Pilot Project 3: THE ROLE OF ACETYLCHOLINE RECEPTORS IN MERKEL CELL POLYOMA VIRUS-INDUCED MERKEL CELL CARCINOMA
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The overall goal of the project is to develop the first multi-omic profile of the cervicovaginal microenvironment in Hispanics.

Inputs	Specific Aims & planned initiatives			Outcomes -- Impact	
	Aims	***Activities***	***Outputs***	***Short-term/ Intermediate***	***Long-term***
• UPR-MSC • MDACC • UPR/MADCC Cores • IAC • PSC Samples from patients with virus-driven Cancer • Large Merkel cell carcinoma (MCC) cohort Expertise: • Skin pathology • Molecular pathology • Neuroscience and nAchR expertise • Confocal microscopy Equipment/Techniques • Confocal microscopy • Light microscopy • Immunohistochemistry • qPCR • Methylation analysis • Immunohisto-chemistry	**Aim 1**. Evaluate the histologic features and MCPyV-status of a large MCC cohort and correlate with clinical parameters and survival. **Aim 2.** Characterize the expression of nicotinic acetylcholine receptors (□-3, □-5, □-7, and □-9) in a large cohort of MCC by immunohistochemistry and qPCR. **Aim 3.** Correlate the expression pattern of nicotinic acetylcholine receptors with immune infiltrate, genome methylation and clinical characteristics of MCC.	• Microscopic examination of MCC tissue. • Determine MCPyV-positive or MCPyV-negative status of MCC tumors in the cohort. • Perform immunohistochemistry to determine nAchR (□-3, □-5, □-7 and □-9) expression in MCPyV-positive and MCPyV-negative MCC. • Perform immunohistochemistry for T-cells (CD3, CD4 and CD8), B-cells (CD20), macrophages (CD68 and CD163) and PD-L1. • Evaluate nAchR expression intensity and distribution in MCPyV-positive vs. MCPyV-negative MCC by confocal microscopy. • Perform genome-wide methylation analysis of MCPyV-positive vs. MCPyV-negative MCC.	• We anticipate identifying histologic parameters that predict overall survival in patients with MCC. • We anticipate identifying immune infiltrate parameters that predict response to immunotherapy and overall survival in patients with MCC. • Understand the expression pattern and distribution of nAchR (□-3, □-5, □-7, and □-9) in MCPyV-positive and MCPyV-negative MCC • Identify differences in genome-wide methylation between MCPyV-positive and MCPyV-negative MCC • 2 publications • Establish UPR-MDACC collaboration to study cutaneous malignancies. *Standardized outputs* • # publications • # high-impact journals • # grants and supplements • # students trained • # collaborations established • # patents	***Learning*** • Increase our understanding of MCC, a rare virus-driven malignancy. • Identify prognostic factors that influence survival in patients with MCC. • The data generated will inform the design of future studies to understand the role of nAchRs in the biology of MCC. ***Action*** • Incorporate prognostic parameters into routine clinical practice.	Utilize knowledge obtained from proposed studies to modify treatment strategies for MCC to improve patient outcomes. Leverage the established UPR-MDACC collaboration to apply for additional funding opportunities to study other cutaneous malignancies.
Process Evaluation				**Outcome Evaluation**	