



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
R1112

Project Title:  
Recruitment of Established Investigators

Award Mechanism:  
Recruitment of Established Investigators

Principal Investigator:  
Copeland, Neal

Entity:  
The Methodist Hospital Research Institute

### Lay Summary:

Dr. Neal G. Copeland returned to the United States in September 2011 and became Director of the Cancer Biology Program, along with his wife and long-term collaborator, Nancy Jenkins, at the newly formed Methodist Hospital Research Institute (TMHRI) in Houston, Texas. For more than 30 years, they have modeled human diseases affecting many organ systems including disorders of the immune, visual, auditory, skeletal, nervous, pigmentation, and hematopoietic systems, in mouse. They have also had a long-standing interest in modeling human cancer in mice and for the past six years have focused exclusively on providing a better understanding of the genetics of cancer with the hope that new drug targets useful in the targeted treatment of human cancer can be identified.

Dr. Copeland received his Ph.D. degree in Biochemistry from the University of Utah in 1976 and carried out postdoctoral training in the molecular biology of retroviruses at the Dana Farber Cancer Institute, Harvard Medical School. Here, he met Dr. Jenkins and they decided to take their first independent positions at The Jackson Laboratory with the intent of using retroviruses as insertional mutagens in mice. In particular, they initiated their studies on the identification of candidate cancer genes in hematopoietic tumors, which is the principal type of cancer induced by retroviruses. They continued this work, as well as many other studies, at the National Cancer Institute-Frederick. Here, Dr. Copeland served as Director of the Mammalian Genetics Laboratory, the forerunner of the Mouse Cancer Genetics Program, which he also headed. In 2005, they reported success in modeling human cancer in mice using the Sleeping Beauty (SB) transposable element system. Using SB, it is now possible to model virtually any type of solid tumor in mice; solid tumors are of course the most common kind of cancer that affects humans. To fully exploit this technology, Dr.'s Jenkins and Copeland moved to the Institute of Molecular and Cell Biology in Singapore, where Dr. Copeland served as the Director, and Dr. Jenkins as Deputy Director, for most of their stay. A massive forward genetic screen for genes involved in the initiation, progression and metastasis of cancer in 16 different models in 11 organ types was performed in their laboratory in Singapore and they returned to the US with a large collection of candidate cancer genes in hand.

At TMHRI, Dr. Copeland will take the most promising candidate cancer (CAN) genes and begin validating them by first determining whether the structure or expression of a CAN gene is altered in human patients samples. For those that are, it will be interesting to determine whether the mutation of a particular gene(s) correlates with patient outcome

and/or response to therapy. Those with high predictive value can eventually be incorporated into patient screening protocols. The gold standard for CAN gene validation is demonstrating that a CAN gene can induce or accelerate the formation of tumors in a mouse model. This approach is very challenging to do given the large collection of genes being identified in mouse and human tumors. Thus, we are currently devising several strategies for the high throughput analysis of CAN genes identified from both mouse and human tumors. Once a robust set of validated cancer genes is developed, it is critical to partner with biotech and/or pharmaceutical companies to use this information to generate targeted therapies for various forms of cancer. Finally, we believe that it may be possible to use transposon-based insertional mutagenesis to identify genes involved in drug resistance and testing this hypothesis will also be a high priority at TMHRI.

Dr. Copeland has served on numerous scientific advisory and editorial boards and has consulted for several biotechnology companies. He is a member of the National Academy of Sciences, USA and is one of the worlds most highly cited biomedical research scientists.