Defining the role of sleep in cancer immunity and metabolism

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Abstract**:** During disease progression, patients with cancer often experience systemic and poorly prognostic signs of illness, including the wasting syndrome, cachexia, and sleep disruption. In turn, disrupted sleep patterns are associated with increased cancer risk. Despite these clinical indications of reciprocal interactions between sleep and cancer, the mechanisms linking sleep disruption and cancer development and progression are largely unknown. We will use integrative techniques from neuroscience, endocrinology, metabolomics, and immunology to systematically dissect the pathways by which alterations in sleep/wake circuitry promote aberrant metabolic and immune responses in both murine and human cancer. We will couple wireless EEG/EMG telemetry with assessment of endocrine, metabolic, and immunological changes in the tumor and host system. We will bi-directionally modulate sleep patterns using optogenetic disruption and induction of sleep. Specifically, we will target dopaminergic neurons in the mesencephalic ventral tegmental area, as their optogenetic activation drives wakefulness, while silencing these neurons generates 'natural' sleep states. We will investigate whether this modulation of sleep reversibly induces endocrine, metabolic, and immunological changes observed during cancer progression. In collaboration with a clinical sleep laboratory at WCMC, we will gather data from human subjects with cancer to confirm the translational relevance of our work. We will analyze data using novel machine learning/AI techniques, unsupervised approaches that will enable confirmation of translational relevance and aid in additional hypothesis generation for reverse translational research. Ultimately, we aim to understand the biological substrates linking sleep and cancer and identify molecular strategies for treatment of patients with cancer and systemic comorbidities.