**Chemotherapy and Radiotherapy Related Differential Methylation Regions**

1, Identify Chemotherapy and Radiotherapy Related Differential Methylation Regions for each drug and Radiotherapy

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Drug** | **KYSE410** | **KYSE150** | **KYSE450** | **KYSE140** | **KYSE30** | **KYSE510** | **COLO680n** | **KYSE180** | **KYSE70** | **TE1** |
| **5FU** | **R** |  | **S** |  |  | **R** |  |  | **S** |  |
| **Vb** |  |  | **S** | **R** |  | **R** |  |  | **S** |  |
| **Ci** | **R** |  |  | **S** | **S** |  |  |  |  | **R** |
| **Pa** |  |  |  | **R** |  |  | **S** |  | **S** | **R** |
| **Dt** | **R** |  |  |  | **S** |  |  | **S** |  | **R** |
| **Nd** |  | **R** |  | **S** |  |  |  |  | **S** | **R** |
| **Mi** |  |  | **S** | **R** | **R** |  |  | **S** |  |  |
| **ChemSum** | **R** |  | **S** |  |  |  |  | **S** |  | **R** |
| **Radiotherapy** | **R** |  | **R** |  |  |  |  | **S** |  | **S** |

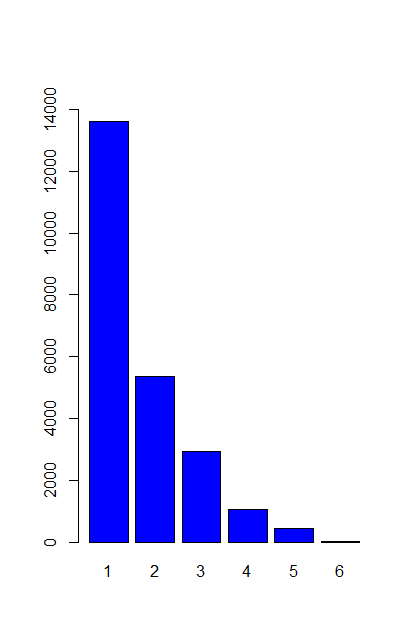


Figure 1. Identify Chemotherapy and Radiotherapy Related Differential Methylation Regions for each drug and Radiotherapy

1A. comparison strategy. 1B. the number of resistant associated DMR for each drug. 1C. the number of DMR probes shared by multiple drugs.

Result:

1, for different drugs, resistance associated DMR were identified. The number of the DMRs for each drugs is of high variation ranging from 300-1500.

2, none common DMRs were identified for all 7 the drugs and Radiotherapy. Only 1 chemotherapy resistant associated DMR (TRPC3, chr4:122872273-122872430) was identified in 5 drugs (5FU, Ci, Dt, Mi, Nd). See table 1 and supplementary Table S1.

3, only 35 chemotherapy resistant DMRs (<0.6%) were shared with Radiotherapy resistant DMRs for each drug, indicating chemotherapy and Radiotherapy resistant are in the different mechanism.

Table 1. common chemo/ Radiotherapy related DMRs

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| CHR | Start | End | Counts | Parts | 5FU | ChemSum | Ci | Dt | Mi | Nd | Pa | Radiotherapy | Vb |
| chr4 | 1.23E+08 | 1.23E+08 | 6 | 1,2,3,4,5,6 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| chr1 | 1216990 | 1217935 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr1 | 12201528 | 12206139 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr1 | 65775047 | 65775606 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr1 | 1.53E+08 | 1.53E+08 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr10 | 11059599 | 11059812 | 5 | 1,3,6,7,9 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 1 |
| chr10 | 21807048 | 21807369 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr10 | 56560675 | 56561216 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr10 | 1.32E+08 | 1.32E+08 | 5 | 1,2,5,7,9 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 1 |
| chr11 | 818837 | 818982 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr11 | 2160462 | 2163078 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr11 | 2721129 | 2722727 | 5 | 1,2,3,4,5 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| chr11 | 67417774 | 67418519 | 5 | 1,3,4,5,6 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| chr12 | 2733651 | 2735088 | 5 | 1,2,3,4,9 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 |
| chr12 | 16757684 | 16760327 | 5 | 2,3,4,5,9 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 |
| chr12 | 54446136 | 54447466 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr12 | 65514972 | 65515082 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr13 | 1.13E+08 | 1.13E+08 | 5 | 1,2,5,7,9 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 1 |
| chr14 | 62034470 | 62036547 | 5 | 1,2,3,4,9 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 |
| chr17 | 1093069 | 1095515 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr17 | 33759430 | 33760407 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr17 | 37021148 | 37024681 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr17 | 38465218 | 38465780 | 5 | 1,2,3,4,5 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| chr18 | 21572477 | 21573018 | 5 | 2,3,4,5,6 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| chr19 | 1131757 | 1133464 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr19 | 3607102 | 3607166 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr2 | 2935638 | 2937561 | 5 | 1,2,4,7,9 | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 1 |
| chr2 | 60961859 | 60963982 | 5 | 1,2,4,7,9 | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 1 |
| chr2 | 1.43E+08 | 1.43E+08 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr2 | 1.92E+08 | 1.92E+08 | 5 | 1,2,3,4,5 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| chr2 | 2.2E+08 | 2.2E+08 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr3 | 5015822 | 5019355 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr3 | 11610060 | 11610292 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr3 | 1.39E+08 | 1.39E+08 | 5 | 2,3,4,5,6 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| chr3 | 1.94E+08 | 1.94E+08 | 5 | 1,2,3,4,9 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 |
| chr3 | 1.96E+08 | 1.96E+08 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr4 | 13546063 | 13546160 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr4 | 40517754 | 40518414 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr4 | 86748445 | 86749537 | 5 | 1,2,3,4,5 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| chr5 | 1.4E+08 | 1.4E+08 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr5 | 1.4E+08 | 1.4E+08 | 5 | 1,2,4,6,9 | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 1 |
| chr6 | 30041989 | 30043921 | 5 | 1,2,3,4,9 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 |
| chr6 | 30923159 | 30924030 | 5 | 1,2,3,4,9 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 |
| chr6 | 45387108 | 45388585 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr6 | 1.34E+08 | 1.34E+08 | 5 | 1,2,3,4,5 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| chr7 | 1.51E+08 | 1.51E+08 | 5 | 1,2,3,4,6 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| chr8 | 1.42E+08 | 1.42E+08 | 5 | 1,2,3,5,9 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 |

Conclusion:

**Please validate the top DMRs in corresponding cell lines, especially 1 and 46 DMRs shared by 6 and 5 chemo/radiotherapy resistant.**