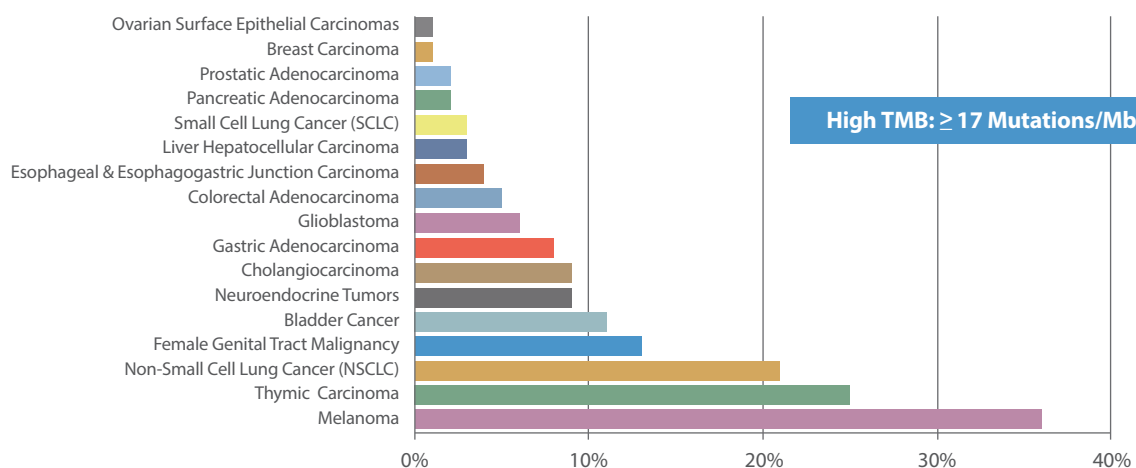




Tumor Mutational Burden – Immune Checkpoint Inhibitors Response

Caris Molecular Intelligence® tumor profiling includes **Tumor Mutational Burden (TMB)** status when Next-Generation Sequencing is performed. TMB is an emerging indicator for predicting response to immune checkpoint inhibitors across a wide spectrum of tumor types, including CRC, melanoma, NSCLC and urothelial carcinomas (bladder, renal, etc.).¹⁻⁶

High TMB Across Caris Molecular Intelligence Cases



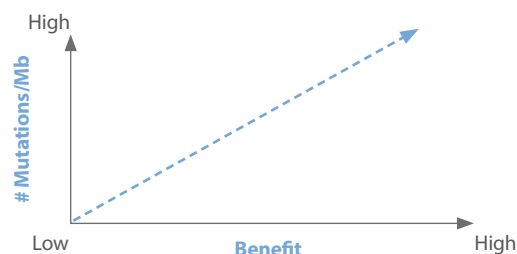
Genomic profiling with Caris Molecular Intelligence can help you make more informed therapy decisions when considering immune checkpoint inhibitors.

How It Works

Tumor mutational burden by Next-Generation Sequencing measures the total number of non-synonymous, somatic mutations identified per megabase (Mb) of the genome coding area (a megabase is 1,000,000 DNA basepairs).

- Non-synonymous mutations are changes in DNA that result in amino acid changes in the protein.^{2,6}
- The new protein changes result in new shapes (neo-antigens) that are considered to be foreign to the immune system.^{2,4}
- Immune checkpoint inhibitors are able to stimulate and allow the immune system to detect these neo-antigens and destroy the tumor.²
- Germline (inherited) mutations are not included in TMB because the immune system has a higher likelihood of recognizing these alterations as normal.⁷

TMB: Immune Checkpoint Indication for Response



Tumors with significant numbers of mutations resulting in altered proteins (neo-antigens) may respond more effectively to immunotherapies.

1. Rizvi NA. Science. 2015; 384(6230):124-128. doi:10.1126/science.aaa1348. – 2. Snyder A. N Engl J Med. 2014; 371:2189-2199. doi:10.1056/NEJMoa1406498. – 3. Camposato LF. Oncotarget. 2015; 6(33):34221-34227. doi:10.18632/oncotarget.5950. – 4. Rosenberg JE. The Lancet. 2016; 387(10031):1909-1920. doi:10.1016/S0140-6736(16)00561-4. – 5. Strickland KC. Oncotarget. 2016; 7(12):13587-13598. doi:10.18632/oncotarget.7277. – 6. Le DT. N Engl J Med. 2015; 372:2509-2520. doi:10.1056/NEJMoa1500596. – 7. Stewart TJ. Oncogene. 2008; 27:5894-5903. doi:10.1038/ncr.2008.268.

To order or learn more, visit www.CarisMolecularIntelligence.com.

