# What Genetic Mutations Are Doctors Looking for in CLL Patients?

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**Andrew Schorr:**
One more thing I'm going to ask you about, and then, I want to go to Dr. Wierda, as well. So, molecular testing. So, what's that, and where does that come in, in CLL?

**Dr. Brown:**
Right. So, molecular testing is looking for particular gene mutations, often by something called next-generation sequencing, which has become the way that we do many of these tests. And many of our cancer centers have panels of genes that we look at that we know are mutated in a particular type of cancer. And so, with CLL, there are certain genes that are mutated at relatively high frequencies. Although, there's no gene that's mutated in most CLLs. So, the most important gene to look at is the TP53, because again, if there's a mutation in that, just like if there's a deletion of 17, chromosome 17, that does affect, eventually, our treatment decisions.

Other mutations that are seen in CLL include NOTCH1, and SF3B1, and ATM are probably the most common. They don't generally affect our treatment decisions, but they may have some prognostic impact. We're still really learning their full significance.

**Andrew Schorr:**
All right. That's what I want to ask Dr. Wierda. So, Bill, you get a report back of your patient, and it's got whether it says NOTCH, or P53, or 17p. And there's someone like me or Michelle, sitting in front of you, and say, "Okay, so what's the significance?" Some of it could be real significant, and maybe you could tell us about that, and some of it, we don't know yet, or maybe not significant. So, take us through that.

**Dr. Wierda:**
Right. So, in terms of an assessment, we will routinely do here, at Anderson, a 29-gene panel. Centers are implementing now, and coming on line with panels of genes that they're sequencing. And not everybody does the same panel. So, I think probably Jennifer's panel is different than the panel that we developed. We have been using ours for a couple of years now, and we have 29 genes that we are sequencing routinely. It's what's referred to as targeted sequencing, so not all the genes—not the whole entire gene for each of those 29 genes is sequenced, but portions of them that are potentially important are sequenced.

And so, we get the results in terms of the mutations that patients have in this 29-gene panel. And as Jennifer said, the most important one is TP53 because, that has implications in prognosis, and also, implications in terms of choice of therapy. And that's the one that we could have the most full discussion about in terms of those components.

The other genes, we're still learning about, and they are not real common. They happen usually—they happen to—they are found in, usually, the minority of individuals. And right now, and over the past couple of years, we've been doing sequencing for this 29-gene panel, and we're looking at clinical metrics such as time to first therapy, such as response to therapy, duration of response to therapy. We're looking at all of those clinical components to try to understand what the significance, what the clinical relevance and significance is for the various mutations that we've identified.

We're now—we have recently submitted a couple of papers, one, that describes the frequency of these mutations in an unselected patient population who's come to MD Anderson to be evaluated. The other paper that we've recently put together, and reported is what gene mutations correlate with time from diagnosis to first treatment. So, we've identified a gene that when mutated is correlated with shorter time to first treatment. But most of them, we're still learning about. TP53, we have the most perspective on and the longest—most data related to this, mutations in TP53.