140	142
[180,]	2	140	142
[181,]	0	142	142
[182,]	1	141	142
[183,]	1	141	142
[184,]	1	141	142
[185,]	1	141	142
[186,]	1	141	142
[187,]	4	138	142
[188,]	4	138	142
[189,]	4	138	142
[190,]	4	138	142
[191,]	4	138	142
[192,]	4	138	142
[193,]	4	138	142
[194,]	4	138	142

[195,]	4	138	142
[196,]	2	140	142
[197,]	1	141	142
[198,]	1	141	142
[199,]	1	141	142
[200,]	1	141	142
[201,]	1	141	142
[202,]	1	141	142
[203,]	0	142	142
[204,]	0	142	142
[205,]	1	141	142
[206,]	1	141	142
[207,]	1	141	142
[208,]	1	141	142
[209,]	1	141	142
[210,]	1	141	142
[211,]	1	141	142
[212,]	1	141	142
[213,]	1	141	142
[214,]	1	141	142
[215,]	2	140	142
[216,]	2	140	142
[217,]	2	140	142
[218,]	2	140	142
[219,]	2	140	142
[220,]	1	141	142
[221,]	1	141	142
[222,]	0	142	142
[223,]	0	142	142
[224,]	3	139	142
[225,]	3	139	142
[226,]	3	139	142
[227,]	0	142	142
[228,]	0	142	142
[229,]	5	137	142
[230,]	5	137	142
[231,]	5	137	142
[232,]	6	136	142
[233,]	6	136	142
[234,]	6	136	142
[235,]	6	136	142
[236,]	4	138	142
[237,]	3	139	142
[238,]	1	141	142
[239,]	1	141	142
[240,]	3	139	142
[241,]	3	139	142
[242,]	3	139	142
[243,]	3	139	142
[244,]	3	139	142
[245,]	3	139	142

[246,]	3	139	142
[247,]	3	139	142
[248,]	3	139	142
[249,]	0	142	142
[250,]	0	142	142
[251,]	1	141	142
[252,]	1	141	142
[253,]	1	141	142
[254,]	3	139	142
[255,]	4	138	142
[256,]	4	138	142
[257,]	6	136	142
[258,]	4	138	142
[259,]	4	138	142
[260,]	4	138	142
[261,]	4	138	142
[262,]	2	140	142
[263,]	1	141	142
[264,]	1	141	142
[265,]	2	140	142
[266,]	2	140	142
[267,]	1	141	142
[268,]	1	141	142
[269,]	5	137	142
[270,]	5	137	142
[271,]	4	138	142
[272,]	4	138	142
[273,]	2	140	142
[274,]	2	140	142
[275,]	3	139	142
[276,]	3	139	142
[277,]	3	139	142
[278,]	4	138	142
[279,]	3	139	142
[280,]	2	140	142
[281,]	2	140	142
[282,]	2	140	142
[283,]	2	140	142
[284,]	2	140	142
[285,]	2	140	142
[286,]	2	140	142
[287,]	5	137	142
[288,]	5	137	142
[289,]	5	137	142
[290,]	5	137	142
[291,]	3	139	142
[292,]	3	139	142
[293,]	4	138	142
[294,]	4	138	142
[295,]	2	140	142
[296,]	2	140	142

[297,]	2	140	142
[298,]	2	140	142
[299,]	3	139	142
[300,]	9	133	142
[301,]	8	134	142
[302,]	8	134	142
[303,]	8	134	142
[304,]	8	134	142
[305,]	7	135	142
[306,]	7	135	142
[307,]	7	135	142
[308,]	7	135	142
[309,]	7	135	142
[310,]	7	135	142
[311,]	6	136	142
[312,]	6	136	142
[313,]	6	136	142
[314,]	1	141	142
[315,]	1	141	142
[316,]	1	141	142
[317,]	1	141	142
[318,]	1	141	142
[319,]	1	141	142
[320,]	1	141	142
[321,]	1	141	142
[322,]	1	141	142
[323,]	1	141	142
[324,]	0	142	142
[325,]	0	142	142
[326,]	0	142	142
[327,]	6	136	142
[328,]	6	136	142
[329,]	6	136	142
[330,]	6	136	142
[331,]	6	136	142
[332,]	6	136	142
[333,]	7	135	142
[334,]	5	137	142
[335,]	5	137	142
[336,]	1	141	142
[337,]	1	141	142
[338,]	1	141	142
[339,]	1	141	142
[340,]	1	141	142
[341,]	2	140	142
[342,]	2	140	142
[343,]	2	140	142
[344,]	6	136	142
[345,]	6	136	142
[346,]	6	136	142
[347,]	6	136	142

