George Daniel Brooks Lectureship
The endowment for the George Daniel Brooks Lectureship was established in December 1991 with a gift from Frances Brooks Corzine. She made the gift in memory of her father, George Daniel Brooks, to support an annual lecture at the Vanderbilt-Ingram Cancer Center. The first lecture was given in 1996 by Alfred G. Knudson, Jr., M.D., on Tumor Specificity in Hereditary Cancer. Knudson was Fix Chase Distinguished Scientist and Senior Member of the Institute for Cancer Research, Fox Chase Cancer Center. Since 1996, annual lectures have been given on highly relevant topics, such as “Mechanisms of Malignant Progression” and “New Concepts and Paradoxes in Cancer Research” by some of the foremost authorities in cancer research.

Upcoming Discovery Lecture:

SIR STEPHEN O’RAHILLY
M.D., FRCP, FRCPI, FRCPATH, FRS, FMedSci
University of Cambridge

April 2, 2015
208 Light Hall / 4:00 P.M.
Diffuse large B cell lymphoma (DLBCL) is a heterogeneous diagnostic category that is comprised of two prominent molecular subtypes, termed activated B cell-like (ABC) and germinal center B cell-like (GCB). These DLBCL subtypes are now viewed as molecularly distinct diseases since they arise from distinct stages of normal B cell development, require distinct recurrent genetic abnormalities to become malignant, have distinct cure rates with current chemotherapy regimens, and respond differentially to targeting agents. We defined a “chronic active” form of B cell receptor (BCR) signaling that activates NF-κB in ABC DLBCLs. Such ABC DLBCLs are killed by knockdown of BCR signaling components, such as the kinase BTK or components of the BCR itself. Over one fifth of ABC DLBCLs have mutations affecting the CD79B or CD79A subunits of the BCR that augment BCR signaling. To attack chronic active BCR signaling therapeutically, we initiated clinical trials in relapsed/refractory DLBCL of ibrutinib, an irreversible and highly selective inhibitor of BTK. Ibrutinib monotherapy induced a high rate of complete and partial responses in ABC DLBCL, while GCB DLBCL tumors rarely responded. Given its excellent safety profile and selective mechanism of action, we are hopeful that ibrutinib can be combined with both chemotherapy and other signaling modulators to achieve cures for these patients. Several rational combinations of targeted agents for the therapy of ABC DLBCL will be presented.

Dr. Staudt received his B.A. from Harvard College in 1976, graduating Cum Laude in Biochemistry. He was awarded a Medical Scientist Training Program fellowship at the University of Pennsylvania School of Medicine and received his M.D. and Ph.D. degrees in 1982. His Ph.D. thesis revealed somatic hypermutation as the mechanism of rapid antibody diversification during normal immune responses. Following Internal Medicine training, he joined Nobel Laureate David Baltimore’s laboratory at the Whitehead Institute as a Jane Coffin Childs Fellow. There he cloned and characterized the first tissue-specific transcription factor, Oct-2. In 1988, he established his laboratory at the National Cancer Institute (NCI), which now focuses on the molecular basis for human lymphoid malignancies and the development of targeted therapies for these cancers. Dr. Staudt is currently Co-Chief of the Lymphoid Malignancies Branch (previously the Metabolism Branch) in the NCI. In addition, he is the Director of the NCI Center for Cancer Genomics, which oversees several large-scale managed programs studying the genomic aberrations in cancer. In 2011, Dr. Staudt was given the honorary title of NIH Distinguished Investigator. He has received numerous awards for his research, including the 2009 Dameshek Prize from the American Society of Hematology for outstanding contribution in hematology and election to the National Academy of Sciences in 2013.