APPLICATION NOTE

OncoKDM Lite: Improving TSO500 data interpretation accuracy from VCF files in oncology routine practice

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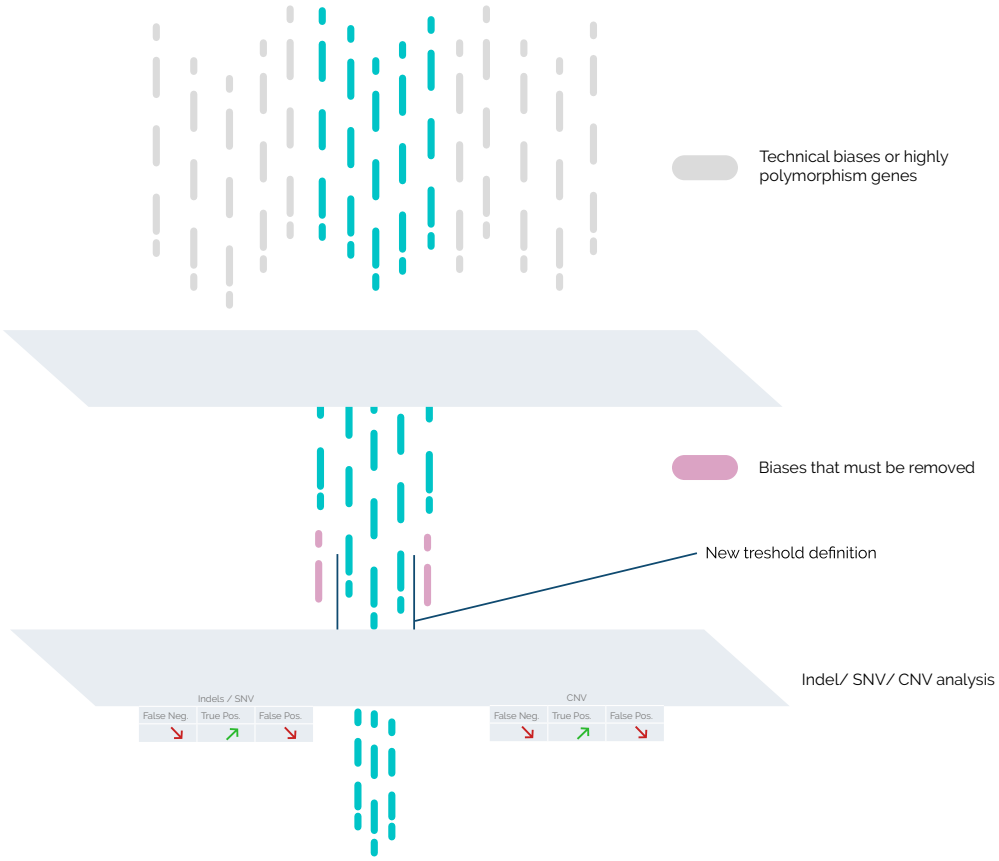
In the era of precision medicine, recent developments in next-generation sequencing and tumor immunology have allowed the discovery that several receptors like CTLA4, PD-1 and PD-L1 could be targeted by therapeutic monoclonal antibodies to cure patients.

Huge efforts have been made to identify predictive markers that could improve the therapeutical benefit of those treatments.

One of the most promising markers is based on the fact that the immunogenicity of a tumor is related with the amount of the neoepitope load generated via hypermutation of the DNA coming from the tumor cells, ideally indel/frameshifts or non-synonymous mutations that generate novel proteins that can be recognized by the immune system. These neoepitopes can then be presented via MHC in order to aid the immune system to target and kill those cells.



Initially, TMB was measured using whole genome and whole exome sequencing to have enough power (meaning bases sequenced). Nonetheless, those technologies are not cost-effective enough to be used in clinical routine.

The TSO500 panel from Illumina that has been launched in early 2019 is the most advanced commercial panel being able to achieve those goals. However, laboratories can quite easily standardize the wet lab, the bioinformatical analyses to get the maximum accurate information from one analysis, such complex panel could require complex strategy and must be validated before to move in clinic.

In addition, it is key to avoid spending time and money to analyze the data several times with different algorithms and parameter for different purposes.

Based on the analysis of about 500 samples, we were able to identify more than 300 variants systematically associated either with technical biases or highly polymorphism. Those ones are filtered out to not generate noise for the oncologist.

Moreover, starting from the VCF generated by default, we defined a new threshold that is reducing the number of false-negative results without increasing the number of false-positive results. We also can perform CNV analysis from this VCF file and here too, we have identified some biases that must be removed. Thanks to this strategy we can analyze the TSO500 data with huge accuracy to provide the best information in combination with OncoKDM Lite.