SPEAKER 1: So in other words, we needed a first treatment that would massively reduce the tumor burden, so that the antibodies that we were going to use were not like dumping water from a pail in the ocean. The treatment that we devised was the crude antecedent of ECP. We knew that the drug 8-Methoxypsoralen, abbreviated 8-MOP, is a unique, naturally occurring molecule in nature that has no activity by itself. If you take it by mouth it's excreted from the body in entirety in 24 hours.

But if it encounters long wave, i.e., low energy ultraviolet light such as would come through a window glass, the drug gets activated instantaneously to as potent a DNA cross linking, chemotherapeutic agent, only where the light and the drug come together, and only for the milliseconds that follow a light exposure.

So we hypothesized that if we could use that drug activated by light shined on blood from patients that had a large number of the malignant cells in their blood already, in other words, a leukemia and tissue phase, pass that blood through an ultraviolet exposure field inside transparent, plastic tubing, and return it to the patient, perhaps we could kill a large number of the malignant cells, rely on the liver, the spleen, other components of the filtering reticuloendothelial system to remove the dying cells, and then, with a smaller tumor burden left, come back with those antibodies.

So we took five of my own patients with therapeutically resistant, chemotherapy resistant, actually, cutaneous T-cell lymphoma in a leukemic phase, and tried this approach. It was the first time that anybody at least has reported treating the blood with a photoactivatable drug. What happened was the extraordinary thing that we now call photopheresis or ECP, because we actually got such a good response, a complete response in fact, in two of those five first patients, that we never got to use the antibody. We just for reasons that we can discuss realized that we were dealing with something very special in this strange, fortunate turnaround.

Indeed, by treating those first two patients, two days in succession at monthly intervals, waiting to see how safe this was, and doing that through three monthly cycles, we were astonished to get complete eradication of their T-cell malignancy. We did it despite the fact we were treating all the cells in the blood that passed through the ultraviolet light field. We did it not only by heavy infiltration of vital organs, but by suppression of the normal immune system, and leading to opportunistic infections of the same type that can kill AIDS patients.

That didn't happen at all. So we were struck with the fact that we had, in two of five patients, somehow induced a tremendous immune reaction by only treating an estimated 3% to 5% of the malignant cells in the body, exposing them to this photoactivated drug, 8-MOP, returning those cells immediately to the patient, and leading to the kind of an immune reaction that no one had seen in any cancer, an immune reaction in which the other 90 plus percent of the malignant cells, which had not been exposed to the light activated drug, disappeared.

We had no idea at that time how this had happened, but we knew a few things. And I knew it, especially as a cutaneous T-cell lymphoma physician confronted with the care of these patients, my own patients with this advanced disease. We had no other therapy available to us in medicine at the time that could do something like that, even though it had only happened in two out of the five patients. The other three patients had advancing disease despite what we did.

But we knew that we had done something that appeared to be, for some mechanistic reason, that medicine at the time, immunobiology of the time, could not explain, had induced in patients that were previously immunologically tolerant of their malignancy, allowing it to progress, we had somehow turned on a selective-- and the keyword is selective, we'll keep coming back to that-- immune reaction, it only knocked off the malignant cells, leaving the rest of the immune system intact.

Since immunology, and at that time, I was also at Columbia, I was the director of the immunobiology component of the Columbia Cancer Center, I knew and my colleagues knew that whatever the principle was that we had landed on, it was something that was not known. And that's how the entire quest that we'll talk about a bit occurred, because these are extremely exciting days. It turns out that we now know that principle, and it changes and opens the entire vista. That's where it came from.