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# ENDING MALARIA? - CRIPSR AND GENE DRIVE

Nikhita Attaluri 12D

#### Introduction - What is Malaria

Despite malaria impacting hundreds of millions of lives a year, it is a deadly disease that we in the developed world don't have to worry much about. About 90% of cases and lives claimed are in the WHO African region, however, this killer disease leaves children under 5 most vulnerable, accounting for 61% of all malaria deaths worldwide.

It is caused by a microscopic Plasmodium parasite which infects mosquitoes. The disease is transmitted when an infected female Anopheles mosquito bites a human. Once the mosquito bites a human, the parasite is released in the human's bloodstream, where it then travels to the human's liver where it spends a few days maturing. After maturing for a few days, the parasite reenters the bloodstream and starts infecting red blood cells causing them to burst. As the parasites continue to infect more red blood cells, the person falls sick with symptoms of the disease. Malaria cannot spread directly from person to person; it is spread most commonly through mosquitos. When a mosquito bites a person with malaria, it becomes infected with the parasite, and when the infected mosquito bites another human, it spreads the disease.

Once diagnosed, there are many treatments and anti-malarial medications to cure malaria completely, yet these treatments vary from the type of malaria and how early the diagnosis is, meaning there is not always a full recovery. However, there is currently no vaccine and the main preventative measures for this deadly disease are anti-malarial medications and mosquito nets; leaving many exposed and at-risk for this disease.

Considering that the disease predominantly affects regions that are developing, treatments are not as easily accessible, therefore, a stronger preventative measure would be highly beneficial.

Once diagnosed, there are many treatments and antimalarial medications to cure malaria completely, yet these treatments vary from the type of malaria and how early the diagnosis is, meaning there is not always a full recovery. However, there is currently no vaccine and the main preventative measures for this deadly disease are anti-malarial medications and mosquito nets; leaving many exposed and at-risk for this disease. Considering that the disease predominantly affects regions that are developing, treatments are not as easily accessible, therefore, a stronger preventative measure would be highly beneficial.

#### **CRISPR and Gene Drive**

With the recent developments of CRISPR gene drives, one of the most promising preventative measures comes from genetically modifying mosquitoes that carry malaria. This could potentially prevent the spread of malaria significantly and possibly even eradicate it, saving countless lives.

CRISPR refers to a sequence of bacterial DNA, which when working in conjunction with the Cas-9 enzyme can be used for gene editing. Researchers can add a gene to an organism's DNA by creating an RNA 'guide' sequence. This guide sequence binds to the organism's original DNA which allows Cas-9 enzyme to cut the organism's DNA at this specific location. Once the DNA is cut, researchers can utilise the cells' DNA repair mechanism to add or delete genes.

This system can be used to create CRISPR Cas-9 gene drives. Gene drives essentially allow modified genes to be passed onto 99% of offspring by inserting the CRISPR system into the genes of organisms. CRISPR gene drives work by using the CRISPR Cas-9 technology to insert the genes for the Cas-9 enzyme and several 'guide' RNAs along with the modified gene into an organism. As a result of this, when the genetically modified mosquito breeds with a wild mosquito, the guide RNA and Cas-9 enzyme previously inserted into the modified mosquito allows the wild mosquito's DNA to copy the altered gene and as well as the drive.

#### Potential uses of this technology

CRISPR enables us to genetically modify the Anopheles mosquito that infects humans. Gene drives allow us to potentially pass on this modification to the wild population, changing the genes of the entire species, at a rate so fast that the parasite can not catch up to the modification. This could mean the end of malaria.

There are different approaches to genetic modification and gene drives as a means of eradicating malaria including making mosquitoes immune to malaria and reducing mosquito populations. These approaches have been taken by numerous researchers and projects, including Target Malaria. Considering that only female mosquitos bite humans and infect them, Target Malaria takes the approach of reducing the mosquito population by biasing sex ratios and causing infertility.

