SPEAKER: So the key, the key scientific questions that needed to be answered, that were begging to be answered, about this therapy, well, how could you explain the tremendous selectivity for a malignant clone or a pathogenic set of T cell clones? How could one explain the absence of classical adverse reactions, at least in the vast majority of patients? And how could one explain the capacity of a treatment in a counterintuitive way, compared to all other treatments, treat both a cancer and auto-reactivity?

Well, the first thing that it pointed to, before we could really get any true traction on the answers, was that there is something else-- not another therapy, but there is something very big and very expansive, called a natural immune system, that naturally does both of those things. Right now, for all healthy individuals, we are silently, without even trying to induce it, having an immune system that is protecting us against incipient cancers, before we will ever see them and most of which we will never see, because the immune system rids us of them in its microscopic track. And at the same time, the immune system, with its over a billion different orchestrated T-cell clones working together, is also very neatly preventing in all of us, or almost all of us, except those that have autoimmune disease, auto-reactivity.

There is tolerance of all of our organs and all of our cells. So what was clear, at least as a tantalizing possibility, was that somehow, what we had landed on was not a new principle, but an uncovered principle, essentially that it was possible to partner with the normal immune system. We weren't inventing a way to do things that the normal immune system does by itself. Somehow, ECP was an on-ramp to that highway called the natural immune system, which also typically does its miraculous stuff without our knowing about it and without causing adverse reactions.

So we had no choice but to really try to find that principle. And it was daunting. If you fast forward to the year 2018 and look at PubMed on the National Library of Medicine, run by the NIH, you'll find some 1,200 peer-reviewed papers, one way or another, providing points of light in that endeavor. But the perspective right from the start was that we knew certain things that could guide the research.

The first thing was, the only way that selectivity, that antigen-specific selectivity and that cellular specificity, the only way that the immune system can do that is through the portal of antigen-presenting cells, the most important of which is called the dendritic antigen-presenting cell. Unless the antigens that were going to be attacked could now be-- were somehow being processed and presented through the dendritic cell population of the patients, this could not happen. So we knew that the target had to be, of our studies and the studies of others, the broad focus had to be, how does ECP, how does the passage of anti-coagulated blood as a 1-millimeter film through the most commonly-used device, right from the start, how does that enable dendritic cells to get into action, when clearly, they had been circumvented, or else we wouldn't be seeing these diseases?