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“Immunity, Microbiome, and Pathogenesis in Alcohol-Associated Cancer Treatment (IMPACT) Study”

Background: Alcohol consumption is an established risk factor for colorectal cancer (CRC), yet the biological mechanisms linking alcohol use to cancer progression and treatment response remain incompletely understood. Emerging evidence suggests that alcohol-associated intestinal dysbiosis and immune dysfunction, particularly senescence and exhaustion of CD8+ T cells, may contribute to impaired tumor immune surveillance. The Immunity, Microbiome, and Pathogenesis in Alcohol-Associated Cancer Treatment (IMPACT) Study aims to characterize potential biological pathways linking patterns of alcohol exposure to altered immune surveillance and intestinal dysbiosis in adults with newly diagnosed CRC. This study will generate preliminary data to inform future investigations of CRC progression and treatment response.

Methods: IMPACT is a mechanistic, observational, cross-sectional case-control pilot study recruiting adults with newly diagnosed CRC through LSU Health and University Medical Center New Orleans Oncology Clinics. Participants will be classified as alcohol-using or non-alcohol-using based on self-reported alcohol consumption and urine ethyl glucuronide (EtG) testing, with cases and controls frequency-matched 1:1 by CRC stage, sex, race, and age (± 10 years). Following informed consent and eligibility screening, participants will undergo clinical and behavioral assessments, dietary evaluation, anthropometric and body-composition measurements, and collection of blood, urine, and stool specimens. Peripheral blood will be evaluated for senescent and exhausted CD8+ T-cell populations, while stool and plasma samples will be analyzed to characterize microbial and metabolomic profiles. A subset of participants initiating immune checkpoint inhibitor (ICI) therapy as part of routine clinical care will undergo repeat assessment approximately six weeks after treatment initiation to evaluate longitudinal changes in immune, microbial, and metabolic measures.

Expected Outcomes: Outcome data are not yet available. The IMPACT Study is expected to provide preliminary evidence regarding associations among alcohol usage patterns, intestinal microbiome characteristics, circulating and intestinal metabolites, and senescent and exhausted CD8+ T-cell populations in CRC. These findings will inform the design and endpoints of future adequately powered studies examining alcohol-associated mechanisms of CRC progression and treatment response.