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**Next generation sequencing has lower sequence coverage and poorer SNP-detection capability in the regulatory regions**

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The rapid development of next generation sequencing (NGS) technology provides a new chance to extend the scale and resolution of genomic research. How to efficiently map millions of short reads to the reference genome and how to make accurate SNP calls are two major challenges in taking full advantage of NGS. In this article, we reviewed the current software tools for mapping and SNP calling, and evaluated their performance on samples from The Cancer Genome Atlas (TCGA) project. We found that BWA and Bowtie are superior to the other alignment tools in comprehensive performance, while SOAP2 has the fastest alignment speed and SHRiMP has the highest coverage. Furthermore, we showed that next-generation sequencing platform has significantly lower coverage and poorer SNP-calling performance in the CpG islands, promoter and 5'-UTR regions of the genome. NGS experiments targeting for these regions should have higher sequencing depth than the normal genomic region.