

Testimony

Before the

Senate Cancer Coalition

Statement of
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Good morning, Senator Feinstein, Senator Hutchison and members of the Senate Cancer Coalition. I am happy to provide testimony today on behalf of Dr. Harold Varmus, the Director of the National Cancer Institute (NCI). My name is Barbara Wold. I am a genome scientist currently on sabbatical from the California Institute of Technology where I am the Bren Professor of Molecular Biology. I came to NCI this year as advisor to the Director to establish NCI's new Center for Cancer Genomics (CCG). The mission of this Center is to develop and apply cutting-edge genome science to prevent cancer and better treat cancer patients.

Cancer is many different diseases, yet all have a common origin: The DNA of tumor cells is mutated or modified in genes that govern cell division, survival and migration, among other important cellular functions. These DNA changes do harm by altering the amount, structure, and function of RNA and protein molecules, which are the active products of our genes. Spectacular improvements in DNA sequencing methods over the past decade now allow us to determine exactly how an individual tumor's DNA has been mutated. This path of discovery has important implications for better prevention, diagnosis, and treatment of cancer.

This morning I want to tell you a few key lessons we have learned by systematically applying modern genomics to breast cancer. I also want to point out how parallel research on other types of cancer is yielding valuable insights into breast cancer and vice versa. I will use the remainder of my time to tell you how this leads us to a compelling opportunity to marry individual patient care with our nation's research enterprise.

Breast cancer is one of the most common cancers with almost 230,000 cases and 40,000 deaths each year in the U.S.¹ Research over the past three decades has taught us that breast cancer, like other adult human cancers, is caused by multiple mutations in the DNA of a cell that ultimately becomes a tumor. Most of the pertinent DNA mutations occur by chance and accumulate over a period of many years to ultimately cause a tumor, although in some patients one of the mutations is inherited from a parent, as is the case for breast and ovarian tumors with inherited BRCA1 and BRCA2 mutations.

We are presently learning an enormous amount about which gene mutations can cause breast cancer as part of The Cancer Genome Atlas (TCGA) program. TCGA is the flagship program in adult cancer genomics, developed and run in a close partnership between the NCI's CCG and the National Human Genome Institute (NHGRI). TCGA, which will be complete in 2014, is creating reference genome and genome-related data for more than 10,000 tumors, including 20 major adult tumor types and 10 rare ones. Each TCGA tumor is characterized by multiple genomic methods in a systematic and rigorous manner, and the resulting reference data are made available to all cancer researchers. Another program in the CCG, TARGET (Therapeutically Applicable Research to Generate Effective Treatment), is leading a similar effort for childhood cancers, with a special emphasis on tumors that respond poorly to current therapies.

One general lesson from work on many cancers is that combinations of mutations in a small number of genes are needed to produce a tumor. We also know that all breast cancers are not identical at the DNA level – far from it. Every tumor has its own genomic “personality,” and each falls into a subset of breast cancers with some commonalities and also some distinctions. For example, we have known for some time that an excess of HER2 proteins, caused by extra copies of the HER2 gene, is associated with an aggressive group of breast tumors. Knowing this about HER2 led to the development of Herceptin, a drug that now provides an effective targeted treatment for many HER2 positive tumors. As is the case for other targetable driver genes, further research is also identifying new drugs aimed at HER2 positive tumors. This will expand the suite of options available to the physician. At the genomics level, the TCGA consortium confirmed 10 previously known breast cancer genes and identified another 10 novel ones. These studies are also showing us that specific drivers found in one tumor type can also be active in tumors from other unrelated tissues. For this reason, studying tumors of one type will often enrich what we know about another type, in unpredictable ways. Moreover, these relationships are likely to change and refine diagnostic categories and suggest different and effective uses of existing drugs.

Learning the specific identity of the driver gene set for an individual tumor is ultimately powerful in the clinic, because it can help the physician assess whether a given drug will be effective in a particular patient. We already do this with estrogen sensitivity and HER2 status in breast cancer, and with EGFR status in lung cancer. The list of such distinctions is growing

¹ N, Noone AM, Krapcho M, Neyman N, Aminou R, Altekruse SF, Kosary CL, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). *SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations)*, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2009_pops09/, based on November 2011 SEER data submission, posted to the SEER web site, 2012. Available at <http://seer.cancer.gov/statfacts/html/breast.html>. Accessed 13 June 2012.

rapidly. Genomic knowledge can also be used to decide against a particular treatment, if the appropriate target mutations are not in play. It is incredibly important that we not waste a patient's valuable energy and time on a treatment that does not fit their tumor. Indeed, some of the most exciting clinical cancer research going on around the country today, at NCI Cancer Centers and elsewhere, uses extensive genome sequence information to guide patient treatment. Learning the DNA signature for each patient will ultimately be an important and routine part of diagnosis and treatment.

Thank you for the opportunity to testify today. I would be happy to answer any questions.