Nonetheless, a lot of research going on right now is still in the trial phase and there haven't been any approvals for the genetically modified mosquitoes to be released into the wild.

#### **Problems and ethical implications**

One of the biggest hurdles faced when considering genetic modification and gene drive are the ethical implications associated with it. Taking into account that this technology has the power to alter the genetic makeup of an entire population quite quickly, many argue that the risks carried with gene drive make the modification needed to cure malaria unethical.

Furthermore, many argue that once the modified mosquitoes are released, the spread of the modified gene would be much slower than in theory, which could lead to the parasite mutating, causing even more harm to humans. However, due to the number of people exposed and at-risk to the deadly disease, many argue that having a way to eradicate malaria and not releasing it quickly would be unethical. As CRISPR gene drives are a very new technology there would have to be very strict and controlled trials to determine the exact outcome.

Gene editing and other advances in biotechnology are posing ethical dilemmas which need to be addressed by scientists and administrators and governments to ensure we benefit from knowledge but avoid pitfalls of endangering other living species and disturbing natural order.

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# ANTIBIOTICS: TOO MUCH OF A GOOD THING?

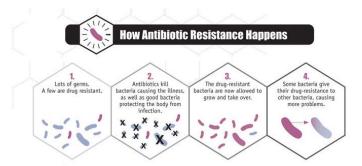
Madelyn Javes 12E

It has been called "A global crisis...one of the greatest threats to health today...a slow moving tsunami" by Dr Margaret Chan, the former World Health Organisation (WHO) director general. It has been identified by the WHO as a priority health issue to every single country. What could this crisis be?

Antibiotic resistance.

What is antibiotic resistance? Well, to answer that, let's look first at what an antibiotic is.

Have you ever had an ear infection? Maybe a throat infection? Did your doctor give you some pills to take to get rid of it? It's likely they were antibiotics. When we get an infection, it's caused by something called a pathogen. The main pathogens that make us ill are bacteria, viruses and fungi. Each of these pathogens are targeted by specific medicines. Viruses, for example the flu, are targeted by antivirals (this is why you shouldn't be given an antibiotic for the flu!), fungi by antifungals and bacteria by antibiotics. These medicines are not interchangeable. For example, only bacteria can be targeted by antibiotics. There are many types of antibiotics too - some work on many kinds of bacteria, and some only work on specific types. They work by stopping the growth (bacteriostatic antibiotic) of or directly killing the bacteria (bactericidal antibiotic) that the doctor thinks is causing an infection.





Most of the time, antibiotics work really well to get rid of bacteria. However, they can fail, because the bacteria aren't responding to them anymore. This is what's called antibiotic resistance.

When bacteria are exposed to the same antibiotics over and over, or are left in the body (perhaps because not all the pills given by the doctor are taken), some bacteria that are naturally slightly resistant to antibiotics survive - this happens because of a mutation in their genes. We have good bacteria in our body, which helps to fight infection. Antibiotics don't discriminate against good and bad and kill both. When the resistant bacteria are left over, it is easier for them to reproduce because of this. They can multiply, and pass on their antibiotic resistant genes to other bacteria, growing freely. These bacteria that become resistant are known as 'superbugs'

## So, why are superbugs causing a global crisis?

Antibiotics are incredibly important to modern medicine. To imagine a life without them, we need only look back before 1928 when the first antibiotic, penicillin, was discovered. Anything that could cause an infection could be fatal, from childbirth to a scrape on the knee. Common illnesses couldn't be treated. These days, it would be even worse. Modern medical advancements such as organ transplants, surgery and chemotherapy depend on being able to prevent or treat infections. People with weakened immune systems due to certain medications or illnesses would be under even more risk. That ear infection you went to the doctor with may not be able to be treated at all.

As it turns out, this is not a future threat. Antibiotic resistant bacteria causes more than 750,000 deaths per year. But let's bring it more local. In 2018, there were 1,218 cases of MRSA, one of the most threatening superbugs in Hong Kong. And the number is expected to keep rising.

