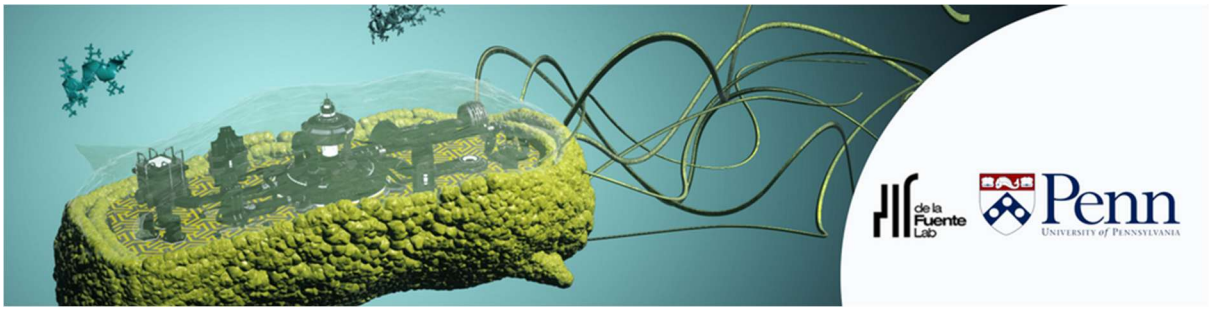

AI Breakthrough Identifies Potent Antivirals with Minimal Data

Philadelphia, PA – April 29, 2025 – In a development that could accelerate the search for new viral treatments, scientists at the University of Pennsylvania have devised an artificial intelligence–based approach capable of identifying promising antiviral compounds from only a few dozen initial candidates.

Their study, "Antiviral discovery using sparse datasets by integrating experiments, molecular simulations, and machine learning," published in the Cell Press journal *Cell Reports Physical Science*, centers on human enterovirus 71, known to cause hand, foot, and mouth disease and sometimes linked to severe neurological complications. By training machine learning models on a set of just 36 compounds, the researchers achieved notable predictive accuracy and experimentally confirmed five potential virucidal agents out of eight shortlisted compounds.

"The recent pandemic underscored the critical need to expedite drug discovery," said Dr. Cesaro, one of the study's co-authors. "Our AI-driven method shows that, even with limited data, machine learning can effectively identify virucidal compounds, accelerating the development of effective solutions and ensuring a swift response to future outbreaks."

"What is exciting about this work is how it merges AI with rigorous experimentation," said Professor Cesar de la Fuente, an expert in AI, antibiotics, and infectious diseases, and the study's corresponding author. "By uniting molecular simulations, machine learning, and targeted lab validation, we are shortening discovery timelines and opening up a new era of data-driven medicine."

"Our molecular dynamics simulations provide crucial insights into how antiviral compounds interact with the EV71 capsid at the atomic level," said Dr. Haoyuan Shi, Cornell '24 Ph.D. "Different compounds exhibit distinct destabilization mechanisms—while urea and NaOH disrupt protein-protein interactions, glutaraldehyde and paraformaldehyde promote cross-linking. Our simulation results, alongside experimental validation and potential machine learning integration, pave the way for more effective antiviral strategies."

While many laboratories rely on large and expensive datasets, the Penn scientists—collaborating with Procter & Gamble and Cornell University—combined molecular dynamics simulations, statistical modeling and laboratory validation to achieve their results. "Through a large-scale unsupervised learning, we were able to derive a rich compound representation that enabled us to model the complex relationship between the representation and virucidal effect even under a scenario with very limited virucidal data," explained Dr. Wan, another key contributor to the project.

By demonstrating that a small yet carefully curated dataset can guide scientists toward viable antiviral options, the research offers a compelling alternative to more resource-intensive methods. The findings, the authors note, could lay the groundwork for tackling other viral threats, particularly when time and resources are in short supply.

Please note that this paper is currently under embargo and will be officially released online at April 29th at 11 AM ET (US).

About Dr. César de la Fuente

César de la Fuente is a Presidential Associate Professor at the University of Pennsylvania, where he leads the Machine Biology Group. He completed postdoctoral research at the Massachusetts Institute of Technology (MIT) and earned a PhD from the University of British Columbia (UBC). His research goal is to use the power of machines to accelerate discoveries in biology and medicine. Notably, he pioneered the development of the first computer-designed antibiotic with efficacy in animal models, demonstrating the application of AI for antibiotic discovery and helping launch this emerging field. His lab is at the forefront of developing computational methods to mine the world's biological information digitally, leading to the identification of over a million new antimicrobial compounds. It is estimated that the work of de la Fuente and his collaborators has multiplied the speed of antibiotic discovery by a factor of several million, saving many years of human research and reducing what once took decades of collective work to just hours. De la Fuente has received over 80 national and international awards, including being elected as a Fellow of the American Institute for Medical and Biological Engineering (AIMBE), becoming one of the youngest ever to be inducted. He has published over 170 peer-reviewed papers in top-tier journals such as Cell, Science, Cell Host Microbe, Nature Biomedical Engineering, and PNAS.

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