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Insight: Micro-robots show promising results in mice – could this be the future of medical treatment in humans?

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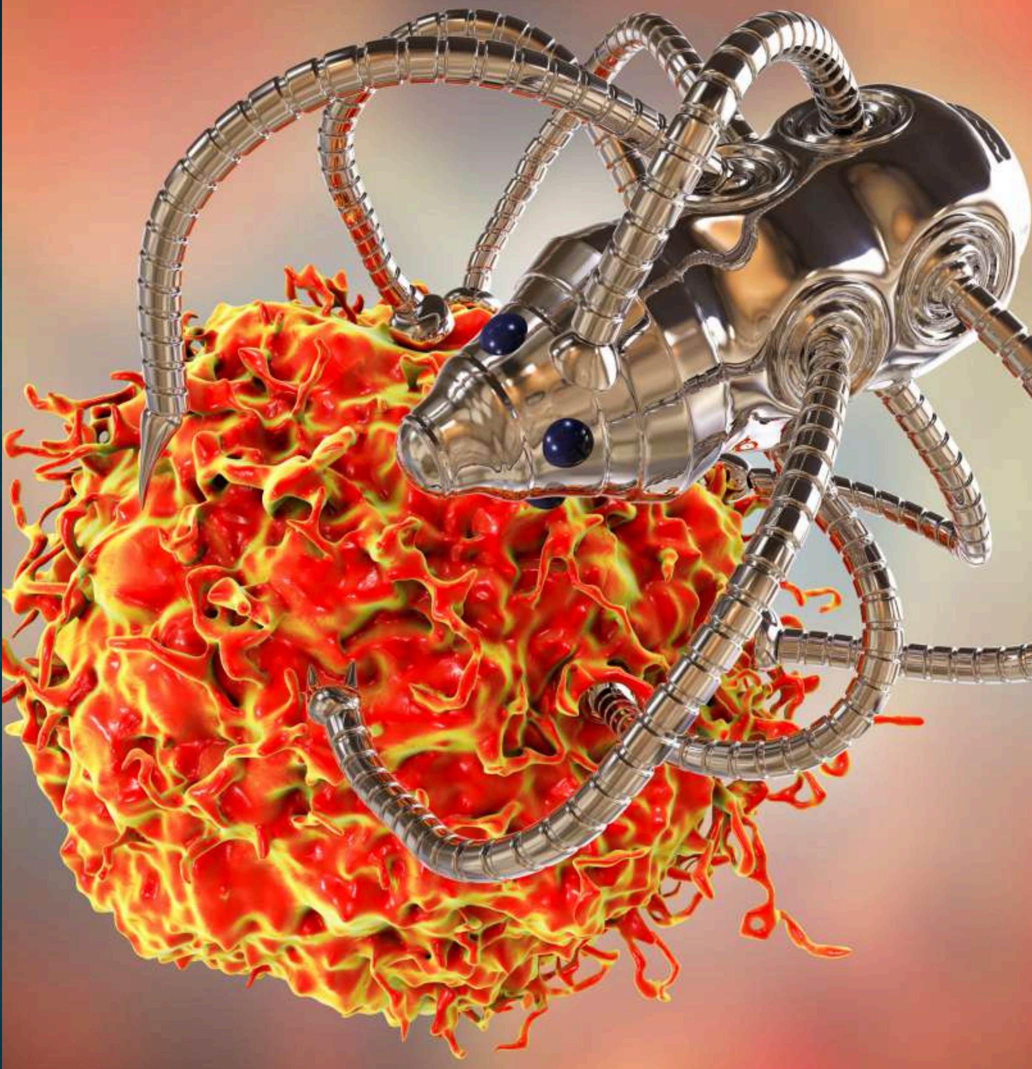