When fighting a superbug, doctors often have to resort to using powerful 'last line' antibiotics. Their use is controlled, but as resistance increases, their use is becoming far more common.

#### What did we do to make this happen?

Mainly, superbugs are caused by the overuse of antibiotics - this is why they're most commonly found in hospitals. Patients not finishing their prescription of antibiotics are also a large factor. Substandard infection control, hygiene and sanitation in health care settings also contribute. There is an overuse of them in livestock farming, to prevent and treat disease in animals too.



There is good news though, researchers are working to develop new antibiotics or alternatives - even in our home town, Hong Kong.

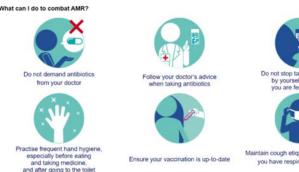
In 2018, at the Hong Kong University of Science and Technology, the key enzyme (a type of protein) behind bacterial resistance to a type of last line antibiotics, called peptide antibiotics, was discovered. Being able to find the cause of resistance is thought to be able to make it easier to develop new antibiotics.

In 2019, at the Hong Kong Polytechnic University and Chinese University of Hong Kong, researchers achieved a breakthrough discovery. They developed a new type of antibiotic, called a 'Nusbiarylin'. This type of antibiotic was tested to be even more effective against common superbugs than current last line antibiotics. Currently, it's still going through trials but is extremely promising.

#### Ok, so what can I do about it?

Well, the best thing you can do about antibiotic resistance is to be educated. Know what an antibiotic is. Know when they can be used (bacteria), and when they can't be used (viruses). And tell other people! The Hong Kong Department of Health has actually written guidelines for this, as shown in figure 2.

Figure 2 - Hong Kong Department of Health guidelines



- 1. Refrain from asking your doctor for an antibiotic for a virus, like a cold or the flu. If you're given medicine, ask if it's an antibiotic.
- 2. If you're given antibiotics, be aware and always follow your doctor's instructions on how to take them. Take all of the medicine and don't stop even if you are feeling better. This helps to ensure there aren't any left over bacteria.
- 3. Have good personal hygiene this will reduce the chance of you getting sick in the first place.

All in all, it's clear that antibiotic resistance is a growing problem. It is already a reality, and a scary one at that. But the goal is not to be scared, but to be aware.

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# THE IMMUNE SYSTEM

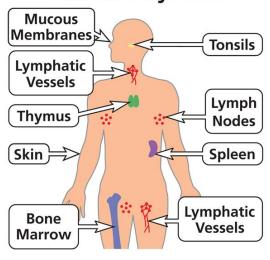
Janice Fok 12N



#### Introduction

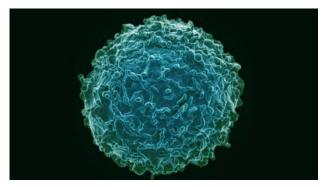
The Immune System is a vital defense system that protects your body from invading pathogens that can cause diseases. The immune system is split into two categories, innate immunity and adaptive immunity. Innate immunity is the immune system that is already present since birth, while adaptive immunity is created when an immune response has occurred. In 1958, Professor Jacques Miller discovered the function of the thymus in the adaptive immune system. When he joined the Walter and Eliza Hall Institute of Medical Research in Melbourne, he worked with Graham Mitchel and discovered the two types of lymphocytes known as T cells and B cells and also the function. The image from AIDSinfo shows a diagram of the immune system.