[348,]	6	136	142
[349,]	6	136	142
[350,]	6	136	142
[351,]	6	136	142
[352,]	7	135	142
[353,]	9	133	142
[354,]	9	133	142
[355,]	9	133	142
[356,]	8	134	142
[357,]	3	139	142
[358,]	3	139	142
[359,]	3	139	142
[360,]	3	139	142
[361,]	2	140	142
[362,]	1	141	142
[363,]	1	141	142
[364,]	1	141	142
[365,]	1	141	142
[366,]	1	141	142
[367,]	1	141	142
[368,]	0	142	142
[369,]	0	142	142

3.2 Count of Transmission of Variants (*TransCount()*)

3.2.1 Window

```
> window <- GRanges(seqnames = "chr14", IRanges(start(gr[100]),
  width = 10000), strand = "*")
> window2 <- GRanges(seqnames = "chr14", IRanges(start(gr[100]),
  width = 1000), strand = "*")

> TransCount(ste, window)

[1] 1106
```

3.2.2 Not in window, but in block

```
> TransCount(ste, setdiff(block, window))

[1] 7727
```

3.2.3 In the whole block

```
> TransCount(ste, block)

[1] 8833
```

3.3 In both windows

```
> TransCount(ste, GRangesList(window, window2))

[1] 1106 48
```

3.4 Not “In both windows,” but in block

```
> TransCount(ste, GRangesList(setdiff(block, window), setdiff(block,
  window2)))
```

```
[1] 7727 8785
```

3.5 Count of Transmission of Rare Variants (*TransCount()*)

```
> ste.rare <- ste[MAF(ste) <= 0.01]
```

3.5.1 In both windows

```
> TransCount(ste.rare, GRangesList(window, window2))
```

```
[1] 26 3
```

3.5.2 Not “In both windows,” but in block

```
> TransCount(ste.rare, GRangesList(setdiff(block, window),
  setdiff(block, window2)))
```

```
[1] 116 139
```

3.6 Holger-style Genotype Matrix

Coercion to matrix for *trio*

```
> geno <- as(ste, "matrix")
> aTDT(geno[, 1:5])
```

```
$stat
```

```
[1] 1.000000 0.000000 0.000000 8.727273 19.565217
```

```
$pval
```

```
[1] 3.173105e-01 1.000000e+00 1.000000e+00 3.134851e-03 9.722321e-06
```

```
$transMinor
```

```
[1] 0 9 2 108 8
```

```
$transMajor
```

```
[1] 1 9 2 156 38
```

Or apply the aTDT method to the SNP Trio Experiment directly.

```
> aTDT(ste[1:5])
```

```
$stat
```

```
[1] 1.000000 0.000000 0.000000 8.727273 19.565217
```

```
$pval
```

```
[1] 3.173105e-01 1.000000e+00 1.000000e+00 3.134851e-03 9.722321e-06
```

```
$transMinor  
[1] 0 9 2 108 8  
  
$transMajor  
[1] 1 9 2 156 38
```

A Classes

A.1 SnpMatrix, DataFrame, GRanges

The four key ingredients are the SNP matrix, the pedigree information as a `DataFrame`, position of the SNPs given by a `GRanges` object, and covariate data given as a `DataFrame`.

```
> sm
```

```
A SnpMatrix with 968 rows and 511 columns
Row names: H_ME-DS10776_2-DS10776_2 ... H_ME-DS11313_1-DS11313_1
Col names: chr14:54383433 ... chr14:54444750
```

```
> ped.DF
```

```
DataFrame with 4139 rows and 6 columns
```

	famid		id
	<character>		<character>
1	4778		H_ME-4778_1-4778_1.2
2	4778		H_ME-4778_2-4778_2.2
3	4778		H_ME-4778_3-4778_3.2
4	4783		H_ME-4783_1-4783_1.1
5	4783		H_ME-4783_2-4783_2.1
6	4783		H_ME-4783_3-4783_3.1
7	20000492	H_ME-20000492_1-20000492_1.1	
8	20000492	H_ME-20000492_2-20000492_2.a.1	
9	20000492	H_ME-20000492_3-20000492_3.1	
...
4131	DS12332		H_ME-DS12332_1-DS12332_1
4132	DS12332		H_ME-DS12332_2-DS12332_2
4133	DS12332		H_ME-DS12332_3-DS12332_3
4134	DS99998	H_ME-DS10193_5-DS10193_5.2	
4135	DS99998	H_ME-DS10193_6-DS10193_6	
4136	DS99998	H_ME-DS10193_7-DS10193_7	
4137	DS99999	H_ME-DS10707_4-DS10707_4.2	
4138	DS99999	H_ME-DS10707_5-DS10707_5	
4139	DS99999	H_ME-DS10707_6-DS10707_6	
	famid		mid
	<character>		<character>
1	H_ME-4778_2-4778_2.2		H_ME-4778_3-4778_3.2
2	NA		NA
3	NA		NA
4	H_ME-4783_2-4783_2.1		H_ME-4783_3-4783_3.1
5	NA		NA
6	NA		NA
7	H_ME-20000492_2-20000492_2.a.1	H_ME-20000492_3-20000492_3.1	
8	NA		NA
9	NA		NA
...
4131	H_ME-DS12332_2-DS12332_2	H_ME-DS12332_3-DS12332_3	
4132	NA		NA
4133	NA		NA

