PROCEEDINGS

LONDON INTERNATIONAL CONFERENCES

eISSN 2977-1870

Nanotechnological Innovations in Healthcare

Halil Tunc* Ahyan Hassan* Hasan Rizvi* Saifullah Alsaaty* Emine Tunc**

Abstract

Nanotechnology is a concept much older and more prevalent than you may think. This article will delve into the applications of nanotechnology in various fields of medicine. Using ideas and research, old and new, this publication uses various studies to explore how nanotechnology saves, improves, and, in some cases, enables life. Frankly, the fields discussed further in this paper have nothing in common other than significant and interesting applications of nanotechnology. However, even with this diverse array of fields, only a fraction of nanotechnology's massive impact across medicinal practice altogether is covered. Nanotechnology has broken into almost every major sector of medicine, finding use from routine practices, such as drug delivery, all the way to extraordinary procedures, such as bone regeneration. This article opens up on the applications of nanotechnology in the cardiovascular, reproductive, antiviral, skeletal, and surgical fields. A substantial amount of research has been conducted to show that nanotechnology is no longer limited to science fiction, and has a major impact that will only grow with time and technology. Doctors and scientists are making full use of nanotechnology's capabilities by using it in any and all cases that require precision and effectiveness that is either impossible or extremely difficult and dangerous when performed by human hands. This makes many treatments less hazardous and more effective, saving and improving an exponential number of lives as time goes on.

Keywords: Nanoparticles, Drug Delivery, Cardiovascular Nanotech, Reproductive Nanotech



https://doi.org/10.31039/plic.2024.11.258

*HS of Endeavor, USA

**University of Texas at Austin, USA

13th London International Conference, July 24-26, 2024



This work is licensed under a <u>Creative Commons Attribution-NonCommercial-</u>

Introduction

What do you think of when you hear the term *Nanotechnology*? You may think of Iron Man or various other major science fiction characters and their inconceivably futuristic feats of engineering and technology, but what if I told you that nanotechnology might not be as futuristic as it seems? Nanotechnology is used across many different fields today, very prevalently and interestingly in medicine. Medicinal nanotechnology spans numerous fields and applications, including antiviral/antibacterial, reproductive, cardiovascular, bone regeneratory, and surgical contexts.

Before we delve into the world of medicinal nanotechnology, however, we need to know what nanotechnology is. Nanotechnology is known as the design, creation, and utilization of pieces of technology that have at least one dimension that measures 100 nanometers or less [1]. Additionally, nanotechnology involves the comprehension and manipulation of matter on a nanometer scale, also known as the nanoscale, which spans between 1 and 100 nanometers. Now, knowing the definition of a term doesn't entail complete comprehension of that topic, so let us explore the vast world of nanotechnology.

Although it may seem more complicated, nanotechnology is simply engineering at the nanoscale, and it has been this way throughout its history. The term "nanotechnology" was first introduced by a professor by the name of Norio Taniguchi at a conference in Tokyo, Japan in 1974. He defines it similarly to the definition I have provided, calling it "the production technology to get the extra high accuracy and ultra fine dimensions, i.e the preciseness and fineness of the order of 1 nm" in his On The Basis of Nano-technology. Even though Taniguchi coined the term he is not a lone figure in nanotechnology's history. Just like many other fields of science and technology, nanotechnology has a "father". Surprisingly, Taniguchi is not this person, this title has been given to American physicist Richard Fenman, who presented the fundamental concept of nanotechnology without using the term in 1959 during his talk *There's Plenty of Room at the Bottom*. His description portrays different ways to manipulate materials in or near the nanoscale for our advantage, even delving into the miniaturization of computers, which was a very novel idea for his time since computers used to fill entire rooms. Feynman and Taniguchi were both very intelligent people who had great ideas, but modern, physical nanotechnology was nonexistent before the scanning tunneling microscope created by Gerd Binnig and Heinrich Rohrer, IBM scientists who won a Nobel prize for this invention. Their invention enables the viewing and control of individual atoms, finally putting a face to the name nanotechnology. Now that we know where nanotechnology came from, let us see where nanotechnology is.

