

# Converting recycled plastics into disease-fighting nanofibers


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IBM Research


# Ninjas vs Superbugs

ADVENTURES IN NANOMEDICINE



**When Alexander Fleming discovered penicillin in 1928, antibiotic seeds were sown in wonderland. But as early as 1947 – just four years after the use of penicillin became common – we began to see bacteria developing a resistance to antibiotics.**

## Rise of the Superbug



As a result of our increased use of antibiotics over the years, strains of bacteria that are naturally drug-resistant and drug-resistant strains have emerged. Today, we still have antibiotics to treat these infections, but they are becoming less effective and are being used in more and more people who are no longer healthy.

Superbugs, including CRE bacteria, Clostridium difficile and MRSA, are one of the biggest health concerns of the 21st century. At least two million Americans are affected by antibiotic-resistant bacteria every year, and 23,000 die.


## MRSA: A Superbug Supervillain


**Methicillin-resistant Staphylococcus aureus**

They're MRSA, a persistent superbug that is a threat because it's always lurking. From mild skin infections to serious infections in the blood, lungs and other parts of the body.

MRSA lives in hospitals, homes, on gym mats, almost everywhere. It's found everywhere it's spreading. Once the bacteria takes hold, MRSA can spread to almost any part of the body at least once in 10 years.

MRSA is always resistant to every antibiotic, including penicillin, ampicillin, nafcillin and methicillin. It causes most infections in the U.S. each year that are antibiotic-resistant. A new genetic mutation and R-factor combined.





## Introducing the Ninja Polymer: MRSA's Worst Enemy

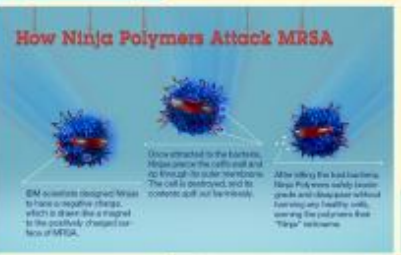
47-77 nm

With the threat of superbugs rising, IBM is developing a better way to fight them – The Ninja Polymer. Made in the lab, this type of individual polymer targets and kills bacteria in an entirely different way than antibiotics.

Unlike our current antibiotics, Ninja attack MRSA, a deadly member of the family. This makes it much harder for MRSA to develop a resistance.

Ninja Polymers are non-toxic and biodegradable. Which means they can be safely absorbed from the body without causing harmful side effects.


## How Ninja Polymers Attack MRSA




IBM scientists designed Ninja to have a negative charge, which is different than a target to the positively charged surface of MRSA.

Once attracted to the bacteria, Ninja penetrate the cell wall and slip through the outer membrane. The cell is destroyed, and its contents spill out harmlessly.

After killing the bad bacteria, Ninja Pink were easily broken down and disappeared without leaving any harmful cells, leaving the polymers that "Ninja" welcome.





## From Semiconductors to Superbug Killers


How exactly did a technology company like IBM end up in nanomedicine?

While exploring new ways to solve silicon-related issues in semiconductors, IBM researchers identified a new kind of polymer that produced an electrostatic charge when charged together.

IBM researchers realized if they could introduce materials at the atomic level to control their behavior and the electrostatic charge in a solid or liquid, they could translate those results to nanomedicine.

IBM researchers were both when IBM researchers put their skills to work on a new kind of drug delivery system. They used their knowledge of semiconductors to create a new kind of drug delivery system. They used their knowledge of semiconductors to create a new kind of drug delivery system.

## The Future of Ninja Polymers




In the future, Ninja could be added to hospital products like mattresses or bed covers – a safer solution for the "bedside" superbug currently in these products.

Ninja Polymers are still in the lab, but IBM's goal is to see them in drug delivery systems to fight our way through and other superbugs, but also get on with the rest of the world.

The Ninja Polymers could also be used in new drug delivery systems, special coatings for prosthetic joints. One day, hospital equipment – from catheters to cardiac monitoring tubes – could be coated with antibacterial polymers.

## Watch Ninjas vs Superbugs to learn more about IBM's new way of fighting MRSA at [ibm.com/ninjas](http://ibm.com/ninjas).



Researchers from IBM and the Institute of Bioengineering and Nanotechnology have made a nanomedicine breakthrough in which they converted common plastic materials like polyethylene terephthalate (PET) into non-toxic and biocompatible materials designed to specifically target and attack fungal infections. This research was published today in the peer-reviewed journal, *Nature Communications*.

