

An Integrated Approach to Targeting Breast Cancer Molecular

Subtypes and Their “Resistance” Phenotypes

Dream Team Leaders:

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BACKGROUND:

This Dream Team's goal is to develop a fully integrated translational research approach to developing more effective, less toxic therapies for the three major breast cancer subtypes. The team combines the expertise of Dennis Slamon, known for his work in developing the important anti-cancer drug Herceptin, and Joe Gray, a molecular biologist who brings understanding of the basic mechanisms that cause breast cancer.

During the past several years, researchers have come to understand that breast cancer is not a single disease but rather a spectrum of conditions that vary in their biology and response to treatment. They have been able to identify three major subtypes; ER positive, HER2 positive and triple negative. This Dream Team is interested in understanding the basic molecular mechanisms which give rise to these subtypes and explain the differences in their clinical behavior.

One of the primary obstacles to effective cancer treatment is the ability of cancer cells to become resistant to treatments that are initially effective. Over a period of time, cancer cells are able to develop ways of “outsmarting” the drugs and agents designed to kill them. This Dream Team will study the driving mechanisms that lead to resistance in the three major breast cancer subtypes. Understanding resistance opens the door to developing innovative therapeutic agents that overcome this critical problem.

Another area of interest is in the role that cancer stem cells play in resistance. Researchers now realize that the growth and spread of many cancers, including breast cancers, are influenced by the existence of these stem cells which are often highly resistant to otherwise effective treatments. The Team will study the ways in which this unique malignant cell population operate across the three major breast cancer subtypes, knowledge that could be important to the developing new treatments for breast as well as other major cancers.

One critical component of this study will be to bring together the vast amount of information that exists about breast cancer into an integrated data base that will form a “discovery platform,” or basis for identifying and validating new drug combinations and targets that can be pursued in clinical trials. The Team expects that these efforts will lead to significantly improved therapies for breast cancer, especially the most difficult to treat forms, within the three year period.

Significance:

Although a great deal of progress has been made in understanding and treating breast cancer, over 40,000 women a year lose their lives to this disease every year in the United States alone. Understanding the molecular diversity of breast cancer has been the driving force leading to the development of new treatments for this disease. Researchers are rapidly moving beyond the “one size fits all” approach into a new era in which breast cancer treatments will be tailored to the biology of the tumor. This project will address the most significant issues related to the three major subtypes of breast cancer and will use that information to develop innovative, less toxic therapies with the potential to improve the treatment outcomes for women with this disease.

The Quote:

“We are at a point today where technology has really enabled us to ask questions at a sophisticated level in ways we were never able to ask before—critical questions that we have had for a long time but couldn’t approach. Now we can begin to ask what exactly is broken within a cell, what converts that normal cell to a malignant one? We can think now about how we might interfere with those pathways that cause cancer.” Dennis Slamon, M.D., Ph.D.

“We have spent the last several decades coming to a deep understanding of some of the events that go awry in cancers, that lead to the development of malignant disease. Where we are today is at a period where we can actually fingerprint each individual tumor so know what’s wrong with it, and I think that we can use our biological understanding to decide which drugs we can use to treat that individual cancer.” Joe Gray, Ph.D.