Nanotechnology, by definition, only exists in the nanoscale, so to understand nanotechnology, we need to understand the nanoscale. The nanoscale can be difficult to comprehend or even imagine, because of how little of its presence needs to be noticed by an average person, if ever. Since this is one of those rare instances, here is an explanation to give you a sense of scale: The smallest perceivable dimension for the human eye is 0.1 millimeters, about the diameter of a strand of hair, which equates to 100,000 nanometers. This doesn't even begin to enter the nanoscale, actually, this only shows that the nanoscale is 1000 times smaller than the smallest unit of measurement visible to the human eye under optimal conditions. To be clear, if you were as big as you can get while still in the nanoscale, the width of a strand of human



hair would be almost as tall as if you stood next to two Burj Khalifas stacked on top of one another at your current size. This sheer minuscularity requires nothing short of either access to very advanced technology or an exceptional imagination to visualize. The nanoscale is like a completely different world, primarily because of the complexities and unusualities exhibited by particles of this size. For example, nanosized particles can have different colors than their larger counterparts, because light is reflected differently based on the arrangement of atoms at the nanoscale.

Nanotechnology is a very complex topic, but this background information should serve as a tool to help fully comprehend its intriguing and bewildering applications in the medical field, and how they help save lives and pull our world towards a better future.

Nanotechnology in Medicine

Delving deeper into the medical applications of nanotechnology, we can see that it is used in a wide variety of ways, solving problems at a cellular level with cancer and reproductive technology to a much larger scale with surgery and bone regeneration. The properties of nanotechnology allow us to solve biological problems we couldn't before due to nanotechnology being much smaller and more precise. The miniscularity of nanotechnology allows it to enter the body in non-invasive ways and help the patient. Nanotechnology is an important advancement in the biomedical industry because of its capacity to alter materials at the molecular and atomic levels, allowing for new levels of accuracy in medicinal applications.

This technology allows for the creation of tailored drug and vaccine delivery systems that can deliver medicinal compounds directly to sick cells, improving therapy efficiency while minimizing side effects. These drug delivery systems are not only used for antiviral and antibacterial purposes, but also for cardiac regeneration or cardiovascular purposes. Furthermore, nanoscale materials are being employed to develop highly sensitive diagnostic instruments that can detect diseases in their early stages, along with improving surgery by making it more precise and non-invasive to the body. Nanorobots and nanostructured implants are two examples of innovations that show promise for improving tissue and bone regeneration and repair. Additionally, nanotechnology is used to aid the reproductive process in moving individual sperm and preserving it in cryostasis. Nanomaterials' distinctive qualities, such as size, surface characteristics, and reactivity, open up new opportunities for customized medicine, giving specific treatment regimens based on individual patients.

Nanotechnology has continually impacted healthcare since its birth, playing a significant role in medical evolution and leading to improved outcomes. In the past two decades, our world has watched nanotechnology take strides toward omnipresence, which has been expedited by intensive research in many healthcare industries. The use of nanotechnological systems in medicine is known as nanomedicine, and it has resulted in significant advances in illness prevention, diagnosis, and therapy. Various nanosystems have been discovered to be more suitable for medicinal applications than traditional ones.

Antiviral and Antibacterial Nanotechnology

Drug Delivery and Diagnosis

Nanotechnology can be used in antiviral and antibacterial procedures to slow down the reproduction pathways of certain diseases by making them more sensitive, enhancing the immune response, developing more efficient diagnostics for identifying and locating the disease, and targeting drug delivery systems to specific parts of the body affected by the disease. When it comes to antiviral and antibacterial processes, nanotechnology has the edge compared to average techniques because it has improved drug loading efficiency, can circulate the drug throughout the body faster, and has ultrasensitive detection capabilities that allow it to detect the virus or disease faster [2].

Nanotechnology is even being used to make better vaccines. These nanotechnological vaccines will be able to enter the body without the use of needles and circulate through the body faster. Moreover, with the usage of nanotechnology, individual vaccines will be able to introduce more than one disease at a time to the body's acquired immune system, concurrently making for a more cost-efficient option. However, these nano-enhanced vaccines are still under development. [3].

To correctly identify which drug or vaccine should be used on the patient, nanoparticles are used to diagnose what type of disease the patient has. Once the disease has been correctly diagnosed and located, the nanotechnology starts circulating the correct drug or vaccine throughout the body [2].

