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NEMPS
(NORTH EASTERN MEDICAL PHARMACOLOGICAL SOCIETY)

Design by **Ashish Debnath** on behalf of **Creative Design,** Dibrugarh, Assam

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From the President's Desk

Nowadays, a range of online and paper-based journals devoted to the study of Pharmacology are published in the world. They are mainly published by universities and academic institutions. Already for 2nd year now, the NEMPSULE has taken a good shape. For various reasons, the journal was unable publish in time.

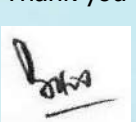
Presently, the bulletin will be equally focused on studying the modernity. The editorial board are trying hard to release 2nd issue dedicated to specific topics of relevance.

Such specificity of a journal necessitates the involvement as authors andanalytical community, who know the subject well within their competence.

We will try to reflect a wide variety of opinions of different experts, so that our reader gets a comprehensive idea of the subject of one's interest. Such approach will allow users to track and evaluate the most important topics that constantly appear in the field of studying the Pharmacology.

How successfully we will achieve the stated goals largely depends on the activity of our potential authors – not only reputable scientists, but also young scientists starting their journey in Pharmacology and ready to participate in the development of the global knowledge system.

Thank you team NEMPSULE



Prof B. K. BEZBARUAH
President, NEMPS
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Message from the General Secretary, NEMPS

It is a matter of pride to pen down the message for the 2nd edition of NEMPSULE - The E-Bulletin of NEMPS as a General Secretary. We have witnessed the evolution of NEMPS since the formation, having organized two successful conferences and published one edition of NEMPSULE.

The first edition of NEMPSULE was a successful endeavour with various scholarly articles and the expectations from the second edition was even more. It's never easy to publish E-Bulletin twice a year, but the editorial team, comprising of the editor Dr.Gayatri Sarma, and the members of the Scientific Committee, Dr. Meghali Chaliha, Dr. Chinmoyee Deori and Dr. Anju L Saikia, had made it possible with their scientific acumen and hard work.

I would like to thank and congratulate the editorial team for the successful publication of the 2nd edition of NEMPSULE.

Long Live NEMPS.

Swapnanil Gohain

Dr. Swapnanil Gohain
General Secretary
NEMPS

From The Desk of The Editor

It gives me immense pleasure in presenting to our readers the second issue of the NEMPSule of the year 2024 and extend a warm welcome to all of you as you embark on this academic sojourn through it's pages.

The NEMPSule, the official e-Bulletin of NEMPS, is designed to encompass topics related to all aspects of Pharmacology and Therapeutics with special emphasis on recent updates. The primary objective of the Editorial team is to maintain the e-bulletin's quality, ensure its continuity while at the same time promote inclusivity. And we are pledged and totally committed towards achieving this objective. But our efforts are futile without the support of the esteemed members of the NEMPS.

NEMPS is a proud association of several eminent pharmacologists of national and international repute. At the same time, NEMPS also has in it's stride a huge bunch of highly energetic and dynamic young members. Dissemination of knowledge among the members of NEMPS would go a long way in building up a strong, confident Association. And the NEMPSule serves as the most deserving platform for the same. Hence, it is my sincere and humble request to all members to heartily contribute articles and extend their wholehearted cooperation in this regard.

This issue of NEMPSule comprises a wide array of topics including Regenerative medicine , Radiopharmaceutical Therapy , Liquid Biopsy, Autophagy and many more. I have tried my level best to keep this issue free from any errata and also make the pages of the e-Bulletin more compatible with mobile phones.

I heartily thank all the contributors of the NEMPSule from the bottom of my heart for taking out time off their busy schedule to pen down a few lines for the e-Bulletin . I also thank the President NEMPS, Dr. Babul Bezbarua Sir and NEMPS General Secretary, Dr. Swapnanil Gohain for their persistant support and advice. I thank all members of the scientific committee Dr. Meghali Chaliha, Dr. Chinmoyee Deori and Dr. Anju L. Saikia, for having offered their valuable time to review the articles.

Long Live NEMPS !
Long Live NEMPSule !

Thanks and regards,

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Recent advances in Radiopharmaceutical Therapy

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Introduction:

Radioligand therapy (RLT) is a form of precision nuclear medicine that may recognize and treat diseases by harnessing the power of radioactive atoms. RLTs are able to deliver radiation to target cells anywhere in the body. RLT have two primary components: the radioisotope and the cell-targeting compound, or ligand. Therapeutic radioisotopes are produced in special nuclear reactors or generators, then shipped to a production facility where the radioisotope is bonded to the cell-targeting compound. The finished product is then placed in vials, sent through quality testing, packaged into special lead-shielded containers, and shipped directly to the hospital or clinic as a ready-to-use therapy. Radioimmunotherapy (RIT, a type of RLT) combines radiation therapy with immunotherapy like Monoclonal Antibodies (MABs) are paired with radioactive materials (radiotracers). These MABs specifically target cancer cells, and the radiotracers emit radiation, delivering it directly to the tumor cells, thus normal tissues are spared due to the antibody's specificity. It's effective when tumor cells express unique antigens.

