

SPEAKER 1: This is a study where we look at lung cancer in never-smokers. This is a particularly interesting question because lung cancer-- naturally, people think it's an environmental disease. How come never-smokers also develop lung cancer? So our hypothesis a long time ago was there is a genetic susceptibility underlying lung cancer. What's triggered, also, why we look at genetic susceptibility is that even among the heaviest smokers, only 10% to 20% develop lung cancer. So obviously supporting the notion of genetic or individual susceptibility. And several studies have been done to look at the genetic effect but are mostly overwhelmed by smoking effect. Because most of the patients in the study are smokers.

Very few are never-smokers. So what do we do differently is we took only the never-smokers so we can purify the gene effect, so to speak. Of course, this is much harder to do. It took us 12 years to collect samples and get real patients into studies. And then it also involved five institutions in the nation. And finally we got our work done. What we found is-- it's very interesting. What we took-- the way to do it is to do it on an unbiased search in the whole human genome, because the Genome Technology is available-- became available in the past two to three years.

And we searched the whole genome for the differences between the never-smoker lung cancer patients and the normal subjects who were also never-smokers. And then we not only found the hits in the genome that associated with the lung cancer in never-smokers, but we also validated it in three different studies which are collaborating with Mayo Clinic. And the gene particularly we are linked to is this GPC5. And what we found is that people harboring a variation in this gene have a 50% increase in their risk of developing lung cancer.

The never-smokers are the people who really never smoked cigarettes all their lifetime or other tobacco products. But in the study, we allowed a few people who smoked less than 100 cigarettes. So those people tested it and really didn't go on with it. So it's really minimal, if any. Some people were mixed with the non-smokers, but non-smokers we typically don't use in this context, because former smokers who already quit smoking are also defined as non-smokers if you look now. So we call it the never-smokers. The three things we looked at is that this is not only gene. We're pretty sure it's not only gene related to lung cancer development in never-smokers. And so we're going to continue to search more to see how this gene habits in fact in the middle of other to-be-defined genes.

Then we can accurately calculate the risk this gene really imposes on a normal individual. That is the first thing. The second thing is that if we try to see whether this gene has any clinical significance in terms of patients' responses to therapies. And they are survivals. That means we need to stratify patients by harboring this gene variation, or not, link to their treatment regimens and their responses. And this also can help to develop new targets of therapy. And then thirdly, this is going to open the era of treating never-smokers and smokers differently in lung cancer. Right now, they basically follow the same treatment regimens. What we will try to do in the next phase is see whether this gene has a differential effect among people who never smoked but have the differential exposure history, or even a family history of lung cancer.

And we can test whether this particular gene behaves differently in a different subset. So if a patient or a general person asks whether they harbor the gene, or whether they are at risk of lung cancer, then this is one of the measures that we can take to answer the question. At least do we know if this person harbors this variant or not. And then at least we can answer the lung cancer you developed is not caused by this variant. If the person is not harboring this variant. And then we can search for other causes. The key message is-- I think, again, I wrap it around three key points. One is that we do have evidence there is a genetic predisposition to lung cancer in never-smokers. And we will soon know whether this genetic change would lead to different therapeutic measures. And that lastly, we also can use it to tease apart which patient could be accounted for by the genetic changes and which patients are not.