



Dr. Weibo Luo was awarded a Department of Defense (DoD) breakthrough award of \$1.64M for the project titled “Defining the Role of RCOR2 in Hypoxia-Induced Immune Evasion and Its Therapeutic Potential in Triple-Negative Breast Cancer”. Duration of the award is three years.

Triple-negative breast cancer (TNBC) is a highly aggressive subtype of breast cancer in women with limited effective treatment options available, which highlights an unmet clinical need of innovative therapeutic approaches for these patients. The tumor microenvironment, comprising tumor cells, stromal cells, blood vessels, and immune cells, is known to be immunosuppressive in TNBC, which provides a specialized niche for tumor growth. Low oxygen (also known as hypoxia) is another hallmark of tumor microenvironment in solid tumors, including TNBC, and drives tumor progression. Accumulating studies have implicated that hypoxia plays a crucial role in tumor immune evasion, enabling cancer cells to evade immune surveillance and subsequently promote tumor growth and metastasis. However, the precise mechanisms of hypoxia-induced immune evasion in TNBC have not been fully defined yet.

The funded proposal hypothesizes that RCOR2 controls hypoxia-induced MHC-II silencing in TNBC cells leading to TNBC escape from cytotoxic CD4+ T cell immunosurveillance and tumor progression. Thus, targeting the RCOR2 complex will block tumor growth and improve immunotherapy in TNBC. Specific Aim 1 will dissect the mechanism by which RCOR2 controls hypoxia-induced MHC-II loss in TNBC. Specific Aim 2 will decipher the mechanism by which RCOR2 controls hypoxia-induced TNBC immune evasion. Specific Aim 3 will target the RCOR2 complex to block TNBC growth and improve immunotherapy in vivo.

Overall, this project will define an innovative epigenetic mechanism of hypoxia-induced immune evasion and has great potential to open up new translational avenues for the treatment of aggressive TNBC.

Dr. Weibo Luo, an Associate Professor of Pathology, is also a member of the Harold C. Simmons Cancer Center. To learn more about the Luo Lab, follow this link: [Luo \(Weibo\) Lab | UT Southwestern, Dallas, Texas.](#)