FUTURISTIC NON-ANTIBIOTIC STRATEGIES TO COMBAT ANTIBIOTIC-RESISTANT PATHOGENS

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THE PROBLEM OF ANTIMICROBIAL RESISTANCE AND THE WAY FORWARD

- Discovery of antibiotics to treat infectious diseases had a phenomenal impact on human and animal health since 1940s.
- When the antibiotic penicillin began to be used in the 1940s it was a life-saving drug and heralded as "the wonder drug".
- Currently, every year, 700 000 patients die globally due to antimicrobial resistance (AMR).
- It has been estimated that this death toll will increase to 10 million by 2050, which would lead to a reduction of gross domestic product (GDP) by at least 2.5%.
- **is the time of antibiotics up?** Although antibiotics have served humanity well for the last 70.

- The cost and complexities of drug discovery and development have shifted the investment equation away from the development of drugs targeting short course therapies for acute diseases and towards long-term treatment of chronic conditions.

- It can take 10-15 years and over $1billion to develop a new antibiotic.

- Companies invest huge amounts of money to bring a new drug to market but cannot recover their costs or make a profit.

- Big Pharma has mostly abandoned antibiotics development, and seven of the 12 companies that successfully brought a drug to market in the past decade went bankrupt or left the antibiotics business because of poor sales.

"This is the only field within pharmaceutical science where you come out with a drug and you don't want it to be used too much"

Anand Anandkumar, CEO of Bugworks

ARE WE HOPELESS?

- Numerous innovative approaches to antibiotics exist for treating resistant bacteria.

ANTIMICROBIAL PEPTIDES (AMPS)

- Plants, animals and fungi have vastly different immune systems, but all make peptides — small proteins — that destroy bacteria.
- Peptides from creatures such as amphibians and reptiles, which are unusually resistant to infection, could yield new therapeutics.
- Peptides with antibacterial activity have been isolated from frogs, alligators and cobras, among others, and some seem to be effective in epithelial cell cultures and at healing wounds in mice.
- These peptides can be modified to increase their potency, and several are in clinical trials.
- synthesizing such molecules can be expensive, a hurdle that scientists must overcome to bring new peptide drugs to market.

PHAGE THERAPY

- Phage therapy dates back to the beginning of the 20th century, even before Alexander Fleming's discovery of penicillin in 1928.
- Phage therapy is extensively investigated as an alternative therapy to combat bacterial infections.
- The technique is gaining popularity in present scenario because phages are ubiquitous, host-specific and harmless and can be administered orally along with food.

- Recombinant phages are developed to deliver antimicrobial proteins in target bacteria. The therapy can be used topically on open wounds, or given intravenously in case of systemic infections.

- their fine specificity toward host bacterium species is a major concern.

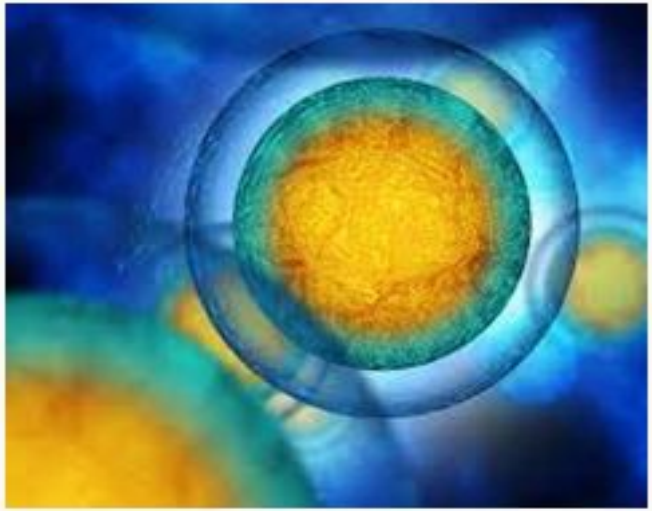
- it is essential that pathogen must be identified before selecting a phage as therapeutic strategy.

