Deciphering the Immune Microenvironment of NF1-associated Peripheral Nerve Sheath Tumors: Identifying Early Biomarkers of Disease Progression and Malignant Transformation

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Background/Objective:

Neurofibromatosis type 1 (NF1) is a multisystem disorder that affects ~1/3000 newborns. Plexiform neurofibromas (PN) are present in about half of cases and can transform (lifetime risk of 8-13%) into malignant peripheral nerve sheath tumor (MPNST), a highly aggressive and metastatic sarcoma with poor survival. Unfortunately, there are currently no reliable biomarkers to identify PN at risk of undergoing malignant transformation. Our research has revealed that a subset of benign-appearing and atypical PN exhibit deregulated immune surveillance and T-cell infiltration that precede malignant transformation. In this study, we are analyzing tumor microenvironment and immune landscape in NF1-related tissue specimens to identify biomarkers of disease progression. To power these studies, this project focused on constructing a dataset of NF1-related samples to be analyzed.

Methods:

701 patients were identified via Cerner billing codes and pathology archives. De-identified clinical data, including presenting symptoms, relevant clinical history, pathology diagnoses, disease features, prior chemotherapeutics/radiation, prior gene profiling, and imaging features were collected.

Results: We selected 86 patients with a total of 175 samples. 81% of patients had a clinical diagnosis of NF1, and 6% had a history of MPNST. Out of the 175 samples, 54 were in the head and neck, 42 in the thorax, 28 in the lower extremity, 27 in the upper extremity, 26 in the pelvis/abdomen, and 15 in the paraspinal region. The leading causes of procedures were pain (41%), growth (40%), and concern for malignancy (27%). The most common tissue diagnoses were neurofibroma (51.4%), PN (20%), and undefined-grade MPNST (11%). Out of the 46 MPNSTs, 30 were primary tumors, 4 metastases, and 12 local recurrences.

Conclusion and Potential Impact:

The results of this study will provide valuable insights to inform preclinical models of NF1-tumorigenesis to validate these findings and identify novel treatment approaches for individuals affected by these rare but devastating tumors.