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Caris Life Sciences’ Molecular Intelligence Platform Characterizes Total Mutational Load in Multiple Tumor Types

7,000 Tumor Database with Total Mutational Load Status Used to Identify Cancer Types that May Respond to Immunotherapies

Platform Enables Detailed Profiling of Total Mutational Load Status and Correlation with Tumor Types

Data Presented in Poster Discussion and Poster Session at the 2017 ASCO Annual Meeting

IRVING, Tex., June 5, 2017 – Caris Life Sciences®, a leading innovator in molecular science focused on fulfilling the promise of precision medicine, today announced results of two molecular profiling studies that provide detailed information on the characteristics of tumors with significant Total Mutational Load (TML). The studies were possible due to the capabilities of the company’s proprietary Caris Molecular Intelligence® Comprehensive Genomic Profiling Plus (CGP+) platform that has been developed for use in personalized medicine and drug discovery and development. The two analyses were presented during a Poster Discussion Session and a Poster Session at the 2017 American Society of Clinical Oncology Annual Meeting in Chicago.

TML measures the total number of non-synonymous, somatic mutations identified per megabase of the genome coding area. TML has been correlated with response to immunotherapy agents such as PD-L1 inhibitors.1,2 It is hypothesized that these drugs are successful in the high-TML population because the increased mutational load results in increased production of neoantigens - antigens that are foreign to the immune system and create an inflammatory microenvironment. These drugs reduce the ability of tumors to evade the body’s immune response and stimulate its ability to attack the neoantigens on the tumor. Because of this relationship, an understanding of the TML landscape in various cancer types should contribute to the identification of potential responders to immune checkpoint blockade. It is well known that tumors that experience high levels of environmental-derived damage (lung cancer in smokers and melanoma) have high levels of TML. The objectives of the two studies presented at ASCO were to use the large database of CMI patients to better characterize TML across a broad range of tumors in order to identify other types that may be candidates for these therapies.

“As immunotherapies continue to change the treatment paradigm in various cancer types, there is an increasing need to use biomarkers to identify patients who may respond and who may not,” said David Spetzler, M.S., Ph.D., M.B.A., President and Chief Scientific Officer of Caris Life Sciences. “Because high TML may be correlated with more favorable response to immunotherapeutic agents, the results of these studies demonstrated that TML status should be assessed in context with other molecular alterations.”
TML Characterization in Solid Tumors
In a June 3 poster discussion session (Abstract #11517), researchers evaluated more than 7,000 tumors from 14 different cancer types to determine the levels of TML using the Caris Molecular Intelligence 592-gene Next-Generation Sequencing (NGS) platform. The mutation level to be categorized as “high” TML was set at ≥17 mutations per million base pairs (megabase; mt/MB). This threshold was based on the mutation rate of colorectal tumors with Microsatellite Instability (MSI), which demonstrate high mutation rates. Mean TML was highest in melanoma (21 mt/MB; 37% of tumors), non-small-cell lung cancer (11 mt/MB; 15% of tumors) and bladder cancer (11 mt/MB; 15% of tumors). Prostate cancer, pancreas adenocarcinoma and renal cell carcinoma had the lowest levels (6 mt/MB; ≤2% of tumors with high TML). Older patient age, male gender, absence of oncogenic mutations and presence of tumor suppressor mutations were associated with a high TML. The authors concluded that TML varied significantly among different cancers and was associated with several patient and molecular characteristics.

“TML has been proposed as a potential predictive biomarker due to its association with tumor immunogenicity so it is important to understand TML levels in tumor types beyond the ones where we already know the nature of immunotherapy response, such as lung cancer and melanoma,” said Mohamed Salem, M.D., Assistant Professor of Medicine at Georgetown University and lead author on the study. “From a biological perspective, it is also interesting to know how alterations in other cancer pathways correlate with TML levels so we can learn more about the molecular nature of TML’s effect on response.”

Spectrum of TML in Genitourinary Cancers
In a June 4 poster session (Abstract #4535), researchers evaluated TML profiles across different genitourinary (GU) cancers. Muhammed Azam Hussain, M.D., of Penn State University, and colleagues also assessed the correlation between TML and PD-L1 expression, another biomarker of response to immunotherapies. The study evaluated 544 tumor specimens from five GU tumor types (bladder, kidney, prostate, penile and testicular) using the Caris Molecular Intelligence 592-gene NGS platform. TML was highest in bladder cancer (14.5%) compared to the other tumor types. TML was rarer in kidney (1.8%), prostate (2.3%) and penile and testicular (0%) tumors. Bladder cancer samples were evaluated in more detail. Urothelial bladder cancers tended to have high TML (16.5%) whereas bladder cancers with a squamous histology were characterized by high PD-L1 expression (37.5%). In addition, there was no correlation between high TML bladder cancers and PD-L1-expressing bladder cancers. The authors concluded that TML varied among genitourinary cancers and that high TML scores did not predict high PD-L1 expression. They proposed additional research to better understand the underlying biology to determine which cancers may respond to immunotherapies.

“Questions regarding characterization and response to immunotherapies for TML in tumors are essential but very complex questions to answer requiring a platform capable of addressing them,” said Spetzler. “Our proprietary Caris Molecular Intelligence platform is designed to provide researchers and clinicians accurate results to such multi-faceted questions enabling them to efficiently obtain TML status as they evaluate therapy options for their cancer patients and further investigate the therapeutic opportunities related to TML.”

1. Rizvi NA. Science. 2015; 384(6230):124-128
About Caris Life Sciences
Caris Life Sciences® is a leading innovator in molecular science focused on fulfilling the promise of precision medicine through quality and innovation. Caris Molecular Intelligence®, the company’s Comprehensive Genomic Profiling Plus (CGP+) molecular testing service and the world’s leading immunotherapy diagnostic expert, assesses DNA, RNA and proteins, including microsatellite instability (MSI), total mutational load (TML) and PD-L1, to reveal a molecular blueprint to guide more precise and personalized treatment decisions. The ADAPT Biotargeting System™, the company’s revolutionary and unbiased profiling platform, is currently being utilized for drug target identification, therapeutic discovery and development, fixed tissue-based companion diagnostics, blood-based cancer screening and biomarker identification. Headquartered in Irving, Texas, Caris Life Sciences offers services throughout the U.S., Europe and other international markets. To learn more, please visit www.CarisLifeSciences.com.

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