AI finds drugs that could fight aging and age-related diseases

July 7 2023, by Vanessa Smer-Barreto

Credit: AI-generated image (disclaimer)

Finding new drugs—called "drug discovery"—is an expensive and time-consuming task. But a type of artificial intelligence called machine learning can massively accelerate the process and do the job for a fraction of the price.

My colleagues and I recently used this technology to find three promising candidates for senolytic drugs—drugs that slow aging and prevent age-related diseases. Our research is published in the journal *Nature Communications*.

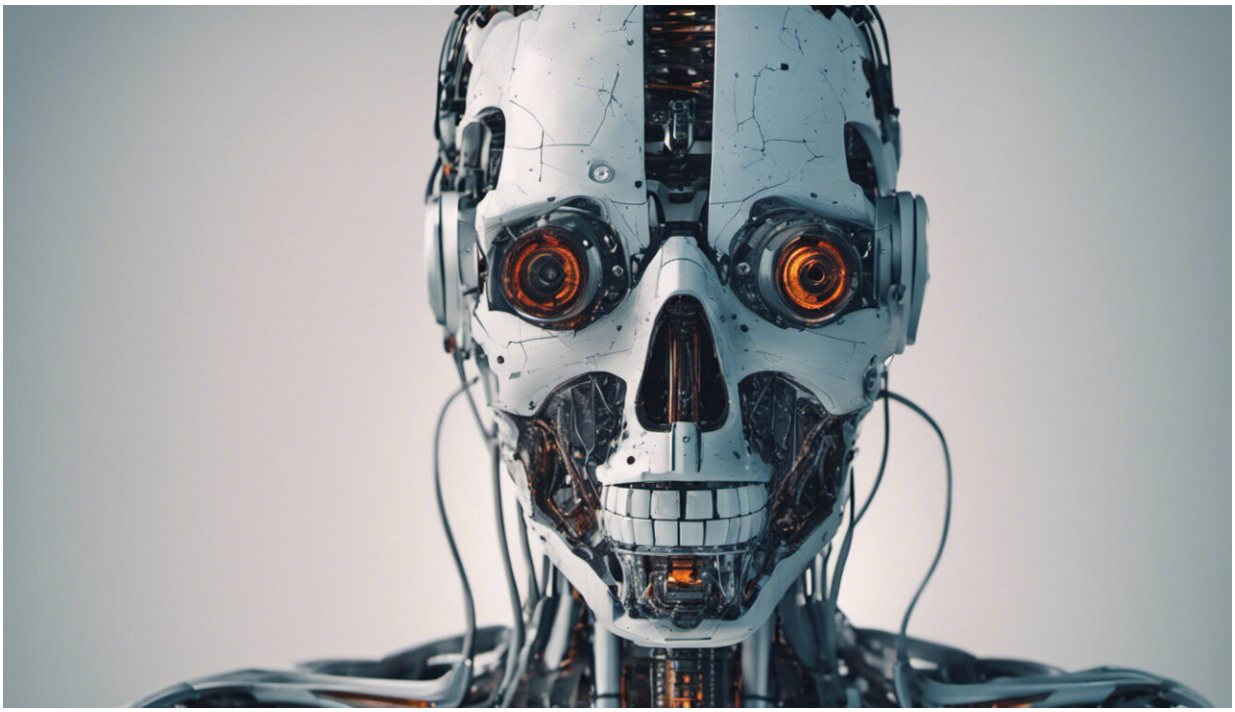
Senolytics work by killing senescent cells. These are cells that are "alive" (metabolically active), but which can no longer replicate, hence their nickname: zombie cells.

The inability to replicate is not necessarily a bad thing. These cells have suffered damage to their DNA—for example, skin cells damaged by the sun's rays—so stopping replication stops the damage from spreading.

But senescent cells aren't always a good thing. They secrete a cocktail of inflammatory proteins that can spread to neighboring cells. Over a lifetime, our cells suffer a barrage of assaults, from UV rays to exposure to chemicals, and so these cells accumulate. Elevated numbers of senescent cells have been implicated in a range of diseases, including type 2 diabetes, COVID, pulmonary fibrosis, osteoarthritis and cancer.

Studies in lab mice have shown that eliminating senescent cells, using senolytics, can ameliorate these diseases. These drugs can kill off zombie cells while keeping healthy cells alive.

Around 80 senolytics are known, but only two have been tested in humans: a combination of dasatinib and quercetin. It would be great to find more senolytics that can be used in a variety of diseases, but it takes ten to 20 years and billions of dollars for a drug to make it to the market.



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Results in five minutes

My colleagues and I—including researchers from the University of Edinburgh and the Spanish National Research Council IBBTEC-CSIC in Santander, Spain—wanted to know if we could train machine learning models to identify new senolytic drug candidates.

To do this, we fed AI models with examples of known senolytics and non-senolytics. The models learned to distinguish between the two, and could be used to predict whether molecules they had never seen before could also be senolytics.

When solving a machine learning problem, we usually test the data on a range of different models first as some of them tend to perform better

than others. To determine the best-performing model, at the beginning of the process, we separate a small section of the available training data and keep it hidden from the model until after the training process is completed. We then use this testing data to quantify how many errors the model is making. The one that makes the fewest errors, wins.

We determined our best model and set it to make predictions. We gave it 4,340 molecules and five minutes later it delivered a list of results.

The AI model identified 21 top-scoring molecules that it deemed to have a high likelihood of being senolytics. If we had tested the original 4,340 molecules in the lab, it would have taken at least a few weeks of intensive work and £50,000 just to buy the compounds, not counting the cost of the experimental machinery and setup.

We then tested these drug candidates on two types of cells: healthy and senescent. The results showed that out of the 21 compounds, three (periplocin, oleandrin and ginkgetin) were able to eliminate senescent cells, while keeping most of the normal cells alive. These new senolytics then underwent further testing to learn more about how they work in the body.

More detailed biological experiments showed that, out of the three drugs, oleandrin was more effective than the best-performing known senolytic drug of its kind.

The potential repercussions of this interdisciplinary approach—involving data scientists, chemists and biologists—are huge. Given enough high-quality data, AI models can accelerate the amazing work that chemists and biologists do to find treatments and cures for diseases—especially those of unmet need.

Having validated them in senescent cells, we are now testing the three

candidate senolytics in human lung tissue. We hope to report our next results in two years' time.

More information: Vanessa Smer-Barreto et al, Discovery of senolytics using machine learning, *Nature Communications* (2023). DOI: 10.1038/s41467-023-39120-1

Provided by The Conversation