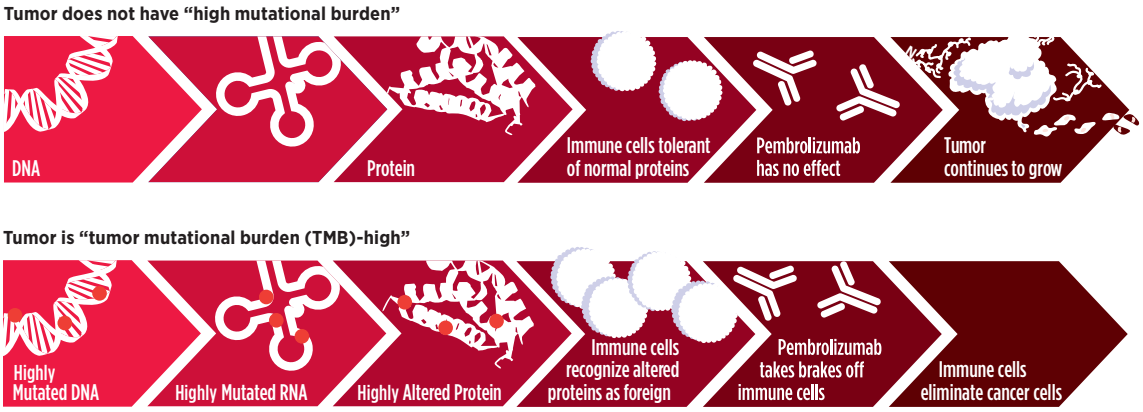
FIGURE 19 MORE PRECISELY IDENTIFYING TUMORS LIKELY TO RESPOND TO CHECKPPOINT INHIBITORS



Precision medicine is broadly defined as treating a patient based on characteristics that distinguish that patient from other patients with the same disease. The U.S. Food and Drug Administration (FDA) approval of pembrolizumab (Keytruda) for the treatment of any solid tumor identified to be tumor mutational burden–high is an example of precision immunotherapy. The scientific rationale underpinning this approval was the result of the dedicated researchers integrating scientific discoveries in the fields of immunology and cancer biology to develop an understanding of why tumor mutational burden–high is an effective biomarker for the use of pembrolizumab. Cancer cells with this biomarker have a much higher number of mutations in their DNA compared with other cancer cells (in the case of this approval it was measured using a defined test as 10 or more mutations per megabase of DNA). These mutations give rise to altered proteins, which are recognized as abnormal, or foreign, to cancer-fighting immune cells called T cells. These T cells are spurred into action when the PD-1 brake that is preventing them from eliminating cancer cells is released by pembrolizumab. In cancer cells that are not tumor mutational burden–high, the dramatically fewer DNA mutations mean fewer altered proteins. The immune cells in this situation accept the protein landscape in the tumor as normal and are unlikely to be spurred into action by pembrolizumab.

American Association for Cancer Research (AACR) Cancer Progress Report 2020