#### **Immune System**



#### How it works

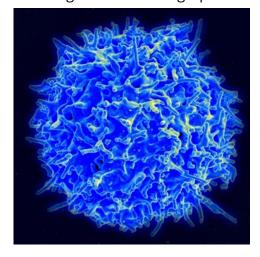
The immune system consists of many different processes and parts. Lymphocytes are a subtype of white blood cell that is involved in the immune system, they include T-cells, B-cells and natural killer cells. These cells move through the blood and look for any foreign invaders that can potentially cause diseases. An immune response occurs when the body is exposed to a pathogen in which the immune system recognizes antigens, which are substances on the surface of cells or pathogens such as viruses, fungi and bacteria and attacks it.



B cells are made from stem cells in the bone marrow. They secrete antibodies that bind to a specific antigen. When an antibody recognizes a specific antigen, it identifies a certain area on the antigen known as antigenic determinants, the antibody then binds on the specific antigenic determinant. This gives a signal to the other immune cells such as cytotoxic T cells to destroy the antigen.

Memory B cells are created after the immune response occurs, which allows the immune system to remember the specific antigen that has previously attacked the body. Should the exact same antigen invades again, a secondary immune response will occur where antibodies will be produced much more quickly. These cells are permanent and will remain in the body for life. The image from NIAID shows a colourised scanning electron micrograph of a B cell.

T cells are made in the bone marrow and matures in the thymus. T cells are required for cell mediated immunity, which does not involve antibodies, instead it involves activation immune cells. When T cells are in the thymus, they differentiate into cytotoxic T cells, helper T cells, regulatory T cells, natural killer T cells and memory T cells. The cell membranes of T cells have proteins known as T-cell receptor which can recognize many types of antigens. Memory T cells are also formed, similar to memory B cells, they are permanent and will trigger a secondary immune response. The image from NIAID shows a colourised scanning electron micrograph of a T cell.



#### **Vaccinations**

Vaccinations provide lifelong immunity to a certain disease. Immunity is when an individual is protected from certain diseases, therefore even if exposed to the disease, the individual will not fall ill. Individuals receive vaccinations either by injection with needle, orally, or nasally.

When an individual gets vaccinated, inactive versions of the certain pathogen are injected, triggering an immune response, producing memory cells.

The first successful vaccine discovered was the smallpox vaccine, which was introduced in 1796 by Edward Jenner, also known as the "Father of Immunology", after observing that those who catch cowpox did not catch smallpox.

#### **Autoimmune Diseases**

Diseases caused by the immune system are known as autoimmune diseases. It occurs when the individual's immune system mistakenly attacks their own healthy tissues. There are over 80 different autoimmune diseases. An example of one is Type 1 diabetes. Type 1 diabetes happens when the immune system mistakenly destroys beta cells in the pancreas that produces insulin. Insulin is the hormone that controls the blood sugar level, converting glucose into glycogen for storage in the liver. It is released when there is a higher concentration of sugar than your body needs. However, as the immune system has destroyed the beta cells, insulin can no longer be produced, leading to a buildup of glucose in the blood (hyperglycemia). Another example is Rheumatoid Arthritis, which mainly affects the joints of hands, feet, wrists, elbows, knees and anklesit occurs when the immune system mistakenly attacks the lining of membranes surrounding your joints known as the synovium. Which leads to weakening and stretching of tendons and ligaments holding the joint together.

#### Conclusion

In conclusion, the immune system is a complex system which protects your body from infections which can cause diseases. It involves the functions of different types of cells and processes which can protect us from any deadly illnesses. There is still research going on to find out more about the functions and parts of the immune system and also finding new discoveries, for example, scientists have been looking at undiscovered ways where the immune system can attack tumour cells.

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# HOW CAN STEM CELLS REVOLUTIONIZE MEDICINE?

James Fung 12W

#### Introduction

The 20th century brought numerous incredible advancements that revolutionized the field of medical science and changed our lives forever. For example, when Alexander Fleming discovered penicillin in 1928, it was considered a miracle drug. This was because penicillin could cure bacterial infections that previously weren't treatable due to the lack of antibiotic drugs, saving millions upon millions of lives. The impacts of these discoveries can be seen through the significant increase in human life expectancy in the UK, from 49.8 in 1901, to 80.96 in 2016. However, despite the fact that the world average life expectancy is now the highest it has ever been in human history, many people today are still plagued by terminal diseases and conditions, such as spinal cord injuries, Parkinson's, diabetes and cancer.

