DNA methylation have been widely reported to be abnormal in human cancers. However, the biomarker or biomarker panel have not been well established for cancer diagnosis and prognosis. In order to accelate these biomarker into clinical application, I proposed two biotechnique methods (MBD-seq and MSD-SNuPET) for methylation based biomarker identification and biomarker/s performance evaluation. In the biomarker identification section, I proposed two novel methods to identify methylation based biomarkers with NGS technique and to validate candidate methylation loci identified from illumina 450K methylation array. In the first study, I proposed a new method, methylation-binding domain-sequencing (MBD-seq), to identify cancer differential methylation regions (DMR) and then these DMR were validated and the best biomarker recombination (panel) were tested in different clinical scenarios: case-control retrospective study and double-blind clinical simulation. By this method, I identified large number methylation biomarkers for bladder cancer including 5 diagnostic biomarker (VAX1, KCNV1, TAL1, PROX1 and CFTR) and 2 recurrence associated biomarker (VAX1 and LMX1A) and 2 differentiation related biomarker (ECEL1 and TMEM26). In the second study, I proposed a low throughput but low cost method: methylation status determined single nucleotide primer extension technique (MSD-SNuPET) to valiate the differential methylation loci identified from public methylation microarray data (such as HM450K array). I applied this method and built a five-gene diagnosis panel including AGTR1, GALR1, SLC5A8, ZMYND10 in non-small cell lung cancer and the panel showed very high prediction performance in different prediction models including SVM, random forest and logistic regression(sensitivity=78%, specificity=97% and AUC=0.91).