SYNTHETIC BIOLOGY: THE KRYPTONITE AGAINST SUPERBUGS

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Antibiotics are medical compounds used to treat infections caused exclusively by bacteria. At a time when bacterial infections were untreatable and accounted for nearly 30 per cent of all deaths, the accidental discovery of penicillin by Alexander Fleming changed the course of mankind. This was a remarkable milestone in human history, where people could live their lives with more vigour and happiness, without the creeping fear that they could lose their loved one to what seemed like a harmless tooth infection or a sore throat. Antibiotics play a pivotal role in modern medicine and are now accessible to everyone. But that doesn't necessarily is always a good thing. This level of widespread availability and lack of supervision can lead to improper or in many cases misuse of the drug. Alexander Fleming when receiving his Nobel Prize for the discovery warned that exposing the bacteria to non-lethal doses of antibiotics can lead to the bacteria gaining resistance towards the drug which would indeed render it useless.

The ineffectiveness of a particular antibiotic against a bacterium can be attributed to one of the following reasons: impermeable cell membrane of the bacteria, lack of target site inside the bacteria where the antibiotic can launch an attack, ability of the bacteria to produce enzymes to neutralize the adverse effect an antibiotic can cause, proficiency of the bacteria to modify the antibiotic's target before it starts the necessary action and finally through the usage of built-in efflux pumps that throw antibiotics out of the cell before it can take effect.

Although impermeable cell membrane and lacking a target are natural traits of the bacteria, other traits are acquired by bacteria either through a random mutation or horizontal gene transfer, a mechanism in which the resistance against a particular antibiotic is transferred due to exchange of genetic information between a non-resistant and resistant bacterium in the same population.

Even though acquiring such resistance is a natural evolutionary process, what's alarming is how human intervention and neglect accelerated this process to the extent where we find ourselves in a treacherous situation with many antibiotics becoming inutile despite the words of caution left to us about 80 years ago by Fleming.

A myriad of reckless actions by humans can be attributed to the current epidemic of antibiotic resistance. Patients missing or not completing the recommended dosage of the prescribed antibiotics gives the leftover bacteria in their system time to adapt to the low concentration levels of antibiotics and in turn pass on their resistance to newer generations. The livestock industry pumps exorbitant quantities of antibiotics into the animals in order to counteract the diseases arising from the abysmal living conditions in the factories. Doctors leaving caution to the wind by overprescribing antibiotics to tackle ailments that don't need them, kick-starting a biological evolutionary arms race. In fact, hospitals have become a major hub of breeding grounds for these antibiotic-resistant bacteria.

We have created a classic case of "What doesn't kill you only makes you stronger".

Today we find ourselves in this desperate situation where some of the most powerful antibiotics that were developed after years of painstaking research have been deemed obsolete by the rise of superbugs. Several combinations of antibiotics are prescribed for diseases that in the past were solved with greater ease by a specific antibiotic. This has significantly

increased the risk of liver damage in patients as their bodies tries to metabolize a multitude of antibiotics. Costs of treatment for these diseases have seen a staggering rise as rarer and expensive antibiotics are being used. This will greatly affect public health as lesser people will now have access to these treatments increasing the chances of outbreaks.

Synthetic biology is the science of engineering selective traits into an organism's genetic code. Recombinant DNA is the technology of piecing together sequences of DNA with the help of enzymes to obtain the desired trait. Molecular cloning which uses living cells and polymerase chain reaction which is done in vitro free of life are used to replicate the chosen DNA sequence. A cloning vector is chosen from plasmids or viruses that signal replication. These DNA segments are then combined by laboratory techniques such as Gibson assembly.

Synthetic biology is seen as the shining beacon of light by the science community that could lead the path to revolutionize several modern industries such as medicine, agriculture, animal rearing, waste management and so on. By harnessing the power to make our own organism, we can significantly reduce the environmental impacts created by these industries currently while also vastly improving their efficiency. This is the future of mankind!

Presently to overcome the problem of antibiotic resistance, scientists have proposed the use of bacteriophages that are genetically modified. These specifically target the bacterial cells and which in combination with antibiotics have shown great promise in ending the war between humans and superbugs. Extensive research is still needed to be approved for mainstream use but we have made major strides in tacking what could have been the end of humanity.

But producing organisms in a lab is not as fun as it sounds. Scientists come in contact with thousands of dangerous pathogens in labs every day which puts their lives and the lives of those around them at serious risk. One error can lead to a biosecurity breach which can cause a major worldwide pandemic that can claim countless lives. Having witnessed firsthand the colossal damage a pandemic has on humans and the global society, there is a huge responsibility on the shoulders of scientists to prevent such happenings if this synthetic biology inevitably takes over.

The possibility of synthetic biology can to some people mean going to war with nature. But it isn't. It is working together with nature, and that is an exciting time to look forward to!

References

1. https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/
3. https://www.frontiersin.org/articles/10.3389/fphar.2019.00513/full
4. https://www.genome.gov/about-genomics/policy-issues/Synthetic-Biology#:~:text=Synthetic%20biology%20is%20a%20field,in%20medicine%2C%20manufacturing%20and%20agriculture.