CORONAVIRUS

Medicine in the time of corona: Fundamental molecular research is “essential”

A pandemic—especially one caused by a mysterious or newly discovered infectious agent—engenders a stark reminder that supporting fundamental research has been a prudent investment of public funds. Fundamental molecular research plays an essential role in the clinic to decipher infectious processes, develop therapeutic strategies, and guide physicians, nurses, and other hospital employees in implementing the most effective application of new knowledge. As the world begins the process of healing from the medical, social, and economic effects of coronavirus disease 2019 (COVID-19), public health is at the forefront of decision-making by lawmakers at both the federal and state levels. Daily news conferences and press releases illustrate the importance of scientists and physicians as major partners in pandemic task forces, guiding politicians in health policy decision-making. Basic molecular research plays a crucial role in helping the world overcome the current pandemic and prepare for the next one.

The first application of fundamental molecular research to COVID-19 was rapid sequencing of the SARS-CoV-2 RNA genome using a process known as next-generation sequencing (NGS). These data immediately delivered the scientific and clinical communities with insight into the singular properties of this coronavirus strain. NGS can provide billions of DNA reads in a single day, a process that was unfathomable only 15 years ago. Now an essential and nearly ubiquitous technology, NGS evolved through the research of biochemists, molecular biologists, and engineers who were supported by grants from publicly funded institutions such as the National Institutes of Health (NIH), National Cancer Institute (NCI), and their counterparts across the U.S. by grants from publicly funded institutions such as the National Institutes of Health (NIH), National Cancer Institute (NCI), and their counterparts across the globe. The second major application of fundamental molecular research to COVID-19 was the development of an assay to identify infected individuals. The method of choice for high-sensitivity detection of the virus in people is reverse transcription followed by polymerase chain reaction (RT-PCR), which takes advantage of the viral genome sequence provided by NGS. A key component of this assay is the reverse transcriptase RNA-dependent DNA polymerase, which converts the viral RNA genome into a DNA molecule that can be amplified and detected. This enzyme was a Nobel prize-winning discovery by NIH/NCI-supported researchers Howard Temin and David Baltimore. Although the PCR amplification methods and instruments were finalized in the private sector, much of the enzymology and nucleic acid chemistry that spurred PCR development was based on publicly funded fundamental molecular research.

Developing COVID-19 therapeutics requires an in-depth understanding of molecular processes involved in the viral life cycle. Antiviral therapies are needed to treat patients with mild to moderate symptoms. Additional therapies are needed for COVID-19 patients who suffer cytokine storm, which progresses to critical stages of respiratory failure, septic shock, and multiorgan dysfunction. Given that COVID-19 is within the family of RNA viruses, researchers are well positioned to begin development of antiviral therapies, as biochemists already have generated a plethora of molecular information about the atomic structures for the main enzyme required for viral replication, the RNA-dependent RNA polymerase, an enzyme which has no known host counterpart. In this case, biochemists and transcription biologists have already identified Remdesivir, an adenosine nucleotide analog that interferes with the action of viral RNA-dependent RNA polymerase activity. Clinical trials of the drug are currently underway, and early results are encouraging. As for the treatment of cytokine storm, again, basic biochemical research in immunology has paved the way for the development of several therapies, including interleukin-6 (IL-6) inhibitors that function by blocking the IL-6 receptor and ameliorate unwanted damage to tissues and organs caused by cytokine release as the result of viral infection.

The ultimate aim for the treatment of all viral infections, including COVID-19, is the development of host and herd immunity, which can be accomplished either through host infection or vaccination. To manage potential pandemics with the least number of casualties, researchers must develop vaccines that can be mass produced on a scale of hundreds of millions of doses within in a few months after a virus appears and that can be rapidly distributed across the globe. Traditional vaccines use either active or weakened virus or destroyed forms of viral particles as the immune response–generating agent. The use of attenuated and destroyed viral particles...
as vaccines is highly effective, but the manufacturing process is arduous and time-consuming. Recombinant RNA and DNA vaccines circumvent these shortcomings of traditional vaccine generation and are in clinical trial for COVID-19. In this case, humankind owes biochemists Paul Berg, Walter Gilbert, Frederick Sanger, and their colleagues a debt of gratitude for their Nobel prize winning fundamental research in developing recombinant DNA technologies. This work resulted from decades-long funding by U.S. and U.K. governmental agencies and, today, allows the design of recombinant RNA and DNA vaccines and many other life-saving medicines that take advantage of this revolutionary technology.

Once the dust from the COVID-19 pandemic settles and the U.S. Congress is back in session, I hope that lawmakers will recognize our society’s dependence on thorough, methodical, mechanistic science and the medicines it provides and ask themselves how many more people might have perished from COVID-19 without the modern methods that arose from the basic molecular research described above. This catastrophe should be a reminder that a healthy investment in all institutes of the NIH and NCI and other federal science agencies will be life-saving when future pandemics arise.

– Ali Shilatifard

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Ali Shilatifard

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