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Caris Life Sciences Study Provides First Systematic Assessment of RNA Expression of Key Molecules Involved in the Infectious Process Leading to COVID-19 in Advanced Cancer

New Data Published in Scientific Reports Reveals Possible Biological Underpinnings of Cancer Patients Hyper-Immune Response to COVID-19 Infection

IRVING, Texas, March 16, 2021 – Patients with cancer demonstrate particularly poor outcomes from COVID-19. Caris Life Sciences[®], a leading innovator in molecular science and artificial intelligence focused on fulfilling the promise of precision medicine, has published results from a study that analyzed a cohort of 38,628 cancer patients to gain insight into why cancer patients have poor outcomes from COVID-19. Investigators identified that ACE2, TMPRSS2, and other proteases that are key factors necessary for viral attachment to and entry into target cells.

Caris' study results have been published in <u>Scientific Reports</u>, A Nature Research Journal, finding substantial variability of expression of ACE2 and TMPRSS2 across tumor types while identifying subpopulations expressing ACE2 at very high levels. This study provides the first systematic assessment of RNA expression of key molecules involved in the infectious process, and offers a biological explanation for why cancer patients do poorly when afflicted with COVID-19.

"In some tumor types, especially in gastrointestinal cancers, expression of ACE2 and TMPRSS2 is highly correlated," said W. Michael Korn, M.D., Chief Medical Officer at Caris Life Sciences. "Furthermore, we found infiltration with T-cell and natural killer (NK) cell infiltration to be particularly pronounced in ACE2-high tumors."

These findings suggest that subsets of cancer patients with specific gene expression profiles may be associated with heightened susceptibility to SARS-CoV-2 infection. For these patients, malignant tumors may function as viral reservoirs and possibly promote the frequently detrimental hyper-immune response leading to poor outcomes.

The disease resulting from SARS-CoV-2 infection, COVID-19, shows particularly severe courses in men and the elderly, a relationship that is further aggravated by comorbidities. Malignant diseases are comorbidities of interest in this context, as cancer patients, whose frequent treatment with immune-suppressive drugs might add to their vulnerability, have demonstrated particularly severe courses of the disease. Despite the similarities of SARS-CoV-2 to other coronaviruses, the biologic underpinnings of increased COVID-19 morbidity remain unclear.

"Taking advantage of a large database of tumors profiled by whole-transcriptome sequencing (WTS), we hypothesized that ACE2 and protease gene expression would vary across tumor types, with high expression presumed to associate with increased risk of infection and severe course of disease," said John Marshall, M.D., Chief, Division Hematology and Oncology, Department of Medicine, Georgetown University. "We found that ACE2 expression varies and correlates with expression of proteases in a tumor type-specific manner, which may underlie the severe disease progression observed in subsets of patients with cancer."

Caris' investigation demonstrates significant differences in ACE2 and protease expression in normal and malignant tissues with a subgroup of patients expressing very high levels of ACE2 RNA. These findings, together with the increased presence of inflammatory cells in tumors displaying high ACE2 levels, might contribute to the developing complex pathophysiologic picture of COVID-19 and help guide prophylactic measures in patients with solid malignancies.

About Caris Life Sciences

Caris Life Sciences[®] is a leading innovator in molecular science and artificial intelligence focused on fulfilling the promise of precision medicine through quality and innovation. The company's suite of market-leading molecular profiling offerings assesses DNA, RNA and proteins to reveal a molecular blueprint that helps physicians and cancer patients make more precise and personalized treatment decisions. MI Exome[™] whole exome sequencing with 22,000 DNA genes, and MI Transcriptome[™] whole transcriptome sequencing with 22,000 RNA genes along with cancer-related pathogens, bacteria, viruses and fungi analysis run on every patient provides the most comprehensive and clinically relevant DNA and RNA profiling available on the market.

Caris is also advancing precision medicine with Caris Artificial Intelligence, combining its market leading service offering, Caris Molecular Intelligence[®] with its proprietary artificial intelligence analytics engine, DEAN[™], to analyze the whole exome, whole transcriptome and complete cancer proteome. This information, coupled with mature clinical outcomes on thousands of patients, provides unmatched molecular solutions for patients, physicians, payers and biopharmaceutical organizations.

Caris Pharmatech is changing the paradigm and streamlines the clinical trial process by assisting biopharma companies with accessing research-ready oncology sites for clinical trials. With over 350 research sites within the Caris Pharmatech Just-In-Time (JIT) Oncology Network, biopharma companies can identify and enroll more patients, faster. Caris Pharmatech Just-In-Time Clinical Trial Solutions focus on rapid site activation and patient enrollment to streamline the drug development process. By implementing Caris' Just-In-Time Trial-Matching System, Caris will automatically match patients to clinical trials and sites can be activated and eligible to enroll patients within one week.

Headquartered in Irving, Texas, Caris Life Sciences has offices in Phoenix, Denver, New York, and Basel, Switzerland. Caris provides services throughout the U.S., Europe, Asia and other international markets. To learn more, please visit <u>CarisLifeSciences.com</u> or follow us on Twitter (<u>@CarisLS</u>).

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