How to widen the hunt for targeted cancer therapy

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(AP) -- Cancer is a tale of two sets of genetic code, your own and your tumor's - and tracing the unique areas of damage makes for a way to target treatment.

Fifty years after the discovery of the first direct genetic link to cancer, scientists are assessing the state of so-called targeted therapy - with nearly 30 treatments on the market and a dozen or so more under study.

"We're still not using the 'C' word, 'cure,'" cautioned personalized medicine director Jeff Boyd of Fox Chase Cancer Center, who helped organized a meeting in Philadelphia on Tuesday to mark the anniversary and examine the future of targeted therapy.

But, he added, "there is real potential to transform many cancers into chronic diseases."

One next challenge is how to expand the number of targets to attack, in part by answering what the new chief of the National Cancer Institute calls the "big questions" about what makes this disease so intractable.

Questions like: What makes a tumor metastasize, or spread through the body? Metastasis is what kills, yet scientists don't know why some tumors spread and others don't, and what programs those tumor cells to invade, say, the liver instead of the bone or the lung - factors that undoubtedly could be new treatment targets.

Starting in October, Dr. Harold Varmus, the NCI's director, will begin quizzing top researchers from around the country about which of oncology's underlying mysteries should be part of his "Big Questions Initiative," a new focus of government cancer research.

Answering those questions "would get you over a roadblock that keeps us from making better progress," Varmus told a meeting of his scientific advisers earlier this month.

For Dr. Otis Brawley of the American Cancer Society, such a project might finally offer clues to a huge problem facing patients today: How to tell who needs the most aggressive treatment, and who would be OK skipping the big guns.

A domino effect of genetic alterations is required to cause any of the 200 diseases collectively called cancer. Some occur in the person, making them more prone to illness. But tumors also have their own genetic signature - four to seven genetic changes that are critical to turning, say, a normal breast or colon or liver cell into a cancerous one, and a pattern of activity that signals how aggressive that malignancy will be. Those unique patterns also offer targets for treatment, drugs that zero in on the particular genetic pathways fueling the person's cancer - and even vaccine-like therapies, a fledgling field that aims to train patients' immune systems to recognize and fight their tumors.

It all started with the 1960 publication of what was dubbed the Philadelphia chromosome, a funny-looking chromosome that two scientists - one from the University of Pennsylvania, one from Fox Chase - spotted only in patients with a specific kind of leukemia. Fast-forward to the 2001 approval of the groundbreaking drug Gleevec, which has turned chronic myeloid leukemia from a fast killer into a disease that many patients today manage with a daily pill. It works by targeting the cancer-causing protein produced by the Philadelphia

chromosome.

Gleevec wasn't the first genetic targeted therapy for cancer - the decades of research sparked by that discovery actually paid off for some other cancers first.

Boyd predicts there will be more than 100 targeted therapies available within several more years, and the real quest is for targets that prove as crucial to holding cancer in check as Gleevec's did.,

Generating particular excitement now are possible new drugs for hard-to-treat breast cancer, compounds called PARP inhibitors that block enzymes needed for cell growth. Also on the radar are earlier-stage experiments with drugs for melanoma and lung cancer that target different genetic pathways involved in spurring cancer growth.

The biggest threat: Funding for cancer research isn't keeping up with the discovery of possible new targets, said the cancer society's Brawley. The NCI's budget has held at around $5 billion for several years, but federal scientists are bracing for possible cuts in 2012.

And because these targeted therapies work differently - shrinking a tumor or slowing its growth - than the tumor-destroying approaches of chemotherapy and radiation, it's harder to prove a benefit.

But Allison Frey, whose aggressive form of thyroid cancer spread to her liver in inoperable patches, says that approach has made her cancer an illness she can manage much like a diabetic manages insulin. For nearly five years, the Lanoka Harbor, N.J., woman has swallowed an experimental pill called Axitinib that shrank those patches and kept them from growing back, working through a pathway that targets a tumor's blood supply.

"Honestly, to me it's just like any other chronic illness," said Frey, who's part of a study at Fox Chase. "I show up for work every day and live life ... with minimal issues."