4134	H_ME-DS10193_6-DS10193_6	H_ME-DS10193_7-DS10193_7
4135	NA	NA
4136	NA	NA
4137	NA	NA
4138	H_ME-DS10707_4-DS10707_4.2	H_ME-DS10707_6-DS10707_6
4139	NA	NA

	sex	dx
	<numeric>	<numeric>
1	1	1
2	1	0
3	2	0
4	2	1
5	1	0
6	2	1
7	2	1
8	1	0
9	2	0
...
4131	1	1
4132	1	0
4133	2	0
4134	2	1
4135	1	0
4136	2	0
4137	1	0
4138	1	1
4139	2	0

> gr

GRanges with 511 ranges and 0 metadata columns:

	seqnames	ranges	strand
	<Rle>	<IRanges>	<Rle>
chr14:54383433	chr14	[54383433, 54383433]	*
chr14:54383470	chr14	[54383470, 54383470]	*
chr14:54383819	chr14	[54383819, 54383819]	*
chr14:54383945	chr14	[54383945, 54383945]	*
chr14:54384030	chr14	[54384030, 54384030]	*
chr14:54384232	chr14	[54384232, 54384232]	*
chr14:54384251	chr14	[54384251, 54384251]	*
chr14:54384291	chr14	[54384291, 54384291]	*
chr14:54384382	chr14	[54384382, 54384382]	*
...
chr14:54443495	chr14	[54443495, 54443495]	*
chr14:54443499	chr14	[54443499, 54443499]	*
chr14:54443514	chr14	[54443514, 54443514]	*
chr14:54443831	chr14	[54443831, 54443831]	*
chr14:54443880	chr14	[54443880, 54443880]	*
chr14:54444016	chr14	[54444016, 54444016]	*
chr14:54444124	chr14	[54444124, 54444124]	*
chr14:54444385	chr14	[54444385, 54444385]	*
chr14:54444750	chr14	[54444750, 54444750]	*

```

---
seqlengths:
  chr14
    NA

```

A.2 SummarizedExperiment

We combine three of the key ingredients when we create the SummarizedExperiment object.

```

> se <- SummarizedExperiment(assays = SimpleList(geno = t(sm)),
  colData = col.DF, rowData = gr)

```

A.3 SNPTrioExperiment

Now, we include the pedigree information as an object of class PedClass. We keep PedClass independent of SNPTrioExperiment for flexibility.

```

> ped <- PedClass(ped.DF)
> ste <- SNPTrioExperiment(se, pedigree = ped)

```

Here is the show method.

```

> ste

class: SNPTrioExperiment
dim: 511 968
exptData(0):
assays(1): geno
rownames(511): chr14:54383433 chr14:54383470 ...
  chr14:54444385 chr14:54444750
rowData metadata column names(0):
colnames(968): H_ME-CSc175_1-CSc175_1_a.1
  H_ME-CSc175_2-CSc175_2 ... H_ME-DS11418_2-DS11418_2
  H_ME-DS11418_3-DS11418_3
colData names(28): vcfid jb_famid ... id ped
pedigree(4139): famid id fid mid sex dx

```

And now we verify that it is indeed an extension of SummarizedExperiment.

```

> getClass("SNPTrioExperiment")

```

```

Class "SNPTrioExperiment" [package "trioClasses"]

```

Slots:

Name:	pedigree	exptData
Class:	PedClass	SimpleList
Name:	rowData	colData
Class:	GenomicRangesORGRangesList	DataFrame
Name:	assays	

```
Class: Assays
```

```
Extends: "SummarizedExperiment"
```

A.4 PedClass

Now we investigate the pedigree slot of the SNP Trio Experiment object.

```
> class(pedigree(ste))
```

```
[1] "PedClass"
attr("package")
[1] "trioClasses"
```

```
> getClass("PedClass")
```

```
Class "PedClass" [package "trioClasses"]
```

```
Slots:
```

```
Name:      rownames      nrows      listData
Class: characterORNULL   integer      list
```

```
Name:      elementType elementMetadata      metadata
Class:      character DataTableORNULL      list
```

```
Extends:
```

```
Class "DataFrame", directly
Class "DataTable", by class "DataFrame", distance 2
Class "SimpleList", by class "DataFrame", distance 2
Class "DataTableORNULL", by class "DataFrame", distance 3
Class "List", by class "DataFrame", distance 3
Class "Vector", by class "DataFrame", distance 4
Class "Annotated", by class "DataFrame", distance 5
```

```
> pedigree(ste)
```

```
PedClass with 4139 rows and 6 columns
```

