| Enzyme  | Sequence                 | Methylation effects                      |
|---------|--------------------------|--|
| EcoRV   | 5'□GAT↓ATC3'             | No methylation effects on digestion      |
| EcoRI   | 5'G↓AATTC3'              | No methylation effects on digestion      |
| HindIII | 5'□A↓AGCTT 3'            | No methylation effects on digestion      |
| NsiI    | 5'□ATGCA↓T3'             | No methylation effects on digestion      |
| NcoI    | 5'C↓CATGG3'              | No methylation effects on digestion      |
| PaeI    | 5'□GCATG↓C3'             | No methylation effects on digestion      |
| DpnI    | 5'G <sup>m</sup> 6A↓TC3' | Does not cut <i>dam</i> <sup>-</sup> DNA |
| EcoRII  | 5'□↓CCWGG3'              | Dcm: completely overlaps – blocked       |
| SnaBI   | 5'TAC↓GTA3'              | CpG: completely overlaps – blocked       |

**Table S1.** The description of each restriction enzyme used in the study.