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Genetics Hold Promise, Challenges for Cancer Care

By E.J. Mundell
HealthDay Reporter

SUNDAY, Sept. 16 (HealthDay News) -- Someday in the future, people may routinely have doctors scan their personal genomes, looking for this or that aberrant gene to help prevent, spot or treat a cancer.

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"We are in the midst of both an evolution and a revolution in cancer care," said Dr. Len Lichtenfeld, deputy chief medical officer at the American Cancer Society.

While gene-specific treatments such as the leukemia "wonder drug" Gleevec are already on the scene, "we still have an incredibly long way to go in terms of how we understand the basic genetics of cancer," he said.

"Right now, we are working still at a very crude level -- the future will be much more dynamic," Lichtenfeld said.

The "genetics generation" has much to be proud of, however. The mapping of the human genome in the late 1990s, the advent of high-output methods to comb through thousands of genes, and a deepening knowledge of the complexities of DNA and RNA are bringing new discoveries each week.

Some of the highlights from just the past year:

- Last August, a U.S. team announced the first-ever gene test aimed at pinpointing which patients with early stage lung cancer will benefit from post-operative chemotherapy, and which can be spared the arduous treatment.
- That same month, Canadian researchers reported on a new model to speed the identification of mutations linked to a silent killer, ovarian cancer. Spotting those genes could pinpoint women at risk.
- A $100 million U.S. project called the Cancer Genome Atlas announced its first major achievement in September -- the mapping of genomes for breast

and colon cancer. Scientists say they were able to identify 100 mutations thought responsible for each of those malignancies.

- In March, British scientists reported that they had pinpointed 100 mutated genes that help drive more than 210 different cancer types. "This set of genes is known to regulate key functions in virtually all cell processes of growth, differentiation," researcher Andrew Futreal, of the Wellcome Trust Sanger Institute in Cambridge, said at the time.
- And, in April, a team at Duke University said it had found genes that encourage breast cancer's spread to the lungs, as well as mutations that hamper chemotherapy's therapeutic effects.

It all looks very promising. But Lichtenfeld said that every DNA discovery has its downside, too.

"The more that we learn, the more complex it is going to get," he said. Indeed, the mapping of the breast and colon cancer genomes revealed that not only were the two cancers radically different in their origins, but that each tumor differed greatly between patients.

It's quickly become a very tangled web, experts say, but that's an inevitable part of the science.

"There may be a period of greatly evolving complexity that we have to get through which will only be sorted out by doing larger numbers across more genes," Futreal said.

Complicating matters further is the emerging field of epigenetics -- the study of how genes change their activity as they respond to their environment.

Still, certain "commonalities" could simplify things. Futreal pointed out that even though hundreds of genes can go awry and cause a cancer, many of these mutations will target the same cellular pathway. So, treatments that repair those broken pathways could fix a host of tumor types, he reasoned.

Today, however, only a small minority of cancer patients are directly benefiting from gene-based diagnostics or treatments. Those include women who carry the *BRCA 1* and *BRCA 2* breast cancer mutations, patients with chronic myelogenous leukemia (CML) who can take Gleevec, and early stage lung cancer patients who may soon benefit from those new prognostic tests.

And even when Americans find out that they *do* carry a certain gene posing an added risk, finding a qualified genetics counselor to sort it all out can be tough. There are only a handful of these experts in Lichtenfeld's hometown, Atlanta, he said, and they're practically unheard of in smaller centers.

"Most physicians simply aren't familiar with all the implications of assessing a woman's risk for breast cancer, for example, [or] of understanding all the genetic issues," Lichtenfeld noted. "So, I think that our theory right now is better than our practice. Our practice clearly needs to get better."

Nevertheless, things are greatly improved from decades past, when a patient with

a family history of cancer was simply told to watch and wait and hope.

In the case of the *BRCA 1* and *BRCA 2* genes -- thought to cause up to 10 percent of breast cancers -- women now have real options to cut their risk, Lichtenfeld said. Using high-tech tests to spot the genes, women can make tough but potentially lifesaving decisions to have a breast removed or to take anti-cancer drugs such as tamoxifen to cut their odds for cancer by up to 80 percent.

Other tests aimed at spotting the *HER-2* cancer gene and its product protein can dictate whether a patient's breast tumor will react favorably to the drug Herceptin.

"Many of these decisions aren't any easier than they were in the past, but at least now, they are much better informed," Lichtenfeld said. "And, looking into the future, this is going to become so much more a part of our diagnosis -- our ability to diagnose before we even *see* cancer. Typing the kind of cancer a patient has, too. And it's all going to become a huge part of cancer treatment."

SOURCES: Len Lichtenfeld, M.D., deputy chief medical officer, American Cancer Society, Atlanta; Andrew Futreal, Ph.D., co-leader, Cancer Genome Project, Wellcome Trust Sanger Institute, Cambridge, England

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