Mechanism of action:

In RIT, the antibody and radioactivity are decoupled, the immunoglobulin is injected days before a small molecule radioligand, and a highly selective ligation is used to drive the in vivo combination of the two components at the tumour site. Thus, the antibody spends most of its time in circulation unlabelled and only becomes a radioimmunoconjugate after it has bound to the tumour and reacts with its rapidly circulating small molecule counterpart. This method is designed to deliver high doses of radiation to malignant tissue while minimizing the radiation dose to healthy organs, by using shorter-lived therapeutic nuclides (e.g., lead-212, bismuth-213, and astatine-211) that are normally incompatible with vectors such as antibodies with slow pharmacokinetic profiles.[1] This procedure contains four essential steps: (1) the administration of an immunoconjugate bearing one half of the system's molecular couple; (2) an interval period during which the antibody accumulates at the tumor and clears from the blood; (3) the injection of a small-molecule radioligand containing the other half of the system's molecular couple; and (4) the in vivo ligation between the two components followed by the rapid clearance of excess radioligand.[1]

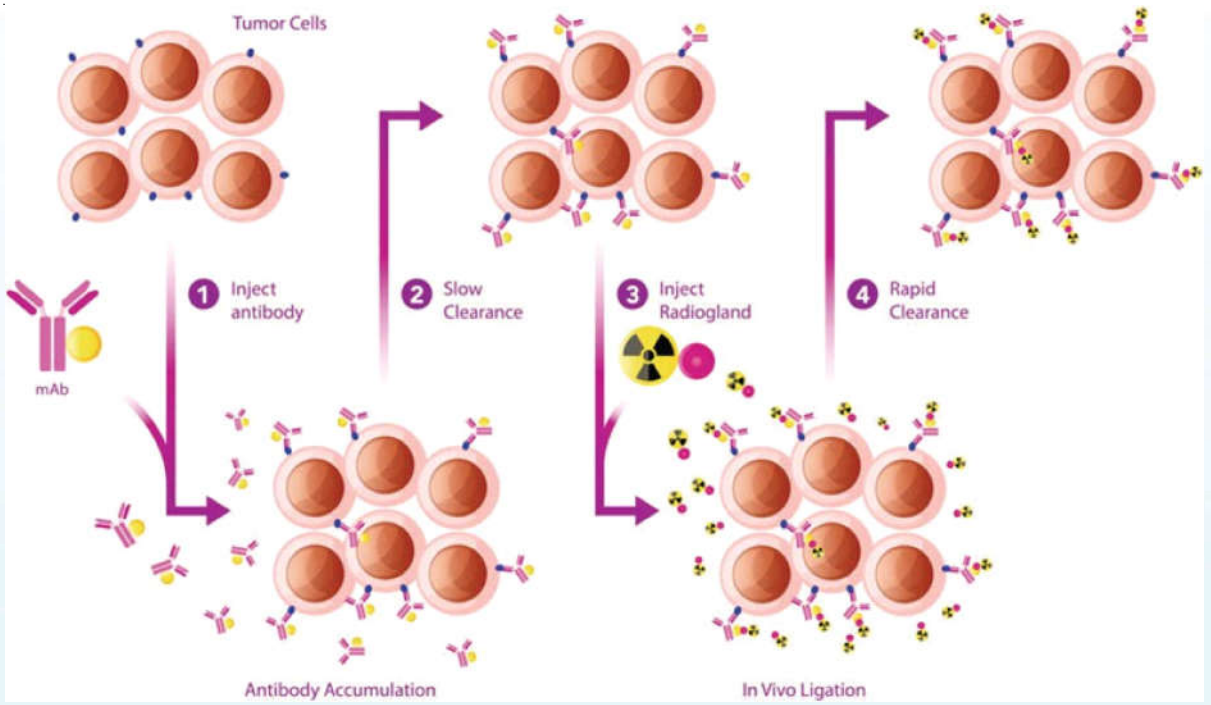

Fig1: Four essential steps in RLT[1]

