Slay Sarcoma Research Initiative
Funded Research at Penn Medicine's Abramson Cancer Center

The Abramson Cancer Center's (ACC) Sarcoma Program brings together brilliant experts from diverse fields – from immunotherapy and basic cancer biology to orthopaedic oncology – within Penn's unique collaborative environment to focus on many different areas of sarcoma research. This compassionate team of experts specialized in the diagnosis and treatment of sarcoma is combined with a cutting edge basic and translational research team who are working to identify innovative treatments for this rare disease. The Slay Sarcoma Research Initiative is funding critical basic science research detailed below.

Uterine leiomyosarcomas are rare malignancies of embryonic connective tissue. Even when there is no evidence of spread beyond the primary site at the time of diagnosis, these cancers often demonstrate aggressive behavior. Effective treatment for uterine leiomyosarcoma is lacking and investigators from the ACC's Sarcoma Program are working to address this gap. By understanding the oncogenic drivers of uterine leiomyosarcomas, therapeutic strategies can be optimized.

Over the last four years, Dr. Robert Giuntoli has been able to develop a productive, collaborative relationship with several individuals at Penn Medicine including Dr. Katherine Nathanson, Dr. Jennifer Morrissette and Dr. Fiona Simpkins. The team of investigators has focused specifically on uterine leiomyosarcoma and additional funding from the Slay Sarcoma Research Initiative will allow them to continue to pursue their goal of developing novel, investigator-initiated clinical trials for women with this disease.

In 2017, initial funding from the Slay Sarcoma Research Initiative supported work to isolate specimens from women with uterine leiomyosarcoma and the successful development of patient derived xenograft models in mice. The team can now not only identify novel targets for treatment of uterine leiomyosarcoma, but can also evaluate the effectiveness of these targets in a relevant patient derived xenograft model.

With the additional funding provided in 2018, Dr. Giuntoli and the team will use next generation sequencing data to identify drugs that target the genetic alterations associated with uterine leiomyosarcoma. These drugs can then be tested in patient derived xenograft models to obtain preclinical data for further investigations. Additionally, the team can develop cell cultures and cell lines which can be utilized in 3D drug screening to identify additional therapeutic targets.

Thus far, the team has learned that approximately 20% of uterine leiomyosarcomas have amplification of CCNE1. CCNE1-amplified cancers heavily rely upon cell cycle checkpoint G2/M for survival. The current hypothesis is that by targeting the cell cycle checkpoint, CCNE1-amplified uterine leiomyosarcoma cells will enter mitosis prematurely resulting in cell death. To test this hypothesis, Dr. Giuntoli and his team will transplant uterine leiomyosarcoma tumor fragments into their uterine leiomyosarcoma patient derived xenograph models. Therapies will be administered based on appropriate protocols and the efficacy of treatments will be determined by assessing tumor growth weekly by ultrasound. These studies may identify a novel treatment warranting further study in clinical trials for uterine leiomyosarcoma patients.

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