Virus Prevention

Using nanotech as a method to treat viruses was seen being used against COVID-19. It was used to slow down the reproduction and mutation of the virus's cells. The reason why the coronavirus thrived so much was its constant ability to mutate and create stronger variants of itself. By using nanotechnology, scientists were able to slow down the reproduction in COVID-19 cells and create a vaccine from weakened and more sensitive cells. As the virus's cells are weakened, the body can easily eradicate them using its white blood cells. Once the white blood cells have fought against the weaker version of the virus, they are more prepared to combat the whole virus [2].

An issue with regular, strong disinfectants was that although they were able to kill the pathogens that caused the virus transmission, unintentional overuse of these disinfectants could make said pathogens resistant to them. This is where nanotechnology can come into play, as the specific surface area, self-cleaning properties, and controlled drug-releasing mechanisms of nanotech can be used as effective alternatives [2].

Cardiovascular Nanotechnology

Atherosclerosis

Nanotechnology is used to precisely distribute and drop off certain drugs to a specific target in the body. This leads to higher efficacy and accuracy, concurrently lowering the chance of mistakes. These medicinal practices have made an appearance in the treatments for 13th London International Conference, July 24-26, 2024



cardiovascular problems. They play a role in the fight against diseases such as atherosclerosis, a disease of the arteries marked by the buildup of fat plaques, cholesterol, and other substances found throughout the artery walls. This plaque buildup causes blood flow to be narrowed or blocked in more serious scenarios. Nanosystems have been created for drug delivery, targeted imaging, and therapeutic interventions in regions affected by atherosclerotic plaque buildup [4].

The progression of atherosclerotic plaque buildup in the arteries plays a large role in worldwide morbidity, leading to many dangerous conditions such as heart attacks, strokes, aneurysms, etc [5]. One key factor essential to this plaque buildup is cholesterol crystals, a solid, crystalline form of cholesterol commonly found in progressive atherosclerotic lesions [6]. Study [7] goes into the idea of nanoliposomes and how they can counter atherosclerotic activity by removing cholesterol crystals. It has been shown that the usage of liposomes can facilitate the extraction of cholesterol from peripheral tissues, acting like "sinks" or "sponges" for the cholesterol, as said in article [7]. Liposomes have a unique structure that can be supplied with hydrophobic and hydrophilic drugs in the different layers of the structure. Moreover, ginsenosides with cholesterol-like structures have replaced cholesterol in the liposomes, improving the stability encapsulation in liposomes. Ginsenoside Rb1 has been reported to show anti-atherosclerotic activity, and due to the similar structure between Rb1 and cholesterol, it can be concluded that implementing Rb1 into liposomes and using this strategy as a nano-sponge for removing cholesterol crystals to reverse atherosclerotic progression can be a very effective way for doing so [7].

Cardiac Regeneration

Regarding the cardiovascular field, nanotechnology is not only used to treat atherosclerosis. It is also essential for the delivery of growth factors for cardiac development. Vascular endothelial growth factor, which is also known as VEGF, is a certain protein found in the body that assists in the development of brand new blood vessels, usually during the development of a baby in the womb, or after muscle tissue has been broken down due to exercise, and more [8]. Lots of research has been put into VEGF being used for cardiac regeneration, as it can be a way to improve blood supply and grow new blood vessels in damaged heart tissue [9]. However, direct intravenous distribution of VEGF has not shown any success. This is likely because of the short in vivo half-life and high instability of VEGF when injected [10]. Because of this, a large interest was seen in creating nanoparticles to deliver VEGF successfully.

In research article [11], a group of mice were experimented on and injected with either VEGF nanoparticles, bare VEGF, or just saline. The researchers found out that the group of mice that were injected with the nanoparticles had a remarkable rise in complete blood vessel mass and linkage in comparison with the naked growth factor treatment. These results show that using nanotechnology to deliver VEGF is a potent treatment to aid in cardiac regeneration.

Reproductive Nanotechnology

Asthenozoospermia

Male infertility is a prevalent issue throughout the world. About 186 million people deal with infertility problems, and the male partner is the problem about half the time [12]. Male infertility occurs when the male partner is unable to successfully fertilize the female partner's egg, and this can be caused by asthenozoospermia, a condition in which a person's sperm has reduced motility, leading to the sperm's inability to successfully swim to the egg. Unfortunately, asthenozoospermia does not have a cure at the moment, however, using nanotechnology may just be the way to approach this worldwide problem.

