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Immune Correlations of Neck Infections with Clinical Outcomes (ICONICO)

Deep neck space infections (DNSI) present significant morbidity and mortality especially when associated with compromise in immunity. They are largely sequelae following the spread of odontogenic, tonsillar, salivary, or foreign body related infections into surrounding neck spaces and beyond. While majority of these are managed with surgical source removal and empiric support therapy, several of them worsen despite these efforts and are associated with poor outcomes. To date, there are no therapeutics for these, beyond additional supportive care. Despite presenting with similar clinical features at admission, patients may have distinctly different outcomes. As such, we do not completely understand the underlying pathophysiology of such different patterns of clinical progression. It has been reported that decreased immune competence is associated with poor outcomes in DNSI. However, comprehensive and serial immune monitoring of DNSI has never been reported. Such immune monitoring represents a critical aspect of our overarching goal of stratifying DNSI patients for subsequent personalized treatment with immune modulatory drugs.

We plan to use multiple approaches to serially elucidate changes in DSNI patient immunity. First, will be the use of enzyme-linked immune absorbent spot (ELISpot) – a highly sensitive immunoassay capable of measuring the frequency of cytokine-secreting cells at the single cell level. Additionally, we will use flow cytometry to enumerate and determine the detailed cellular phenotypes at a single cell level to ascertain predictive utility. Finally, we will determine systemic concentrations of key cytokines. This temporal description of the immune function in patients with DSNI is expected to serve as a prognostic indicator for clinical outcomes including long-term risk of mortality, sepsis, pneumonia, and end organ damage. These data may also provide a target for immunomodulation to improve clinical outcomes. Here, we hypothesize that immune metric(s) can be associated with clinical outcomes of DNSI patients.

Prediction modeling of baseline phenotype and function will be performed with the primary clinical outcome(s) being follow-up surgical intervention. We will determine the predictive value for each immunological readout at each timepoint and compare these values with: 1) repeat imaging following surgery typically triggered by worsening clinical conditions, 2) return to OR following first surgery, 3) escalation of care to a higher level, 4) need for prolonged protection of the airway and 5) wound healing duration.

The investigative team of Dr. Krishnan, DDS, and Dr. Caldwell, PhD, are well situated to conduct this proposed study. Dr. Krishnan is an experienced physician / scientist with 12+ years of treating complicated DNSI. Dr. Caldwell has been studying the immunology of infections for 22+ years and is currently involved in multiple immune monitoring studies. Finally, as the tertiary care service for the region, the division of Oral and Maxillofacial Surgery at UC is a key site for treating DSNI patients.

This study is designed to fill a critical gap in knowledge assessing the phenotype and functional immune state in patients with DSNI to potentially predict clinical outcomes. If altered immunity is associated with poor outcomes, then the growing repertoire of immunomodulatory agents may translate into successful treatments for DSNI patients. If this study proves successful, assessing the ex vivo response of DSNI patients' WBCs to candidate immunoadjuvant therapies with methodologies used in this application could represent a step towards personalized medicine. Additionally, these data would allow new investigations for underlying mechanisms causing improper resolution of the DSNI.