New Jersey State Commission on Cancer Research
LAY ABSTRACT OF RESEARCH PROJECT

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Project Title: **Clinical Impact of SNPs in the P53 Pathway**

Description: **This study examines the role of specific genetic variations in the risk of developing breast cancer, the characteristics of breast cancer behavior, and how those variations can be exploited for treatment.**

Genetic information in the form of DNA is transmitted from parents to offspring and accounts for human uniqueness. Despite outward differences between any two people, the vast majority of genetic information is identical. It is uncommon for people to be born with mutations in genetic information that lead to the early onset of various diseases including cancer. However, it is clear that some individuals are at a higher risk of developing cancer than others and that some develop their cancers at an age much earlier than might be expected. The portion of DNA not identical between individuals contains variations known as single nucleotide polymorphisms (SNPs). It is known that some of these relatively common genetic variations are associated with the development of a wide variety of cancers, including breast cancer. DNA contains long sequences of molecules. Altering one molecule, as by a SNP, changes the genetic code but may not produce any recognizable change in cell function. Therefore, the laboratory is working on identifying SNPs producing measurable changes in cell function, especially in response to stressors such as chemotherapy or radiation, and on identifying the result of those changes at the molecular level. Much of the work has focused on three genes known as mdm2, akt1 and p53. These genes function individually but have a complex network of interactions between them modulating cell behavior. Abnormal expression of these genes, common in breast cancer, may be accounted for, in part, by the presence of SNPs in these genes. Tumor growth for the majority of breast cancers is hormone-dependent and effective strategies for treatment have focused on manipulating hormones. A SNP in the mdm2 gene appears to become functional in the presence of an active estrogen growth signal pathway and may alter the effectiveness of hormonal manipulation. Likewise, other molecules may be used such as genistein, also known to act through the hormone pathways, to take advantage of the presence of this SNP and make treatment more effective. The investigators have built a database of clinical information, blood specimens, and DNA specimens on over 500 breast cancer patients. The next phase of work will focus on analysis of tumor tissue. In the proposed study, the overall goal is to determine how the presence of SNPs in these specific genes alters breast cancer risk, tumor characteristics and tumor behavior in response to chemotherapy and hormonal manipulation. The work will also increase understanding of how various combinations of SNPs may affect breast cancer outcome. Knowledge of cancer cell behavior will enable better treatment interventions and strategies for prevention in those individuals with increased risk.