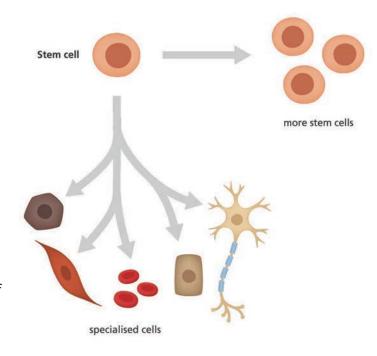
#### What are stem cells?

To understand why so many scientists believe stem cells could be the answer to many of humankind's medical problems, we must first find out what stem cells are. Stem cells are undifferentiated cells which are capable of undergoing a process called differentiation to become specialised cells. Cellular differentiation is a process in which a cell changes from one cell type to another, usually more specialised cell type. These specialised cells can include nerve cells, muscle cells, liver cells, etc. Stem cells are also able to divide continuously to produce more stem cells of the same type. There are 4 main categories of stem cells, totipotent stem cells, pluripotent stem cells, multipotent stem cells and unipotent stem cells.

#### **Totipotent stem cells**

Cell potency refers to the range of potential cells a cell can differentiate into. Stem cells with greater potency are able to differentiate into a wider range of cells. Totipotent stem cells have the greatest potency out of all the stem cells, as they are able to differentiate into all embryonic cells, as well as extraembryonic cells, such as umbilical cord cells and placenta cells.

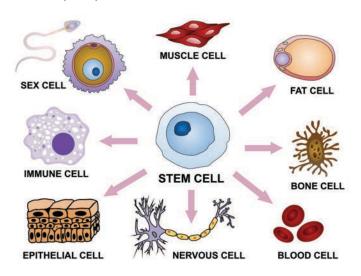




Totipotent stem cells can be acquired from the morula, which is a clump of cells resulting from the division of a fertilised egg cell, before the dividing fertilised egg cells start specialising into pluripotent cells. While it is possible to convert a fully differentiated cell back to a state of totipotency, the conversion process is complicated and not fully understood by scientists. Some scientists believe that cells that undergo this process are not converted to fully-totipotent cells, but are instead converted to a 'complex cellular variation' of totipotency.

#### Pluripotent stem cells

Although pluripotent stem cells are not able to specialise into as many cell types as totipotent cells, they are still incredibly valuable for scientific research. Pluripotent stem cells can differentiate into all the specialised cells, tissues and organs that can be found in our body. An example of pluripotent stem cells are embryonic stem cells. These cells can be obtained from the inner cell mass of blastocysts, which are groups of cells formed in the early development of mammals. Another example is induced pluripotent stem cells.



These pluripotent stem cells are reprogrammed from specialised adult somatic cells, like blood cells and skin cells. This is done through the forced expression of specific genes. Initially, induced pluripotent stem cells were thought to be able to replace embryonic stem cells due to their similarities and completely eliminate the need to use embryos for research. However, studies have shown that induced pluripotent stem cells could potentially cause tumours and that, combined with a low replication rate and early deterioration,

have hindered its full replacement of embryonic stem cells.

#### Multipotent stem cells

Multipotent stem cells can specialise into a few closely-related types of cells. These are usually found in most body organs and tissues and are responsible for replacing damaged or dead cells. There are many examples of multipotent stem cells. An example is hematopoietic stem cells, which can be found in the bone marrow. These stem cells are able to specialise into blood-related cells, such as white blood cells, red blood cells, platelets, etc. However, these stem cells can't specialise into cells belonging to other organs, such as brain or liver cells. Another example is umbilical cord stem cells. When a baby is born, the umbilical cord can be stored to be a future source of stem cells for the baby. These cells can act as a substitute for bone marrow stem cells and are less likely to be rejected by the body as they have not developed cell-surface molecules that will be attacked by the body's immune system.

