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New Epitopes on Tumor Cells as Target for Cellular Immunotherapies †

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Abstract: Solid tumors represent most overall cancer types, but their heterogeneity would require an individualized treatment option. The current helpful approach is based on immunotherapy, but the main problem is represented by the lack of targets. Finding new epitopes (neoantigens) presented to the immune system is a new challenge for researchers worldwide. We analyzed 156 blood and tumor DNA samples using the Next Generation Sequencing method to identify SNVs in hotspot regions of 50 genes associated with tumor development. Data interpretation used Ion Reporter and Oncomine Reporter software. Next, the data were introduced in NetCTLPan epitope prediction software, which generated 8-11-mers with a high-affinity prediction for MHC class I binding and triggering cytotoxic immune response. We identified 89 tumor-specific non-synonymous mutations in 31 genes, inducing substitutions of at least one AA in specific protein structures. Genes such as APC, TP53, KDR, PTEN, PIK3CA, and JAK3 presented more than one mutation, but not all SNVs had tumorigenic significance. We used the NetCTLPan artificial neural network, which predicted specific interactions between epitopes and MHC class I molecules, TAP's transporting ability, and proteasomal cleavage. The ranking of the identified epitopes is based on an algorithm that ponders all the analyzed parameters. The number of epitopes capable of eliciting immune response varied depending on the gene, but we could identify at least one new epitope per gene, which could be used in priming the cytotoxic T lymphocytes. This method could be used for personalized immunotherapy in cancer patients.

Keywords: next-generation sequencing (NGS); mutations; epitope prediction; immune response; cancer.

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Conflicts of Interest

The authors declare no conflict of interest.