Acceptance speech

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Carl H. June, awardee in the Biology and Biomedicine category (18th edition)

It is a profound honor to accept the 18th Frontiers of Knowledge Award in Biology and Biomedicine. To receive this recognition alongside my esteemed colleague and friend, Michel Sadelain, is a privilege that underscores a fundamental truth about scientific progress: breakthroughs are rarely solitary voyages. They are the result of shared vision, complementary discoveries, and decades of collective persistence.

I want to express my deepest gratitude to the BBVA Foundation and the international committee for recognizing the paradigm shift that cell and gene therapy represents. By honoring our work, you are shining a spotlight on a revolutionary frontier in medicine – one where we no longer rely solely on synthetic chemicals or radiation to fight disease, but instead harness the exquisite, natural power of life itself.

To understand the journey that brought us here, we must look at how medicine has traditionally viewed the human immune system. For generations, we understood our white blood cells – specifically T cells – as specialized soldiers designed exclusively to fight off external invaders: viruses, bacteria, and parasites. But when faced with cancer, this brilliant defense system is often blinded or hijacked. Cancer cells are clever; they arise from our own tissue, allowing them to hide in plain sight, evading the immune system's radar.

The question that drove our research decades ago was simple yet audacious: Could we use genetic engineering to give these cellular soldiers a new set of eyes?

The answer emerged in the form of what we now call CAR-T cell therapy. Through a meticulous process, we extract T cells from a patient's own blood. In the laboratory, we use genetic engineering to insert a synthetic blueprint – a chimeric antigen receptor, or CAR. This blueprint instructs the cells to build a precise radar system targeted directly at a specific protein found on cancer

cells. When these reprogrammed cells are infused back into the patient, they are no longer blind. They are a living, breathing medicine – highly trained, fiercely targeted, and capable of multiplying inside the body to seek out and destroy tumors while sparing healthy tissue.

When we began this work, the skepticism was immense. Many believed that introducing genetically modified cells into humans was too dangerous, or that the cells would not survive long enough to make a difference. But science moves forward on the shoulders of persistence.

I will never forget the turning point in 2010 when we treated our first patients – adults with advanced, late-stage leukemia who had exhausted every standard treatment. We hoped the cells would survive for a few weeks. To our absolute amazement, the therapy didn't just work; it far exceeded what we had seen in the laboratory. A single infusion led to complete remission. Those engineered CAR T cells persisted in the patients' bodies for over a decade, serving as vigilant sentinels. What was once a highly experimental concept had become medical history: the world's first truly "living drug."

Today, CAR-T cell therapies are approved worldwide, and more than 50,000 patients – including many children who had run out of options – have received these treatments. But as we celebrate these milestones, we must recognize that we are only at the beginning of the frontiers of knowledge. The next grand challenge is already underway: replicating this success in solid tumors, such as breast, lung, and pancreatic cancers, and extending this technology to tackle autoimmune diseases and infectious threats.

An endeavor of this magnitude requires a global village. I am profoundly grateful to the brilliant generation of students, postdocs, and technicians at the University of Pennsylvania, whose tireless hands and minds built this reality over the past 30 years. I want to thank my wife Lisa and my family, whose unconditional support has sustained me through the long, demanding hours of a research career.

Science is an international language, and our journey has been deeply enriched by global partnerships. I would be remiss if I did not mention the incredible spirit of collaboration we have shared with the scientific community right here in Spain. Brilliant researchers, such as Dr. Manel Juan at the Hospital Clínic de Barcelona, spent time in our Philadelphia lab to master these techniques, taking them back to establish pioneering academic CAR-T programs that have made these therapies more accessible throughout Spain and elsewhere in the world. This award belongs to that entire global ecosystem of translation.

Finally, thank you, BBVA Foundation, for celebrating the spirit of exploration. Together with Michel, I accept this award with the firm conviction that the boundaries of what is medically possible will continue to expand, bringing hope to patients and families across the globe.