

Dear Dr Kariko,

In the first months of 2020, few people in the world knew about messenger RNA vaccines. When the pandemic hit us, our level of preparedness was limited. Among the resources that were ready was the technology on which the first licensed vaccines against COVID19 were developed. The speed of development and the very high efficacy of mRNA vaccines astonished the world and suddenly provided immense hope that the control of the pandemic was within reach and that all the suffering it caused could come to an end.

Within the largest vaccination campaign in history, mRNA vaccines saved a huge number of lives and tremendously helped societies deal with the pandemic. The technology was more advanced than the capacity of the world to share it and important challenges remain to make mRNA vaccines available to low resource countries. Yet, by further highlighting global inequities in access to health care, mRNA vaccines are forcing us to face these inequities and to create mechanisms to decrease them.

The success of mRNA vaccines is also fueling massive research and investments in vaccines against other infectious diseases, cancer as well as other diseases involving the immune system. It is also opening fascinating opportunities to use mRNA in protein replacement therapies for many diseases. Several universities have opened RNA centers to advance therapeutic applications of RNA. At the origin of this revolution was your visionary, yet simple idea. As mRNA is the template that cells use to synthesize proteins, introducing synthetic mRNAs into a cell should allow us to induce the synthesis of any protein when and where it is needed. You then found that in vitro transcribed RNA was inflammatory, preventing its clinical use. You could have given up at that stage, but you pursued your research to understand why this RNA was inflammatory. This led you to discover, with your colleague Drew Weissman at the University of Pennsylvania, that modifying one of the components of the mRNA could make it non-inflammatory. This work was published in the journal *Immunity* in 2005. The revolution that this article was announcing took time to unfold and you met significant skepticism in the scientific community. In the following years, you developed processes to purify modified RNA and delivery systems to use them as therapeutics, in collaboration with biotech companies. It is all this work that made possible the rapid development of efficacious mRNA vaccines against COVID-19.

When the wise person is asked “When is the best time to plant a tree?”, the answer is “Twenty years ago”. “But then, when is the next best time?”, the answer is “Now”. Dr Kariko, the huge impact your work has had and will continue to have in medicine, is reminding us how essential it is to have a vision, to be courageous and to invest a time and efforts in research that may only deliver many years later. As we are harvesting the fruits of the tree you planted years ago, it is essential that we plant new trees to be better prepared for the challenges we will face in the future.

Dr Kariko, your achievements are amazing but you remain a humble person. When we first met, you did not want to talk about you. You preferred to talk about your daughter Susan. Of course, any parent would be proud of a daughter who has won two gold medals at the Olympic games with the US rowing team. But your wish was to praise a young woman for her achievements. Young adults and adolescents are usually considered for who they will

become and not for who they are and what they can accomplish, and they are often dismissed in many societies. Young people are often experts at planting trees and your words inspire us to give more space to the young generation and to allow them to prepare the challenges they will face with us, or alone. This young generation has all the reasons to be discouraged, to be hesitant about what they can accomplish and to doubt about the potential of their actions. Natsume Soseki wrote "The wind does not know which leave will fall first". Your life and your work are showing that even if we are unsure about how and when our actions will help, a vision and persistence can make an enormous difference. May this Doctor Honoris Causa be a humble contribution to the recognition of your work.