"ADVANCES IN CANCER RESEARCH"

Department of Health & Human Services
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Statement of
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Good morning, Senator Specter. I am Dr. Richard Klausner, Director of the National Cancer Institute. I am pleased to have the honor of appearing before the Subcommittee today.

After twenty years of our 'War on Cancer', we have some victories to report--some cancers, previously carrying a rapid death sentence are now, incredibly, curable -- overall cancer mortality rates are, for the first time, beginning to fall.

Yet, as we sit here this morning, over 450 people will be newly diagnosed with cancer and over 150 more Americans will die. The progress we have made is a direct result of research which has begun to illuminate the causes of cancer--allowing effective prevention for some cancers, development of vastly improved methods of early detection and diagnosis and producing new therapies of increasing efficacy. The good news is that we have tested the very premise of the war which this Nation has supported--the premise that progress is predicated on research---and found that premise to hold true. But as the grim statistics and the stories of the tens of millions of survivors and families and friends of survivors and of those who have not survived tell us, we have a long way to go.

I believe we are at a defining point in this war. It is hard to adequately describe the profound advances in the science of cancer research and in the revolutionary technologies that give us powerful tools to attack these diseases--but let me try.

All cancer arises because of the slow accumulation of changes in the set of the 80-100,000 instructions that determine the behavior of each of our cells. There is no one cause of these changes and no one cause of cancer. Chemicals, like those found in tobacco smoke, viruses, radiation, sunlight and the inevitable mistakes made each time each cell copies the DNA on which those instructions are written, all contribute to cancer. Identifying cause is the key to prevention. Diet, exercise, hormones and our genetic makeup, in ways still mysterious, profoundly modify the risks of cancer.

Cancer is not something that just happens--it arises out of a long process that we are only now actually unravelling. All cancer evolves from pre-cancer and we can now begin to design how to detect and treat pre-cancer. Let me give you an example. Colorectal cancer

is the second most common cancer killer. In the vast majority of cases, there is a loss of the function of one specific gene product called APC. This was actually discovered by studying a relatively uncommon hereditary colon cancer syndrome. This molecular change results in the activation of another gene which instructs the cells to make an enzyme that is one of the targets of anti-inflammatory drugs like aspirin. This, coupled with observations that aspirin and other anti-inflammatories may prevent colon cancer, is leading to the search for new and more effective drugs and to clinical trials that are aimed at this specific target in hopes of preventing the development or recurrence of this cancer. This is the type of process that we are ready to repeat for new preventions and new therapies--not blind guesses but targeted choices based upon real knowledge of the machinery of each cancer. Will it work? We will not know if we do not try and we will not know what to try if we do not capture the opportunities for discovery.

We can, I am convinced, develop new ways to predict the behavior of each cancer, whether it needs to be treated, whether it will respond to therapy and what therapy will actually work. This is the new promise of molecular diagnostics. The explosion of new ideas about the specific machinery of cancer cells is beginning to result in the design of therapies against cancer much like the use of antibiotics, anti-cholesterol agents and the new anti-HIV drugs. Some of these new strategies are based on turning off the motors that make cancer cells grow, some are based on strategies to trick cancer cells to commit suicide, some on harnessing the immune system to seek out and destroy cancer cells and some on destroying the unique ways that cancers assure their own blood supply. All of these are based on specific knowledge about cancer. That is where the research is taking us.

One recent therapeutic advance illustrates how cancer therapy is being altered by our new understanding of the molecular characteristics of cancer. Researchers at the NCI, in collaboration with extramural investigators, have been testing new treatment regimens for a particularly aggressive form of lymphoma. A 5-drug regimen resulted in an apparent cure, or long-term remission in about 50% of the patients. The remainder either failed to respond or rapidly relapsed. What was different? In virtually all of the relapsed patients, their cancer cells harbored a mutation in the p53 gene, a gene whose loss of function is implicated in over 50% of all human cancer. What had been called one cancer was clearly at least two distinct diseases. Recently, the investigators evaluated a newer regimen with three additional drugs and have observed long-term remission, hopefully cure, in 90% of all of these patients. This example illustrates a principle that is guiding a transformation in oncology. We can begin to identify the defining characteristics of any cancer. It is this set of alterations that will define the actual targets for therapy.

Imagine engineering a virus to only kill tumor cells--a virus tailored to recognize a gene altered in 50% of all human cancers. It has been done and is now being tested in clinical trials. This year, 20,000 new patients will be enrolled onto one of over 500 NCI-sponsored clinical trials. This is the only way to test the therapies and preventions of tomorrow which must replace the inadequate therapies of today. Despite the size of our national clinical trials system, only 2% of cancer patients enter clinical trials limiting the number of promising leads tested and the speed with which we answer critical questions.

This is a time in cancer research that all of us approach with a new optimism. We know the road to take. Unfortunately, we don=t know how long that road is. We, at the National Cancer Institute, have been planning for how we must be prepared to make new investments in the extraordinary opportunities now available. The challenge before all of us is to step up to these new opportunities to make sure that, however long the road is, it is one we travel at full speed.

Mr. Chairman, that concludes my prepared testimony. I would be pleased to answer any questions.