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Making Cancer History®

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Artificial Intelligence & Therapeutics For the Next-Generation of Immunotherapies: From the Laboratory to the Clinic and Back

Abstract:

Cancer immunotherapy has recently delivered impressive results. However, major roadblocks prevent the deployment of immune-oncology approaches to the majority of cancer patients, especially those with solid tumors. Chimeric antigen receptor (CAR) T-cell therapies, for example, are far from being successfully implemented. A bottleneck in modern immunotherapy of cancer is the identification of molecules that allow effective targeting of the tumor while leaving normal tissues untouched. Historically, all major clinical developments have been focusing on tumor-associated antigens (TAA). The landscape of TAAs, however, is restricted, with TAAs limited to cancer/testis antigens, which showed promising pre-clinical and clinical results but are targetable in only a limited number of malignancies. Furthermore, the magnitude of the immune response against hyper-expressed antigens is hindered by the general low affinity of T-cell receptors (TCRs) for self-antigens. Recent efforts have, therefore, been directed towards the discovery and validation of neoantigens that arise from mutations in cancer cells. Emerging alternatives to neoantigens are mutational hotspot antigens and cancer-specific isoforms of widespread proteins. Here, we describe the advantages and the drawbacks of each antigenic class in the field of immunotherapy, as well as novel in silico prediction tools for the high-throughput analysis of large “omics” datasets, which will dramatically speed up the discovery of new cancer-specific immunodominant antigens with high potential of being translated to the clinic.