The potent power of basic research

As the world reels from the seemingly unrelenting scourge of the SARS-CoV-2 virus, one ray of hope stands out as likely to provide a shield against further infection. An array of vaccines is emerging from scientific research that is proving protective against several variants of the virus, inhibiting serious disease and death in those vaccinated. Despite the incredible promise of these vaccines, some hesitate to take them. They express in part a concern about the apparent rapidity with which these vaccines emerged from laboratories and appeared in vaccination clinics.

In fact, the roots of these vaccines stretch deep into the past. The successful development of these vaccines is a story of triumph through basic research by scientists the world over. Yet that basic research, at the time of its conception, might not have appeared to predict the death-defying impact that we see from today’s vaccines. Basic research has sometimes been criticized for a lack of immediate connection to practical results that benefit the funders of such research, often taxpayers of the countries in which the research is conducted. The question has been posed: Why should we fund scientists to perform experiments directed to results that at the time may seem to lack relevance to immediate societal issues? The answer is that the critical scientific advances of today that directly benefit the public are often enabled by basic research from years, even decades earlier.

The history of the development of the mRNA vaccines for the SARS-CoV-2 virus, the Pfizer-BioNTech vaccine and the Moderna vaccine, provides an interesting example. This story testifies powerfully to the critical role basic research plays in support of great scientific discoveries that advantage so many. A key component of these vaccines is the carrier that conveys the required mRNA from outside the body into the cells where it can be read and the peptides made from its coding. That carrier is a lipid nanoparticle, and it has a surprising history.

In the late 1970s, the field of lipid polymorphism emerged from a number of laboratories around the world. During the previous decade, biologists and biophysicists had only just reached consensus that the lipid bilayer remained at the center of our understanding of cell membrane structure, this non-bilayer morphology opened avenues of investigation on membrane structural dynamics.

One avenue led to an explosion of ideas on new macromolecular structures from lipids that might encapsulate molecules of biological interest. Another avenue led to a deeper understanding of membrane fusion, the process by which, for example, the influenza virus enters a cell to infect it. All of this was basic research. However, it was not clear at the time how such basic research would connect to a practical application with profound implications, namely, vaccines for a worldwide pandemic.

One of the fundamental challenges facing development of an mRNA vaccine was the packaging of the mRNA for delivery to cells. The structure to hold the mRNA must stabilize and protect the mRNA from degradation while circulating in the blood. The structure must also allow the particle to penetrate the cell plasma membrane to deliver the mRNA into cells where it can function by coding for peptide synthesis. The basic research on structures formed by lipids and their dynamics mentioned above provided the inspiration for scientists to imagine solutions to these two challenges. Knowledge of lipid polymorphism from basic research decades before the actual vaccine development enabled conception of the lipid nanoparticle that was effective at encapsulating the mRNA. Basic research also developed a fundamental understanding about lipid structural dynamics that would facilitate insertion of a lipid nanoparticle with the accompanying mRNA into the cell, providing a pathway to address the second challenge.

This example of vaccine development is only one of many examples in which basic research has led to advances that benefit the people of the countries that supported the work. Often, those benefits are not limited by demographic boundaries but eventually affect the entire world’s population. To ensure similar benefits extending into the future of humankind, basic research is critical infrastructure.

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