



## How Do We Approach Cancer Genetic Evolution Over Time?

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### **Dr. Swanton:**

The topic of my talk was titled "The Clinical Implications of Cancer Evolution". We've known for several years now that cancers evolve in a branched evolutionary manner, so they don't evolve in a linear manner. They evolve in a branch manner. What does that mean? It means that there is enormous diversity, genetic diversity in a cancer mass either in the primary site, in the lung, for example, or at other sites of disease.

And we have to know how the cancer evolved very early on so we know what mutations are present in every tumor cell typified in lung cancer by—for example, epidermal growth factor receptor mutations or BRAF mutations, are present in every tumor cell, and they make good and robust drug targets. But the problem is over time resistance occurs to therapy in almost all patients, and the reason for that is because of the branch mutations, the mutations that are present in some cells but not others spring up and resist therapy over space and time.

And so what we're trying to do is develop better approaches to target tumors to prevent resistance from occurring, and the way in which we're proposing to do this is by using the body's immune system to recognize mutations that are present in what we call the trunk of the tumor's evolutionary tree, that is, mutations that are present in every tumor cell so that when you offer patients an immunotherapy like a vaccine or a cell therapy you're targeting tumor cells at all sites of disease, not tumor cells but not others. And what we're trying to do is develop new therapies that can do that effectively.

And we're also trying to understand how resistance to those therapies might occur in the future through immune-based approaches such as loss of molecules that present mutations to the immune system and what have you. So broadly speaking, that's what my talk was about.

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