	famid	id
	<factor>	<factor>
1	4778	H_ME-4778_1-4778_1.2
2	4778	H_ME-4778_2-4778_2.2
3	4778	H_ME-4778_3-4778_3.2
4	4783	H_ME-4783_1-4783_1.1
5	4783	H_ME-4783_2-4783_2.1
6	4783	H_ME-4783_3-4783_3.1
7	20000492	H_ME-20000492_1-20000492_1.1
8	20000492	H_ME-20000492_2-20000492_2_a.1
9	20000492	H_ME-20000492_3-20000492_3.1
...
4131	DS12332	H_ME-DS12332_1-DS12332_1
4132	DS12332	H_ME-DS12332_2-DS12332_2

4133	DS12332	H_ME-DS12332_3-DS12332_3
4134	DS99998	H_ME-DS10193_5-DS10193_5.2
4135	DS99998	H_ME-DS10193_6-DS10193_6
4136	DS99998	H_ME-DS10193_7-DS10193_7
4137	DS99999	H_ME-DS10707_4-DS10707_4.2
4138	DS99999	H_ME-DS10707_5-DS10707_5
4139	DS99999	H_ME-DS10707_6-DS10707_6

	fid	mid
	<factor>	<factor>
1	H_ME-4778_2-4778_2.2	H_ME-4778_3-4778_3.2
2	NA	NA
3	NA	NA
4	H_ME-4783_2-4783_2.1	H_ME-4783_3-4783_3.1
5	NA	NA
6	NA	NA
7	H_ME-20000492_2-20000492_2_a.1	H_ME-20000492_3-20000492_3.1
8	NA	NA
9	NA	NA
...
4131	H_ME-DS12332_2-DS12332_2	H_ME-DS12332_3-DS12332_3
4132	NA	NA
4133	NA	NA
4134	H_ME-DS10193_6-DS10193_6	H_ME-DS10193_7-DS10193_7
4135	NA	NA
4136	NA	NA
4137	NA	NA
4138	H_ME-DS10707_4-DS10707_4.2	H_ME-DS10707_6-DS10707_6
4139	NA	NA

	sex	dx
	<factor>	<factor>
1	1	1
2	1	0
3	2	0
4	2	1
5	1	0
6	2	1
7	2	1
8	1	0
9	2	0
...
4131	1	1
4132	1	0
4133	2	0
4134	2	1
4135	1	0
4136	2	0
4137	1	0
4138	1	1
4139	2	0

A.5 geno accessor

```
> class(geno(ste))

[1] "SnpMatrix"
attr(,"package")
[1] "snpStats"

> getClass("SnpMatrix")

Class "SnpMatrix" [package "snpStats"]

Slots:

Name:      .Data
Class: matrix

Extends:
Class "matrix", from data part
Class "array", by class "matrix", distance 2
Class "mMatrix", by class "matrix", distance 2
Class "structure", by class "matrix", distance 3
Class "vector", by class "matrix", distance 4, with explicit coerce

Known Subclasses: "XSnpMatrix"

> geno(ste)

A SnpMatrix with 968 rows and 511 columns
Row names:  H_ME-CSc175_1-CSc175_1_a.1 ... H_ME-DS11418_3-DS11418_3
Col names:  chr14:54383433 ... chr14:54444750
```

A.6 RowData

```
> rowData(ste)

GRanges with 511 ranges and 0 metadata columns:
      seqnames      ranges strand
      <Rle>        <IRanges> <Rle>
chr14:54383433 chr14 [54383433, 54383433] *
chr14:54383470 chr14 [54383470, 54383470] *
chr14:54383819 chr14 [54383819, 54383819] *
chr14:54383945 chr14 [54383945, 54383945] *
chr14:54384030 chr14 [54384030, 54384030] *
chr14:54384232 chr14 [54384232, 54384232] *
chr14:54384251 chr14 [54384251, 54384251] *
chr14:54384291 chr14 [54384291, 54384291] *
chr14:54384382 chr14 [54384382, 54384382] *
...          ...          ...
chr14:54443495 chr14 [54443495, 54443495] *
chr14:54443499 chr14 [54443499, 54443499] *
chr14:54443514 chr14 [54443514, 54443514] *
```

```

chr14:54443831    chr14 [54443831, 54443831]    *
chr14:54443880    chr14 [54443880, 54443880]    *
chr14:54444016    chr14 [54444016, 54444016]    *
chr14:54444124    chr14 [54444124, 54444124]    *
chr14:54444385    chr14 [54444385, 54444385]    *
chr14:54444750    chr14 [54444750, 54444750]    *
---
seqlengths:
chr14
NA

```

A.7 ColData

B Validity