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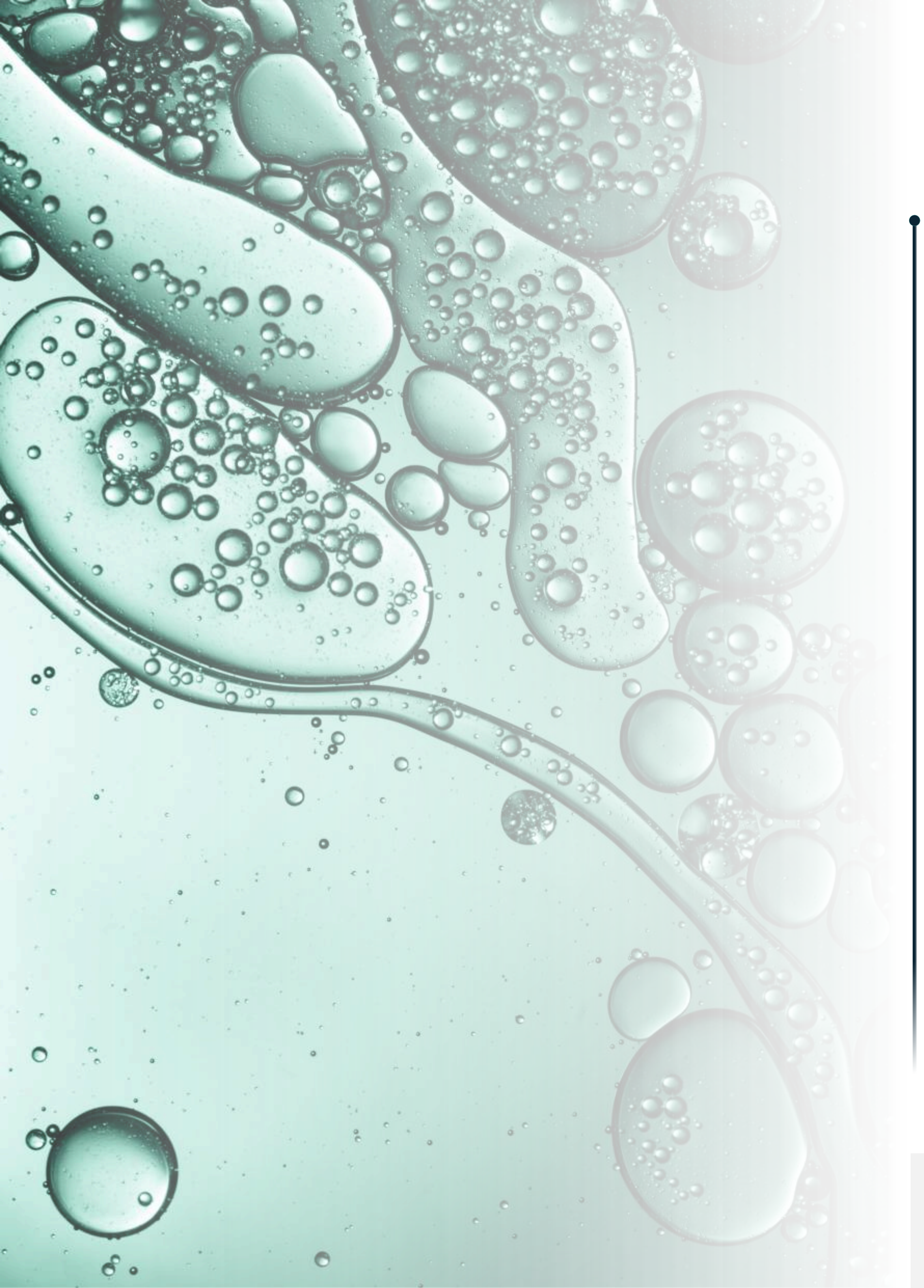

Introduction

Nanoengineers at the University of California San Diego have developed microscopic robots, called microrobots, that can swim around in the lungs, deliver medication, and be used to clear up life-threatening cases of bacterial pneumonia. In mice, the microrobots safely eliminated pneumonia-causing bacteria in the lungs and resulted in 100% survival. While within three days of infection, all untreated mice died.[1]

Although not a new phenomenon, this article looks at the University of California San Diego study results, the evolution of micro and nanorobots, and what it means for future research in the life sciences industry.

