Exploring new research to combat disease-causing viruses

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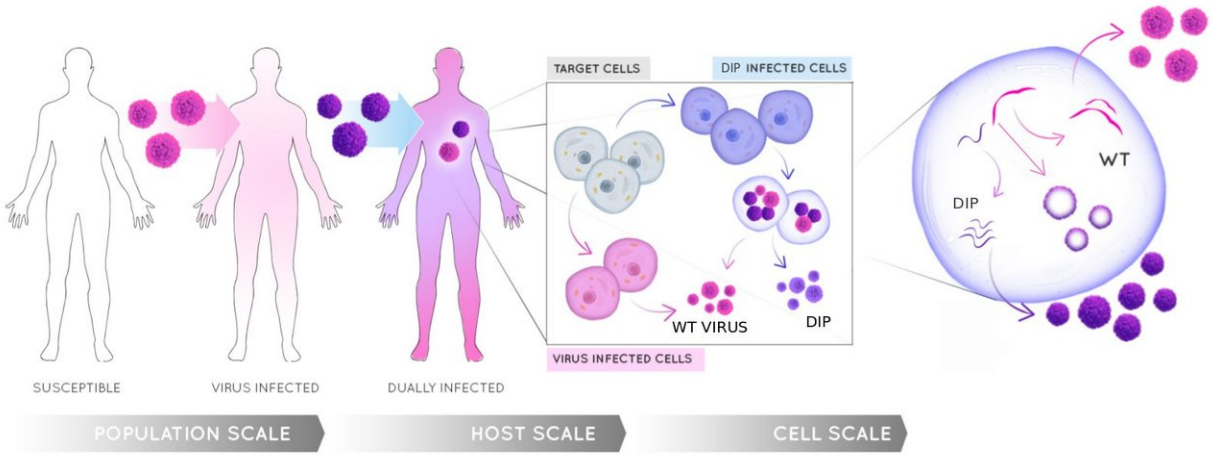

Mathematical and computational modeling of virus and defective particles competition at single cell, tissue, organ and host level will allow inference of antiviral design principles. These principles are then used to engineer the defective particle in the lab. Credit: IBM

According to the US Center for Disease Control, the number of worldwide cases of poliomyelitis has decreased from 350,000 in 1988 to 407 in 2013. While the decline has been steady, polio has still not been eradicated. To try and help solve the problem, biologists and mathematicians from IBM, UCSF, Stanford University, and the University of Haifa are working side-by-side on a DARPA-funded research project to engineer a new type of antiviral agent against viruses

such as polio.

I recently joined IBM Research from Inria, the French National Institute for computer science and applied mathematics, where I was studying the durability of plant resistance to viruses. My transition to study human pathogens has been fascinating as I have been able to create a common language for our team to help bridge the gap between biology, math and informatics.

Our research team will focus on establishing design principles to engineer potential antiviral agents relying on Defective Interfering Particles (DIPs). They are defective versions of viruses, lacking essential elements to complete their life cycle. When co-occurring with their parent, disease-causing viruses, DIPs act as parasites by stealing the very essential elements they lack. This interference hinders the parent virus and enables the antiviral agents to replicate and spread, until the virus is completely gone and no more of the essential elements the agents lack remain available. After displacing the virus, the antiviral agents will die out because of their inability to survive alone. Defective versions of viruses naturally occur because of errors during viral replication; they have been observed, for example, in influenza A, dengue, and Ebola and are, in some cases, maintained in virus populations. Our team of researchers aims to produce models, which could potentially aid medical researchers to engineer DIPs that lack specific elements and are optimized for specific features, so they might be used as an efficient therapy. For this task, IBM researchers will use massive computational power and contribute their recognized expertise in mathematical modeling of diseases to help renowned world-class experimental and theoretical biologists at UCSF, Stanford University, and the University of Haifa.

Unlike existing drugs that stop viral replication by blocking known viral or cellular processes, DIPs can compete and co-evolve along with

viruses. Like DIPs, vaccines also use a defective version of viruses, but as a preventive treatment building immune memory rather than a curative treatment based on competition and co-evolution. One interesting area for future exploration is whether the transmission mechanisms of DIPs between individuals might allow for new methodologies of health care delivery.

The research collaboration will focus on poliovirus, the virus responsible for poliomyelitis, a highly infectious disease that mainly affects children, and 1 in 200 infections leads to irreversible paralysis. In 1988, the Forty-first World Health Assembly adopted a resolution for the worldwide eradication of polio. It marked the launch of the Global Polio Eradication Initiative (GPEI). Wild poliovirus cases have decreased from an estimated 350,000 cases in more than 125 endemic countries then, to 22 reported cases in 2017. Endemic transmission is continuing in Afghanistan, Nigeria and Pakistan1.

An ongoing problem preventing full eradication of the disease is the occurrence of vaccine-derived poliovirus, a new instance of the disease caused when the vaccine strain mixes with other closely related viral species. It represents a serious threat to public health. Unfortunately, vaccine-derived poliovirus types have emerged in several places, mainly Democratic Republic of Congo, Nigeria, Syrian Arab Republic, and Pakistan.

The project proposed by IBM researchers and our collaborators could point the way forward for exploring new methods to help accelerate disease eradication in the face of vaccine-derived poliovirus. The defective and parasitic nature of DIPs may someday be used to reduce and even completely suppress the occurrence of the vaccine-derived disease types, while also helping to prevent the virus from spreading just as effectively as with traditional vaccines.

Our goal is to help extend this idea to other viral species to develop a general strategy, which might be used by public health actors for eradication of all viral diseases.

More information: Kia Guarino et al. Violence, insecurity, and the risk of polio: A systematic analysis, *PLOS ONE* (2017). DOI: 10.1371/journal.pone.0185577

Margarita Pons-Salort et al. Preventing Vaccine-Derived Poliovirus Emergence during the Polio Endgame, *PLOS Pathogens* (2016). DOI: 10.1371/journal.ppat.1005728

Our Progress Against Polio. www.cdc.gov/polio/progress/index.htm

Provided by IBM