In 2016, a study was conducted and published in the journal *Nano Letters* about a potential solution. In this study, a group of researchers developed nano-motors that are meant to attach to individual sperm and help move the sperm so it can reach the egg. This is done by using a small, metal helix that fits around the sperm's tail and "drives" the cell using magnetic energy, thereby creating artificially motorized sperm cells, or 'spermbots'. Once the sperm arrives at the egg, the motor is meant to fall off the cell. Lab testing showed successful results, however, this is not ready for *in vivo* experiments yet, as researchers still face some issues such as the uncertainty of how the female body would react when these metal helices enter her body [14].

Sperm Cryopreservation using Zinc Oxide Nanoparticles

Cryopreservation of sperm is the process of freezing a male's sperm so that it can be used at a later date. When the sperm is required, it is thawed and can be utilized in different procedures known as ART, or assisted reproductive technologies, which include in vitro fertilization (IVF) or intrauterine insemination (IUI). This process of freezing one's sperm is usually done for those who deal with infertility issues. However, it comes with many risks, as a large portion of the frozen sperm dies during the freezing/thawing process. Additionally, many of the sperm cells that do survive end up being damaged and are unable to perform basic physiological functions, thereby deeming them useless for reproductive purposes [15]. Not only that, but one of the main issues that sperm cells deal with during the freeze/thawing process is damage to the DNA [16]. However, sperm cryopreservation can be improved with the implementation of zinc oxide nanoparticles.

Zinc is known to be an essential mineral for sperm integrity, motility, and overall quality. It can also help in preventing oxidative stress, which is a very detrimental issue that many sperm cells deal with during cryopreservation. Studies have demonstrated that the utilization of zinc/zinc oxide NPs (nanoparticles) has enhanced the integrity of the sperm membrane and reduced cell damage during the freeze/thaw process in human [16] and bull [17, 18] sperm. Additionally, higher fertility rates were found when experiments were conducted using frozen rooster sperm that was supplemented with zinc/zinc oxide NPs [19].

Bone Regeneration Using Nanotechnology

Our bones can repair small injuries on their own, but the same cannot be said for larger injuries. Whether you like it or not, whenever you have a broken or fractured bone, that bone

isn't the only organ that is affected [20]. Due to this, it is best to get the bone checked out or fixed as fast as possible so it doesn't lead to any other problems. Scientists have found a way to use nanotechnology to heal larger injuries to the bone [21]. There are three main ways to heal the bone. The first way is to help the natural healing capabilities of the bone work on their own. The second way is to use nanotechnology to target certain cells and help them grow faster. The third and final way is to use nanotechnology to build the bone [22].

When delivering drugs to cells to speed up or aid in the process of regeneration, the main type of nanotechnology used for transporting the drugs is biodegradable. When using these nanosystems, factors such as the desired surface area, the amount of the drug, and the type of drug needed, must be considered because different drugs react differently with other substances. The biodegradability and biocompatibility of the polymer that the nanoparticles are made of must also be carefully considered. Biodegradable nanotechnology can be created from various different materials, ranging from natural polymers to synthetic polymers. Drugs are not the only entities that can be delivered using nanotechnology; growth factor genes can also be directly transferred or delivered. However, efficiently delivering the genes while keeping proper form and stability is a large worry. In their article *Tissue engineering by* modulated gene delivery, Yamamoto, Masaya, and Yasuhiko Tabata state, "For successful gene transfection, the carrier vector should be small enough to be internalized into the cell and capable of escaping recognition by the endosome lysosome processing to protect the DNA until it reaches the target cell." [22]

To rebuild the bone using nanotechnology, we need to consider the materials that the nanotechnology will use to make the bone. There are many different combinations of materials to use, but it is hard to replicate the stiffness and flexibility of natural bone. The new bone must also correlate with the original weaker healing properties of the bone. The replicated bone also needs to maintain the original structure of the bone and continue the original flow of blood [21].