The field of micro-robotics covers the robotic manipulation of objects[2] with dimensions in the millimeter to micron range as well as the design and fabrication of autonomous robotic agents that fall within this size range. Nanorobotics is defined in the same way only for dimensions smaller than a micron.

[1] University of California San Diego. (September 2022). *Tiny swimming robots treat deadly pneumonia in mice. University of California San Diego.* URL: https://jacobsschool.ucsd.edu/news/release/3508

[2] Nelson, B.J., Dong, L., Arai, F. (2008). *Micro/Nanorobots. In: Siciliano, B., Khatib, O. (eds) Springer Handbook of Robotics. Springer, Berlin, Heidelberg.* URL: https://doi.org/10.1007/978-3-540-30301-5_19

How do they work?

The microrobots are made of algae cells whose surfaces are speckled with antibiotic-filled nanoparticles. The algae provide movement, which allows the microrobots to swim around and deliver antibiotics directly to more bacteria in the lungs. The nanoparticles containing the antibiotics are made of tiny biodegradable polymer spheres coated with the cell membranes of neutrophils, a type of white blood cell.

What's special about these cell membranes is that they absorb and neutralize inflammatory molecules produced by bacteria and the body's immune system. This gives the microrobots the ability to reduce harmful inflammation, which in turn makes them more effective at fighting a lung infection.[3]

[3] Levin, D., (2022) Q&A - Roboticist Bradley Nelson: *Making microbots smart, knowablemagazine.org*. URL: https://knowablemagazine.org/article/technology/2022/making-microbots-smart

Treatment with microrobots was also more effective than an IV injection of antibiotics into the bloodstream.

The study results

The work is a joint effort between the labs of nanoengineering professors Joseph Wang and Liangfang Zhang, both at the UC San Diego Jacobs School of Engineering. Wang is a world leader in the field of micro- and nanorobotics research, while Zhang is a world leader in developing cell-mimicking nanoparticles for treating infections and diseases. Together, they have pioneered the development of tiny drug-delivering robots that can be safely used in live animals to treat bacterial infections in the stomach and blood. Treating bacterial lung infections is the latest in their line of work.

The team used the micro robots to treat mice with an acute and potentially fatal form of pneumonia caused by the bacteria Pseudomonas aeruginosa. This form of pneumonia commonly affects patients who receive mechanical ventilation in the intensive care unit. The researchers administered the microrobots to the lungs of the mice through a tube inserted in the windpipe. The infections fully cleared up after one week. All mice treated with the microrobots survived the past 30 days, while untreated mice died within three days.[4]

Treatment with microrobots was also more effective than an IV injection of antibiotics into the bloodstream. The latter required a dose of antibiotics that was 3000 times higher than that used in the microrobots to achieve the same effect. For comparison, a dose of microrobots provided 500 nanograms of antibiotics per mouse, while an IV injection provided 1.644 milligrams of antibiotics per mouse.[5]

The team's approach is so effective because it puts the medication right where it needs to go rather than diffusing it through the rest of the body.

[4] Nield, D., (2022) *Tiny Robots Have Successfully Cleared Pneumonia From The Lungs of Mice. Sciencealert.com.* URL: https://www.sciencealert.com/tiny-robots-have-successfully-cleared-pneumonia-from-the-lungs-of-mice

[5] Baker, H., (2022). *Army of swimming microbots eradicate deadly pneumonia infection from mice lungs. LiveScience.com.* URL: https://www.livescience.com/microbot-army-cures-pneumonia-in-mice

The evolution of microrobots and what this means for future research

The concept of micro and nano robots is not exactly new considering nanopharmaceuticals has been around for nearly 30 years. However, researchers have designed and built a multitude of micro- and nanoscale systems for diagnostic and therapeutic applications, especially in the context of cancer, that could be considered early prototypes of nanorobots[6].