#### **Unipotent stem cells**

Unipotent stem cells have the least potency out of all the stem cells as they can only specialise into one cell type. Skin cells are an example of unipotent stem cells. Skin stem cells can renew and specialise but are only able to produce more skin cells.

#### **Stem Cell Therapies**

Currently, the only stem cell therapies that have been approved by the US Food and Drug Administration utilise multipotent bone marrow stem cells or stem cells from umbilical cord blood to treat blood and bone marrow cancers. An example of an effective stem cell therapy is bone marrow transplants. If a patient suffers from blood cancers, like leukaemia, and decides to go through chemotherapy, the existing bone marrow stem cells will be killed during the process. New bone marrow stem cells can be transplanted to replace damaged or destroyed cells. This technique has helped save countless people who were suffering from blood cancers.

Since embryonic stem cells can replace damaged or destroyed cells that don't regenerate naturally, there is hope that in the future, we will be able to develop cures and therapies for terminal diseases and conditions using embryonic stem cells. There are a few experimental embryonic stem cell therapies that are currently undergoing human trials while some are still being further researched. Theoretically, if scientists are able to study all cell types via embryonic stem cells, they could possibly develop treatments for every single disease. Currently, a lot of work is being put into treatments for terminal diseases, like diabetes, Parkinson's and conditions like injured spinal cords and damaged heart muscle.

While stem cell therapies could seem like a miracle treatment, caution is still required before deciding to undergo any stem cell treatments. This is because stem cell therapies that aren't approved by the FDA can cause various adverse effects. These can range from minor effects, such as bacterial infections, to more severe ones, such as blindness, kidney failure, paraplegia or even death. In 2016, a woman from Australia passed away after receiving an adipose tissue-derived stem cell transplant that was not approved by the Australian regulatory agencies. This demonstrated to the world that it can be potentially life-threatening to undergo unapproved and unsafe stem cell therapies, so it is extremely important for thorough testing to be done on a treatment before releasing it to the public.

Potential uses of Stem cells Stroke Baldness Traumatic brain injury Blindness Learning defects Alzheimer's disease Deafness Parkinson's disease Amyotrophic lateral-Missing teeth sclerosis Wound healing Myocardial Bone marrow infarction transplantation Muscular (currently established) dystrophy Spinal cord injury **Diabetes** Osteoarthritis Multiple sites: Rheumatoid arthritis Crohn's disease Cancers

## Controversies surrounding embryonic stem cells

While embryonic stem cells have shown great potential for use in medicine, there are controversies surrounding stem cell research and stem cell

therapies. This controversy mainly surrounds the fact that currently, to acquire these embryonic stem cells, the developing embryo needs to be killed. As a result, the issue boils down to whether life starts at conception or at birth. One side believes life starts at birth, while the other believes life starts at conception.



The former group do not see the destruction of embryos as unethical, as they don't consider embryos to be life, while the latter group tend to strongly oppose the use of embryonic stem cells, as they believe that since life starts at conception and since an embryo has the ability to develop into a human being, killing it counts as murder. A more morally acceptable option for these people could be to obtain embryonic stem cells from excess, unwanted embryos donated by willing couples after an IVF process. Instead of being discarded and wasted, those extra embryos can be put to good use and can further our understanding of embryonic stem cells.

#### Conclusion

Personally, I support embryonic stem cell research. I believe that life starts at birth and that an embryo, which is incapable of surviving on its own, does not constitute a proper human being. While I understand the arguments presented by opponents of embryonic stem cell research, I believe that there should be further research on embryonic stem cells and their potential therapies. Since the development of these treatments can save the lives of millions of people worldwide who are affected by terminal diseases or conditions and help them live normal lives, I think embryonic stem cell research is justified.