US: 888.979.8669 | MIClientServices@caris.com

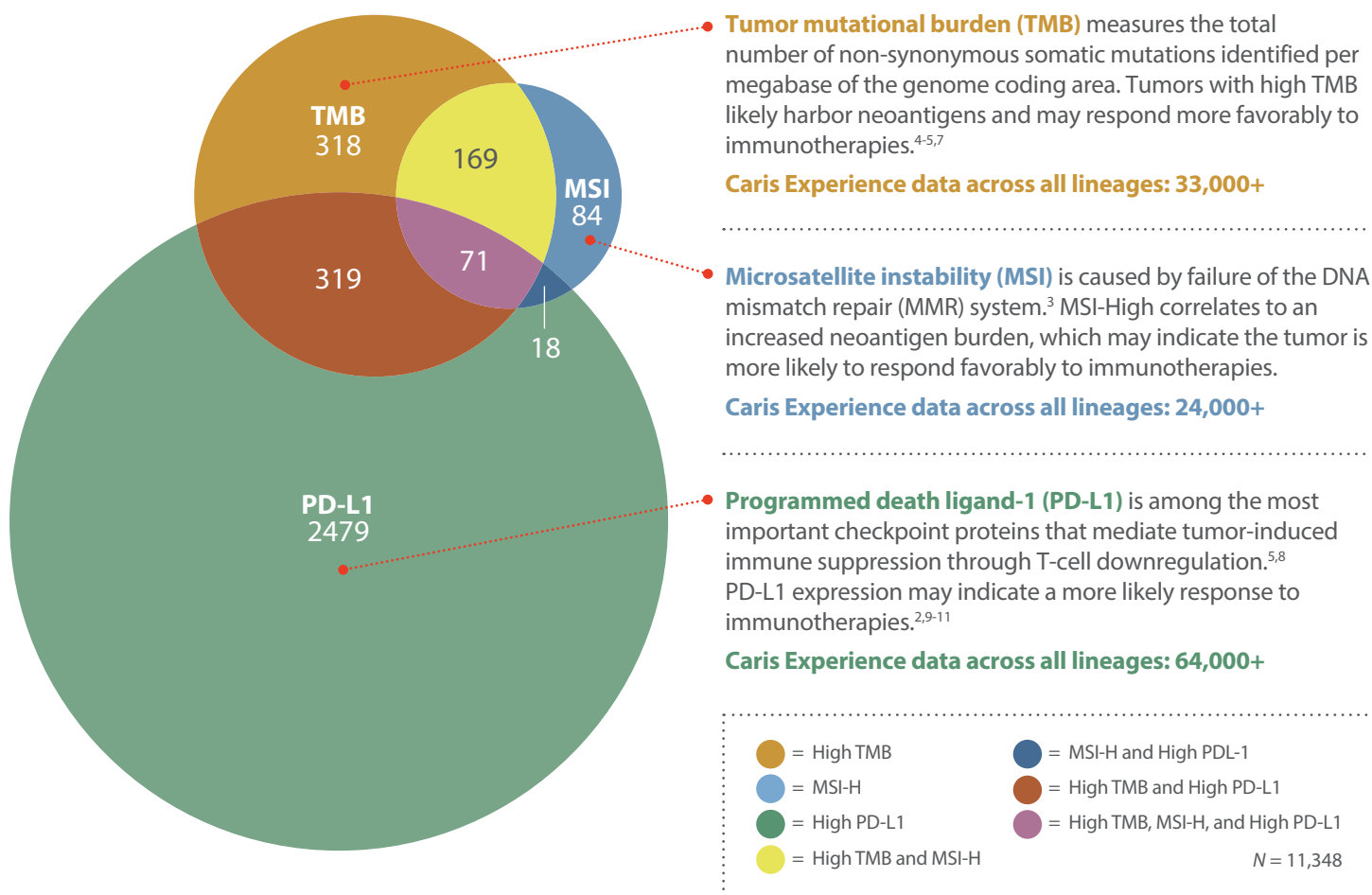
Intl: 00 41 21 533 53 00 | EUCustomerServices@caris.com



Unlock the Power of Immunotherapies

By harnessing the body's immune system to detect and destroy tumor cells, **immune checkpoint inhibitors** are rapidly ushering in a new era of precision medicine.¹⁻⁴ Although immune checkpoint inhibitors have demonstrated durable clinical responses across several tumor types, these therapies are costly and may present toxic side effects.^{1,3-6}

Understanding the relationships between TMB, MSI and PD-L1 can help oncologists make more informed immunotherapy decisions.¹²



Identify Patients More Likely to Respond to Immunotherapies through Comprehensive Genomic Profiling PLUS (CGP+) with Caris Molecular Intelligence.

1. Topalian SL. N Engl J Med. 2012;366(26):2443-2454. doi:10.1056/NEJMoa1200690. – 2. Patel SP and Kurzrock R. Mol Cancer Ther. 2015;14(4):847-856. doi:10.1158/1535-7163.MCT-14-0983. – 3. Le DT. N Engl J Med. 2015;372:2509-2520. doi:10.1056/NEJMoa1500596. – 4. Rizvi NA. Science. 2015; 384(6230):124-128. doi:10.1126/science.aaa1348. – 5. Rosenberg JE. The Lancet. 2016; 387(10031):1909-1920. doi:10.1016/S0140-6736(16)00561-4. – 6. Motzer RJ. N Engl J Med. 373:1803-1813. doi:10.1056/NEJMoa1510665. – 7. Snyder A. N Engl J Med. 2014; 371:2189-2199. doi:10.1056/NEJMoa1406498. – 8. Mellman I. Nature. 2011;480:480-489. doi:10.1038/nature10673. – 9. Borghaei H. N Engl J Med. 2015;373:1627-39. doi:10.1056/NEJMoa1507643. – 10. Garon EB. N Engl J Med. 2015;372(21):2018-2028. doi:10.1056/NEJMoa1501824. – 11. Taube JM. Clin Cancer Res. 2014;20(19):5064-5074. doi:10.1158/1078-0432.CCR-13-3271. – 12. Vanderwalde A. Cancer Med. 2018 Feb 13. doi: 10.1002/cam4.1372.