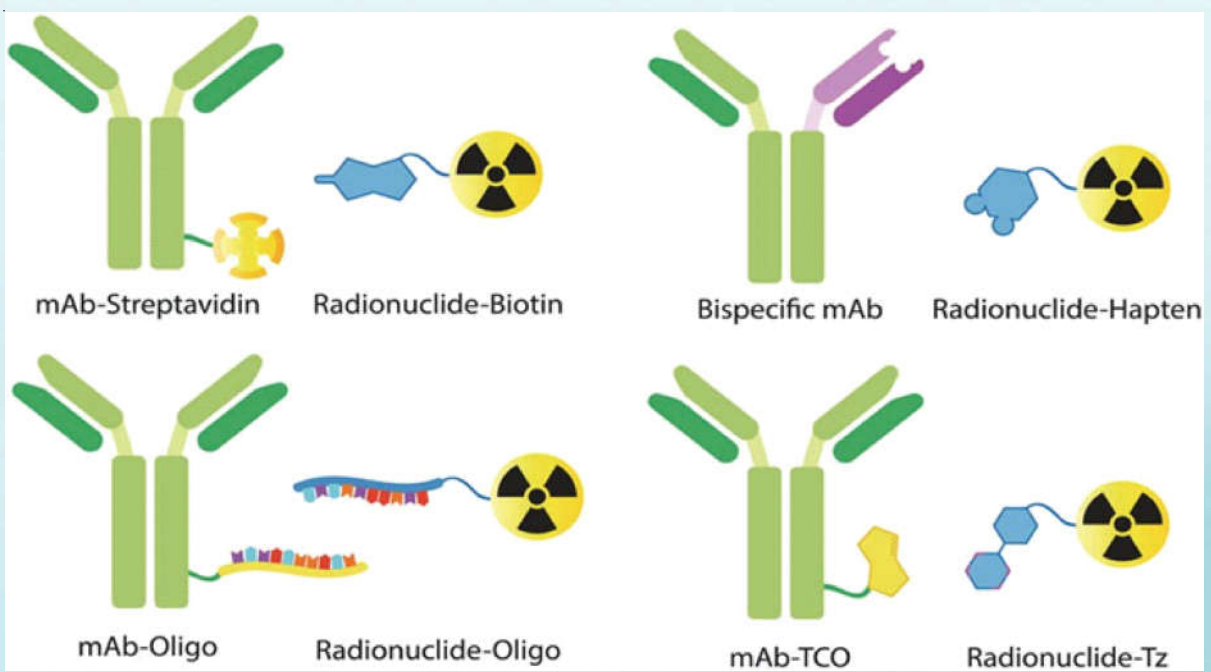

Fig: 2 Four different approaches to in vivo Targeting. *TCO: trans*-cyclooctene, *Tz :* tetrazine[1]

Targeting strategies based on streptavidin and biotin: A variety of molecular couples have been used for in vivo targeting, including streptavidin and biotin, bispecic antibodies (bsAbs), complementary oligonucleotides, and biorthogonal click chemistry. It contains the following steps: (a) a streptavidin-modified mAb is administered before a radiolabeled biotin; (b) To decrease the radiation dose to the blood and other healthy tissues, a galactose-bearing, biotin-based clearing agent is used between the administration of the mAb-streptavidin and the radioligand; (c) To prevent natural biotin from blocking

the binding sites on streptavidin, a biotinylated mAb and an avidin-based clearing agent have been used. In this approach, a biotin-modified antibody is administered first. Subsequently, avidin is injected to bind circulating biotin and circulating immunoconjugate and rapidly clear both to the liver. Streptavidin is then injected to bind the tumor-associated mAb-biotin immunoconjugate, followed, finally by a biotin-based radioligand.[1]