Over a billion people are affected by fungal infections every year, ranging in severity from topical skin conditions like athlete's foot to life-threatening fungal blood infections. The infection is more likely to occur when the body's immune system is compromised due to an illness like HIV/AIDS, cancer or when receiving antibiotic treatment.

There is a pressing need to develop efficient and disease-specific antifungal agents to mitigate this growing drug resistance problem. Traditional antifungal therapeutics need to get inside the cell to attack the infection but have trouble targeting and penetrating the fungi membrane wall. Also, since fungi are metabolically similar to mammalian cells, existing drugs can have trouble differentiating between healthy and infected cells.

Recognizing this, IBM scientists applied an organic catalytic process to facilitate the transformation of PET, or waste plastic from a bottle, into entirely new molecules that can be transformed into antifungal agents. This is significant as plastic bottles are typically recycled by mechanical grinding and can mostly be reused only in secondary products like clothes, carpeting or playground equipment.

## How it Works

These new antifungal agents self-assemble through a hydrogen-bonding process, sticking to each other like molecular Velcro in a polymer-like fashion to form nanofibers. This is important because these antifungal agents are only active as a therapeutic in the fiber or polymer-like form.

This novel nanofiber carries a positive charge and can selectively target and attach to only the negatively-charged fungal membranes based on electrostatic interaction. It then breaks through and destroys the fungal cell membrane walls, preventing it from developing resistance.

According to Dr Yi Yan Yang, Group Leader, IBN, "The ability of these molecules to self-assemble into nanofibers is important because unlike discrete molecules, fibers increase the local concentration of cationic charges and compound mass. This facilitates the targeting of the fungal membrane and its subsequent lysis, enabling the fungi to be destroyed at low concentrations."

Leveraging IBM Research's computational capabilities, the researchers simulated the antifungal assemblies, predicting which structural modifications would create the desired therapeutic efficacy.

"As computational predictive methodologies continue to advance, we can begin to establish ground rules for self assembly to design complex therapeutics to fight infections as well as the effective encapsulation, transport and delivery of a wide variety of cargos to their targeted diseased sites," said Dr. James Hedrick, Advanced Organic Materials Scientist, IBM Research – Almaden.

The minimum inhibitory concentration (MIC) of the nanofibers, which is the lowest concentration that inhibits the visible growth of fungi, demonstrated strong antifungal activity against multiple types of fungal

infections. In further studies conducted by Singapore's IBN, testing showed the nanofibers eradicated more than 99.9% of *C. albicans*, a [fungal infection](#) causing the third most common blood stream infection in the United States, after a single hour of incubation and indicated no resistance after 11 treatments. Conventional antifungal drugs were only able to suppress additional fungal growth while the infection exhibited [drug resistance](#) after six treatments

Additional findings of this research indicated the nanofibers effectively dispersed fungal biofilms after one-time treatment while conventional [antifungal drugs](#) were not effective against biofilms.

The in vivo antifungal activity of the nanofibers was also evaluated in a mouse model using a contact lens-associated *C. albicans* biofilm infection. The nanofibers significantly decreased the number of fungi, hindered new fungal structure growth in the cornea and reduced the severity of existing eye inflammation. These experiments also showed mammalian cells survived long after incubation with the nanofibers, indicating excellent in vitro biocompatibility. In addition, no significant tissue erosion is observed in the mouse cornea after topical application of the nanofibers.

"A key focus of IBN's nanomedicine research efforts is the development of novel polymers and materials for more effective treatment and prevention of various diseases," said Professor Jackie Y. Ying, IBN Executive Director. "Our latest breakthrough with IBM allows us to specifically target and eradicate drug-resistant and drug-sensitive fungi strains and fungal biofilms, without harming surrounding healthy cells."

**More information:** K. Fukushima, S. Liu, H. Wu, A. C. Engler, D. J. Coady, H. Maune, J. Pitera, A. Nelson, N. Wiradharma, S. Venkataraman, Y. Huang, W. Fan, J. Y. Ying, Y. Y. Yang and J. L. Hedrick, "Supramolecular High Aspect Ratio Assemblies with Strong

Antifungal Activity," *Nature Communications*, (2013) DOI:  
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