Since our bones are a natural composite, it is very important to maintain their original and natural generation. The Department of Orthopedic Surgery at Northwestern University Feinberg School of Medicine states that "researchers have long focused on developing nanostructured ceramic/polymer composite materials with the purpose of recreating the composition and function of natural bone." By using natural polymers, researchers hypothesize that the natural regeneration of the bone would still work as usual [21].

The nano-systems work by first locating an injury in the bone, such as a fracture. The nanoparticles then fill the gap by creating a structure that is compatible with the original structure of the bone. Therefore, the blood flow can continue as usual, and the structure of the bone is repaired.

Nanotechnology in Surgery and Clinic Diagnostics

The problem with the surgical process is that even though the surgeon knows what to do, there is still a chance of failure in surgery due to human error. Especially when surgery is conducted in areas that can end the patient's life with one error or mistake made. Scientists



have found a solution to this problem, that being nanotechnology. Nanotechnology would greatly lower the chances of human error in surgery since the robots are minuscule and their movements are substantially precise when compared to human surgeons. This can increase the life expectancy of the surgery, and allow surgeries in parts of the body that would be impossible for humans to conduct now possible. Nanotechnologies can also help improve surgeries by making them more non-invasive to the human body and increase the safety of surgery and diagnostic processes used hand in hand with surgery.

Nanotechnology can have a huge impact in the field of surgery as, according to *Indian* Journal for Surgery, it is a minimally invasive way to treat patients. This is due to the fact that people recover faster whenever lighter trauma is applied to them [23]. Nanobots enter the patient's body through cavities; spaces in the body that can hold organs and other bodily structures. Once in the body, the nanobots are controlled by a surgeon to perform meticulous and exact surgery within cells. In comparison, humans are not able to achieve this precision, as scalpels are many times larger than a cell. Nanobots also use femtosecond laser systems which are capable of targeting individual organelles within a cell without harming other parts of the cell. Femtosecond lasers are lasers that emit "ultrashort optical pulses" in bursts with durations between femtoseconds (1 fs = 10-15 s) [23]. These lasers are in the category of "ultrafast lasers or ultrashort pulse lasers capable of creating intensities in the range of 10^13/cm^2 [23]." Their precision allows them to manipulate biological structures with ease.

Nanotechnology has also heavily impacted diagnostic processes including MRI, ultrasound, and nuclear imaging. Our current imaging diagnostic processes have limitations as to what they can do. Nanotechnology solves this with fluorescent semiconductor nanocrystals (QDs or Quantum Dots), according to the British Journal of Surgery(BJS). QDs are useful for imaging techniques used currently as they can emit fluorescence at a variety of wavelengths which are changed according to their size. As said in [24], these quantum dots have size-tunable emission spectra (the emission spectrum being the spectrum of frequencies of electromagnetic radiation emitted as electrons move from a high to a low energy state) ranging from ultraviolet to near-infrared. In the spectrum, transitions vary between different substances and the different transitions from high to low radiate different wavelengths: the makeup of the emission spectrum. That being said, quantum dots are also ideal for non-invasive imaging, and can be used to identify and monitor diseases in the long term. QDs can be used in a sentinel lymph node biopsy, which is a procedure used to find out if cancer has spread from its origin or not, for staging breast cancer metastasis, which is when the cancer cells have broken away from the hearth. Additionally, QDs can be found in magnetic resonance imaging technology. Using QDs in MRI takes advantage of the high sensitivity of QD fluorescence to different wavelengths and the impressive spatial resolution of MRI, improving the collected data in MRI scanning [24].

Nanotechnology solves the problems in surgery and makes surgical processes much safer for the patient by making current practices used non-invasive. However, nanobots will not completely take the roles of surgeons, as surgeons would be needed to operate the nanobots, and instead, the nanobots would assist the surgeons in making surgery less life-threatening to the patient. Nanotechnology can help in diagnosing the problems to be fixed in surgery more precisely and efficiently than currently used technology. Nanobots will remove human error



from surgical processes and improve diagnostic processes, advancing current medicinal equipment and technologies.

