Genetic Testing and Targeted Therapy

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Andrew Schorr:
So, Dr. Keating, so we have blood tests when we're diagnosed, and maybe you do these other kinds of tests, FISH testing. You're looking at the genetics, which I would say is typically very important now in really many cancers; certainly in CLL. What is your specific gene that's gone sort of haywire, or a number of—and that's what they're referring to, here, now with these numbers? What's your profile of CLL? Yours may be different from mine, probably is.

So do you need a different approach?

Dr. Keating:
You probably don't know what a FISH test is. It's not like in Seattle where they're throwing fish in the market, and the guy's catching it, etc. But it's called a fluorescence in situ hybridization. And it had to be developed because acute leukemia, you could take a bone marrow and incubate them for 24 or 48 hours, and a number of cells would divide. And when they divide, their chromosomes become easier to identify, and you can line them up so that you have your 22 pairs of chromosomes 1 through 22, and women two X chromosomes and in men an X chromosome and the Y chromosome. And the Y chromosome is shorter. So men have basically lost the common sense gene.

So women have a double dose. Sorry, chaps. But we have been replacing them with testosterone, so it's not a bad tradeoff. But what happens is that you can't line up in CLL, because the cells are not dividing very rapidly at all. So you have to develop a probe that you can lay on nondividing cells, and it will search out a particular area on chromosome 11 or 12 or 13 or 17 and stick to it. And because we have pairs of chromosomes, you have two little areas where they're sticking to. You put a fluorescent probe on that's red or green or any other color, and you have two little dots.

But in CLL, it's a disease of loss of chromosomal material, predominantly. So you lose part of number chromosome 11, so you only have one 11 dot, and one 13 dot and one 17 dot. But the trick is that you have three number 12s so that you have these four basic groups. And if nothing is wrong with either of those, you call it negative, which is really just noninformative.

And there are big, big studies looking at fancy sequencing of genes, but still you have the most common ones involved, these four little areas. The other areas are basically research areas, but the FISH test is crucial, and it's evaluating what your disease is going to behave like. So the FISH test is key. I keep reading with interest of all the progress that's being made in the sequencing of chromosomes.

But one thing that is never really spoken about publicly is that the sequencing is done on only about 3 to 4 percent of the DNA in all the chromosomes, because they're the ones that make enzymes. And the rest of it used to be called junk DNA. And it doesn't matter whether you're Darwinian, or you think that God created, it and it just happened.

Neither one of them is going to end up with junk. So they're now finding that all the so-called junk material is really, really important in a whole bunch of cancers, and certainly in CLL.

Andrew Schorr:
And so what's important is to get the right test, so you get targeted therapy. And also sometimes if you're at a treatment, key time for you, like you come out of—you've been diagnosed but now months or years down the road and it's time for treatment based on all the symptoms we described. Maybe you need a test again. Or you had a treatment and now the effectiveness of that treatment has worn off, and there's a new decision to be made; being tested again. So it's not just one time, right, Nicole?

Dr. Lamanna:
Right. I think this is a really important point, because I think we all see folks who are missing some of these key, crucial tests.

And it's something that we're surprised we still see in the community, that it's just not being done. And these tests really do have implications that may affect your treatment. So this is certainly—whether you're newly diagnosed or you've had some sort of therapy before and then might need new therapy, it should be tested again. Because things do evolve and change over time, and so that's really, really important.