



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP120459

Project Title:  
Contribution of the BRIGHT transcription factor to autoimmune Diffuse  
Large B-cell Lymphoma

Award Mechanism:  
Individual Investigator

Principal Investigator:  
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Entity:  
The University of Texas at Austin

### Lay Summary:

Lymphoma is a cancer of white blood cells, or lymphocytes. The two major types of lymphoma are Hodgkin lymphoma and non-Hodgkin lymphoma. There are two types of lymphocytes, T cells and B cells. Diffuse Large B-Cell Lymphoma (DLBCL) is the most common non-Hodgkin lymphoma in the world, constituting approximately 30% of newly diagnosed cases. There are several forms of DLBCL, and the worse form is called Activated B-Cell (ABC)-DLBCL. ABC-DLBCL is very aggressive, fast-growing, and can move outside the lymphoid system to form deadly tumors all over the body. Autoimmunity is a misdirected immune response that occurs when the immune system goes awry and attacks the body. Autoimmunity can cause a broad range of human illnesses and is also strongly associated with certain human cancers, including ABC-DLBCL. Unlike most cancers, ABC-DLBCL is thought to originate from autoreactive B cells and requires continued stimulation by a self or "autoantigen" to grow. There are a number of genes whose products (proteins) represent "gold standards" for distinguishing ABC-DLBCL from other types of DLBCL. BRIGHT is such a gene. The BRIGHT protein functions in the cell nucleus as a "transcription factor" because it reads the DNA code of other genes into proteins. In addition, BRIGHT functions on the cell membrane to control how much signal the cell is receiving from the outside; ie, in the case of ABC-DLBCL, the autoantigen. We hope to find out whether BRIGHT causes ABC-DLBCL by determining what genes are turned on or off by BRIGHT. We will develop a model by transferring the BRIGHT human gene into mice. We will use specialized genetic technology to determine whether BRIGHT over-expression or mutation (to only produce the membrane-associated form) results in mouse tumors that resemble human ABC-DLBCL. These studies will lead to a better understanding of the genetics underlying this dreadful disease and provide novel insights into new anti-cancer drug development.