Conclusion

Nanotechnology has applications in various fields of science, engineering, and even commercial production, but nowhere is it as interesting, as innovative, and as important as it is in medicine. While nanotechnologies open more than just a few doors to new opportunities anywhere they are implemented, this has the most meaning in medicine. Nanotechnology is a great tool that can help ease uneasy lives, give hope to hopeless cases, and shed light on the darkest corners of human anatomy and physiology. In this article, we have explored the applications of nanotechnology in the antiviral/antibacterial, cardiovascular, and reproductive fields and the more specific cases of surgery and bone regeneration. However, this is only a sliver of what nanotechnology is doing, let alone what it can do, to further the safety and efficiency of medicinal practices to save and elongate human lives. With nanotechnology, we can learn the unknowable, furthering our knowledge of ourselves and the world around us, and use this knowledge for the greater good of humanity, but as it can be used to help, it can be used to harm. Just as with biotechnology, the general public's access to in-depth knowledge of nanotechnology and its creation can cause devastation with ease of access to powerful information and technology, which is why specific knowledge should be kept with the caution used for nuclear bombs. Just as nanotechnology can be used to deliver life-saving drugs, it can be used to deploy life-threatening poisons, and just as it can be used to improve the pumping of a heart, it can be used to stop one. Although this may seem terrifying, it is extremely preventable, as I mentioned before, by simply safeguarding the information from the wrong hands. As long as it is used, kept, and understood in the right way, nanotechnology is paving the way for an amazing, knowledgeable future.

As humans, there is a limit to what we can do with our comparatively large and imprecise hands and physical forms, but there is no limit to what we can do with our minds, and nanotechnology is about the size of a thought.

References

- 1. Nanotechnologies. (n.d.). https://ec.europa.eu/health/scientific_committees/opinions_layman/en/nanotechnologies/index.htm
- 2. Tiwari, S., Juneja, S., Ghosal, A., Bandara, N., Khan, R., Wallen, S. L., Ramakrishna, S., & Kaushik, A. (2022, March). Antibacterial and antiviral high-performance nanosystems to mitigate new SARS-COV-2 variants of concern. Current opinion in biomedical engineering. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8632437/#:~:text=Some%20common%20advanta ges%20of%20nanomaterials,drug%20circulation%20time%20in%20%2D%20vivo%2C
- 3. Applications of nanotechnology. Applications of Nanotechnology | National Nanotechnology Initiative. (n.d.). https://www.nano.gov/about-nanotechnology/applications-nanotechnology
- 4. Omidian, H., Babanejad, N., & Cubeddu, L. X. (2023, July 12). Nanosystems in Cardiovascular *Medicine: Advancements, applications, and future perspectives.* MDPI. https://doi.org/10.3390/pharmaceutics15071935
- 5. Atherosclerosis. Johns Hopkins Medicine. (n.d.). https://www.hopkinsmedicine.org/health/conditions-and-diseases/atherosclerosis
- 6. SUGIYAMA, N., HASEGAWA, H., KUDO, K., MIYAHARA, R., SAITO, R., MARUKI, C., TAKASE, M., KONDO, A., & OISHI, H. (2022, July 27). Cholesterol crystals in the retrieved thrombus by mechanical thrombectomy for cerebral embolism: A case report and literature review. NMC Case Report Journal. https://doi.org/10.2176/jns-nmc.2022-0095
- 7. Gong, F., Wang, Z., Mo, R., Wang, Y., Su, J., Li, X., Omonova, C. T. Q., Khamis, A. M., Zhang, Q., Dong, M., & Su, Z. (2022). Nano-sponge-like liposomes remove cholesterol crystals for antiatherosclerosis. Journal of Controlled Release: Official Journal of the Controlled Release Society, 349, 940–953. https://doi.org/10.1016/j.jconrel.2022.07.021
- 8. Dr. Ananya Mandal, M. (2023, August 18). What is VEGF?. News. https://www.newsmedical.net/life-sciences/What-is-VEGF.aspx
- 9. Entering a new era in vascular and Cardiac Regeneration Research. (n.d.-a). https://www.astrazeneca.com/what-science-can-do/topics/next-generation-therapeutics/entering-anew-era-in-vascular-and-cardiac-regeneration-research.html
- 10. Pretorius, D., Serpooshan, V., & Zhang, J. (2021, January 19). Nano-Medicine in the cardiovascular system. Frontiers. https://doi.org/10.3389/fphar.2021.640182
- 11. Golub, J. S., Kim, Y., Duvall, C. L., Bellamkonda, R. V., Gupta, D., Lin, A. S., Weiss, D., Robert Taylor, W., & Guldberg, R. E. (2010). Sustained VEGF delivery via PLGA nanoparticles promotes vascular growth. American Journal of Physiology-Heart and Circulatory Physiology, 298(6). https://doi.org/10.1152/ajpheart.00199.2009
- 12. Professional, C. C. medical. (n.d.). What is male infertility?. Cleveland Clinic. https://my.clevelandclinic.org/health/diseases/17201-male-infertility
- 13. Medina-Sánchez, M., Schwarz, L., Meyer, A. K., Hebenstreit, F., & Schmidt, O. G. (2015). Cellular cargo delivery: Toward assisted fertilization by sperm-carrying micromotors. Nano Letters, 16(1), 555–561. https://doi.org/10.1021/acs.nanolett.5b04221