Since 1995, more than 50 nanopharmaceuticals, basically some sort of nanoscale device incorporating a drug, have been approved by the US Food and Drug Administration. If a drug of this class possesses one or more robotic characteristics, such as sensing, onboard computation, navigation, or a way to power itself, scientists may call it a nanorobot.

It could be a nano vehicle that carries a drug, navigates to or preferentially aggregates at a tumor site, and opens up to release a drug only upon a certain trigger[7]. Scientists can manipulate the shape, size, and composition of nanoparticles to improve tumor targeting, and newer systems employ strategies that specifically recognise cancer cells. Still, precise navigation to tumor sites remains a holy grail of nanorobot research and development[8].

A 2016 meta-analysis assessing the efficiency of nano-delivery vehicles tested in animal studies in the previous 10 years revealed that a median of fewer than 1 percent of the injected nano vehicles reached the tumour site, and that this could be only marginally improved with active targeting mechanisms, such as surface decoration with specific antibodies or peptides for tumor-specific receptor binding[9].

Therefore, making this recent study at the University of California is significant as although it was not a cancer trial, it has shown positive results by administering treatment straight to the source which could lead to future studies on how this could work for other forms of treatment[10].

[6] Schuerle, S., Danino, T., (2020). *Bacteria as Living Microrobots to Fight Cancer. The Scientist.* URL: https://www.the-scientist.com/features/bacteria-as-living-microrobots-to-fight-cancer-67305

[7] Cappelleri, D., Bi, C., Noguera, M., (2019) *Tumbling Microrobots for Future Medicine. American Scientist.* URL: https://www.americanscientist.org/article/tumbling-microrobots-for-future-medicine

[8] Schmidt, C.K., Medina-Sánchez, M., Edmondson, R.J. et al. *Engineering microrobots for targeted cancer therapies from a medical perspective. Nat Commun 11, 5618 (2020).* URL: https://doi.org/10.1038/s41467-020-19322-7

[9] Nelson, B. J., Kaliakatsos, I. K., & Abbott, J. J. (2010). *Microrobots for minimally invasive medicine. Annual review of biomedical engineering, 12, 55–85.* URL: https://doi.org/10.1038/s41467-020-19322-7

[10] Cappelleri, D., Bi, C., Noguera, M., (2019) *Tumbling Microrobots for Future Medicine. American Scientist.* URL: https://www.americanscientist.org/article/tumbling-microrobots-for-future-medicine

Conclusion

MICROROBOTS AND BACTERIA

To overcome these difficulties, scientists have found that bacteria could be a solution by ensuring that micro and nanorobots have better target accuracy. This would work by microscopic organisms swimming autonomously through fluids, driven by molecular motors that spin their cilia or flagella in a corkscrew-like fashion, a very effective propulsion mechanism at this scale that has inspired much nanorobotics that try to mimic this functionality.

Researchers have fabricated helical, magnetic swimmers that can be spun forward by a rotating magnetic field, for example. But bacteria, especially in treating cancer, are more than just role models for efficient swimming; some are actually therapeutic. In addition, microbes can sense biochemical cues and adjust their trajectories accordingly, similar to the envisioned onboard computation.

THE FUTURE OF MICRO AND NANO ROBOTS

Micro and nanorobots have the potential to revolutionise many aspects of medicine. These untethered, wirelessly controlled, and powered devices will make existing therapeutic and diagnostic procedures less invasive and enable new procedures. We look forward to seeing further developments on how these devices will advance in the future.

[11] Nelson, B. J., Kaliakatsos, I. K., & Abbott, J. J. (2010). Microrobots for minimally invasive medicine. Annual review of biomedical engineering, 12, 55–85. URL: https://doi.org/101146/annurev-bioeng-010510-103409

"With all the advances in the medical world at present this one really has the potential to be a game changer. Less intrusive than surgery and has the potential to tackle a number of illnesses, diseases, and conditions. Engineering has the potential to really help the life sciences world by working alongside them to advance treatment and be able to deliver targeted treatment easier than before. I am very excited to see what the future hold for Nanobots within Life Sciences."

Senior Consultant - Regulatory Affairs
Compass Life Sciences

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