

Castrillon and Mani Awarded NCI Multi-PI R01



Drs. Diego H. Castrillon and Ram Mani were awarded a National Institutes of Health (NIH) National Cancer Institute (NCI) R01 award of \$2.8 million, for a five-year project titled “Mechanisms and Consequences of PAX2 Inactivation in the Initiation of Endometrial Carcinogenesis”.

Endometrial cancer, one of the most prevalent malignancies affecting women, has seen a steady increase in incidence: 2024 marked the first year where deaths from endometrial cancer surpassed those from ovarian cancer. This cancer disproportionately affects African American and Hispanic women, highlighting significant healthcare disparities.

While surgery can be effective for early-stage cancers, the five-year survival rate for advanced cases remains below 20%. Despite its clinical impact, endometrial cancer receives less funding and research attention compared to other cancers, necessitating innovative research directions.

PAX2 Silencing: A Critical Discovery

Recent studies from the Castrillon and Mani laboratories have identified PAX2 silencing as a pivotal event in endometrial cancer. PAX2, a transcription factor essential for uterine development, is silenced in over 80% of endometrial cancers, making it the most known signature molecular feature in endometrial cancer. Evidence suggests that PAX2 silencing is often the initiating event in endometrial carcinogenesis, frequently observed in both cancerous and precancerous endometrial tissues.

Unlike other cancer-causing genes, PAX2 is not mutated but silenced through epigenetic mechanisms. The research aims to uncover the specific epigenetic processes responsible for PAX2 repression and to better understand PAX2's role as a tumor suppressor. By investigating these mechanisms, the Castrillon and Mani laboratories hope to advance our understanding of endometrial cancer and pave the way for new therapeutic strategies and improve outcomes for women affected by this disease.

Castrillon and Mani are faculty members of the Department of Pathology and members of the UT Southwestern Harold C. Simmons Comprehensive Cancer Center.