- 14. Ozdemir, D. (2021, September 23). Watch nanobot carry lazy sperm to fertilize living eggs. Interesting Engineering, https://interestingengineering.com/health/watch-nanobot-carry-lazysperm-to-fertilize-living-eggs
- 15. Hai, E., Li, B., Zhang, J., & Zhang, J. (2024). Sperm freezing damage: The role of Regulated Cell Death. Cell Death Discovery, 10(1). https://doi.org/10.1038/s41420-024-02013-3
- 16. Isaac, A. V., Kumari, S., Nair, R., Urs, D. R., Salian, S. R., Kalthur, G., Adiga, S. K., Manikkath, J., Mutalik, S., Sachdev, D., & Pasricha, R. (2017). Supplementing zinc oxide nanoparticles to cryopreservation medium minimizes the freeze-thaw-induced damage to spermatozoa. Biochemical and Biophysical Research Communications, 494(3-4), 656-662. https://doi.org/10.1016/j.bbrc.2017.10.112
- 17. Falchi, L., Khalil, W. A., Hassan, M., & Marei, W. F. A. (2018). Perspectives of nanotechnology in male fertility and sperm function. International Journal of Veterinary Science and Medicine, 6(2), 265–269. https://doi.org/10.1016/j.ijvsm.2018.09.001
- 18. Hozyen, H. F., Shamy, A. A., Fattah, E. M., & Sakr, A. M. (2023). Facile fabrication of zinc oxide nanoparticles for enhanced buffalo sperm parameters during cryopreservation. Journal of Trace Elements and Minerals, 4, 100058. https://doi.org/10.1016/j.jtemin.2023.100058
- 19. Khodaei-Motlagh, M., Masoudi, R., Karimi-Sabet, M. J., & Hatefi, A. (2022). Supplementation of sperm cooling medium with zinc and zinc oxide nanoparticles preserves rooster sperm quality and fertility potential. *Theriogenology*, 183, 36–40. https://doi.org/10.1016/j.theriogenology.2022.02.015
- 20. Tanaka, M., Izumiya, M., Haniu, H., Ueda, K., Ma, C., Ueshiba, K., Ideta, H., Sobajima, A., Uchiyama, S., Takahashi, J., & Saito, N. (2022, April 2). Current methods in the study of nanomaterials for Bone Regeneration. Nanomaterials (Basel, Switzerland). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9000656/
- 21. Lyons, J. G., Plantz, M. A., Hsu, W. K., Hsu, E. L., & Minardi, S. (2020, July 17). Nanostructured biomaterials for bone regeneration. Frontiers, https://www.frontiersin.org/journals/bioengineeringand-biotechnology/articles/10.3389/fbioe.2020.00922/full
- 22. Walmsley, G. G., McArdle, A., Tevlin, R., Momeni, A., Atashroo, D., Hu, M. S., Feroze, A. H., Wong, V. W., Lorenz, P. H., Longaker, M. T., & Wan, D. C. (2015, July). Nanotechnology in bone tissue engineering. Nanomedicine: nanotechnology, biology, and medicine. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4476906/
- 23. Mali, S. (2012). Nanotechnology for surgeons. *Indian Journal of Surgery*, 75(6), 485–492. https://doi.org/10.1007/s12262-012-0726-y
- 24. Loizidou, M., & Seifalian, A. M. (2010, March 4). Nanotechnology and its applications in surgery. OUP Academic. https://academic.oup.com/bjs/article/97/4/463/6150283