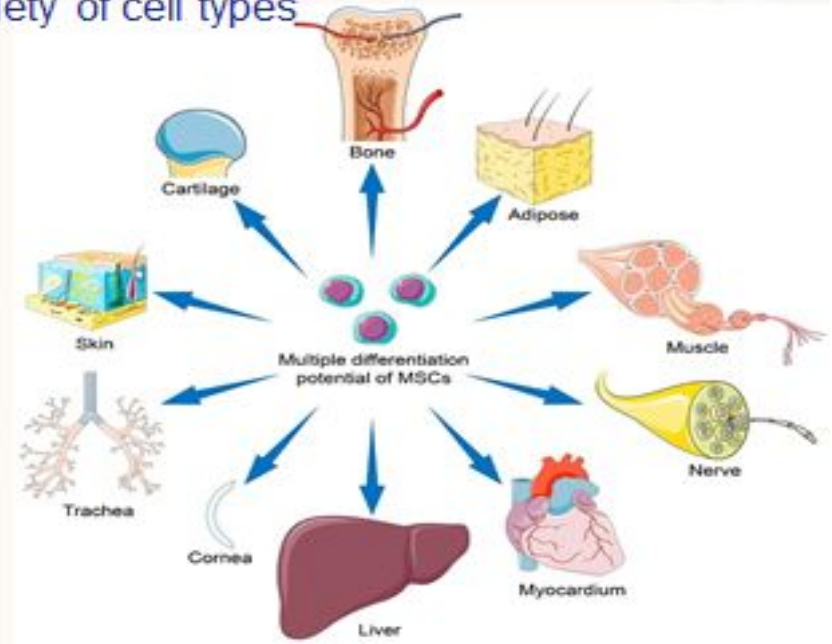
ENZYBIOTICS

- The term is derived from a combination of the words "**enzyme**" and "**antibiotics**."
- Proteolytic enzymes called endolysins have demonstrated particular effectiveness in combating a range of bacteria and are the basis for enzybiotic research.
- Endolysins are derived from bacteriophages and are highly efficient at lysing bacterial cells.
- Lysins can be engineered to kill several pathogens including Gram-negative bacteria.

STEM CELL-DERIVED ANTIMICROBIAL PEPTIDES

- Also known as mesenchymal stromal cells or medicinal signaling cells are multipotent stromal cells that can differentiate into a variety of cell types





- Mesenchymal stem cells (MSCs) have been extensively studied for several decades to develop a safe and promising therapeutic product against a broad range of chronic diseases.

- Human MSCs synthesize factors that behave as antimicrobial peptides (AMPs) that eradicate the bacteria.

- Secretome from MSCs, which significantly reduces the bacterial infections including the antibiotic-resistant MRSA, represents a hopeful approach.

NANOANTIBIOTICS

- Nanoparticulate materials can either be used to deliver antimicrobial substances or may contain antimicrobial substances.
- due to less toxicity and enhanced antimicrobial activity, nanoparticles are regarded as promising therapeutic candidates for future applications in biomedical sciences.
- Nanoantibiotics have antibacterial properties of their own via several mechanisms.
- Due to these diverse mechanisms of action, nano-antibiotics are likely to be effective against antibiotic resistant bacteria.

FECAL MICROBIOTA TRANSPLANT (FMT)

- Fecal microbiota transplant (FMT), also known as a stool transplant, is the process of transferring fecal bacteria and other microbes from a healthy individual into another individual.

- Few studies have shown that FMT is an effective treatment regimen for people with *C. difficile* infection along with other gastrointestinal diseases, such as irritable bowel syndrome, colitis, constipation, diarrhea and several other neurological conditions such as Parkinson's, multiple sclerosis, etc.

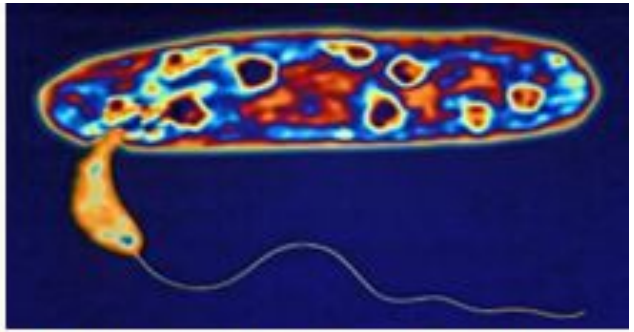
QUORUM-SENSING INHIBITORS

- Formation of biofilms and quorum sensing are the two important attributes of bacterial species enhancing the chances of their survival under adverse environments.

- Quorum sensing is one of the main methods of intracellular communication between bacteria.

- natural and synthetic molecules can block quorum sensing, which are under study in experimental models with interesting results.

PREDATORY BACTERIA



- Bacteria cause infection, but some can also fight it by preying on fellow microbes.
- The best-known species, *B. bacteriovorus*, is found in soil. It attacks prey bacteria by embedding itself between the host's inner and outer cell membranes, and begins to grow filaments and replicate.
- This preliminary research is attracting attention.
- Several US agencies are funding groups studying predatory bacteria.

METALS

- Metals such as copper and silver are the oldest antimicrobials.
- They were favored by Hippocrates in the fourth century BC as a treatment for wounds.
- Because metals accumulate in the body and can be highly toxic, their use may be restricted mostly to topical ointments for skin infections.
- An exception is gallium, which is toxic to bacteria that mistake it for iron, but is safe enough in people to be tested as an intravenous treatment for lung infections.

SUMMARY

- Antibiotic resistance can affect the people or animals at any stage of life.
- It is advisable to develop alternative therapies to lessen the dependence on chemical therapeutics.
- Clinicians should avoid unnecessary prescription and over prescription of antibiotics to the patients having normal infections and advise the patients to follow good hygiene such as hand washing and appropriate infection control measures.

THANK YOU