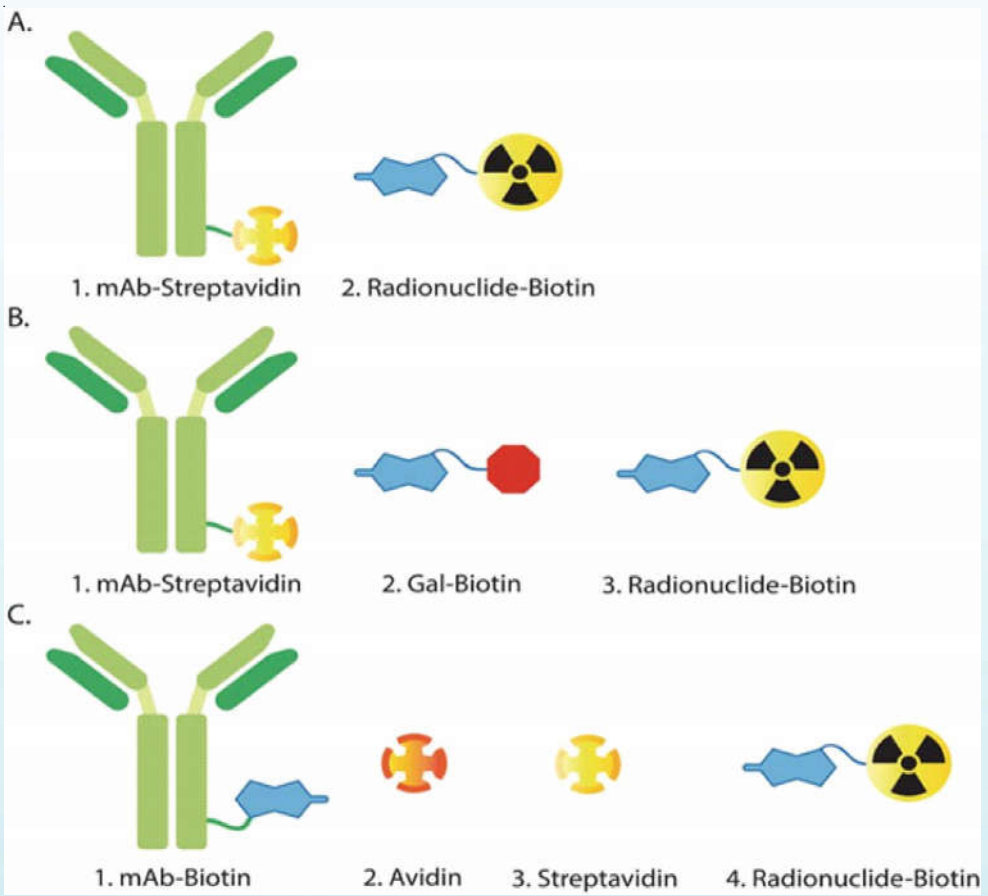

Fig. 3 Targeting strategies based on streptavidin and biotin[1]

Targeting strategies based on bispecic antibodies and radiolabeled haptens: (a) A tumor-specic Fab fragment chemically linked to a radiometal-chelator- specic Fab fragment with a monovalent radiometal- chelator complex used as the radioligand. (b) Two chelators linked together with a peptide chain, thereby forming a bivalent radioligand that can bind two bsAbs. (c) A tumor- specic Fab fragment chemically linked to a histamine-succinyl-glycine (HSG)-specic Fab fragment. The radioligand consists of two HSG haptens linked together with a peptide chain that contains a functional group to which a chelator or other radiolabeling prosthetic group can be attached. (d) A tri-Fab scaffold containing two anti-tumor Fab fragments and one anti- HSG Fab fragment. [1]

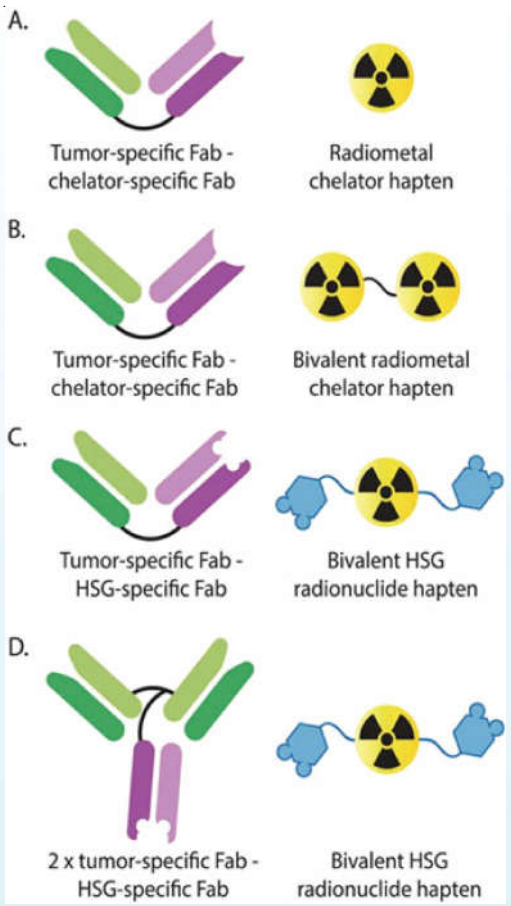

Fig:4 Targeting strategies based on bispecic antibodies and radiolabeled haptens[1]

Recent advances:

Targeting systems based on bispecific antibodies and radiolabeled haptens have generated exciting clinical data with both 68Ga- and 177Lu-labeled radioligands. Recently, the US Food and Drug Administration (FDA) approved Pluvicto™ (lutetium Lu 177 vipivotide tetraxetan), for the treatment of adult patients with a certain type of advanced cancer called prostate-specific membrane antigen–positive metastatic castration-resistant prostate cancer (PSMA-positive mCRPC) that has spread to other parts of the body. [2]

Radioligand therapy (RLT) has shown promising efficacy in the treatment of various cancers: Disease Control: In a study involving patients with advanced sarcoma and other cancers, the disease control rates according to the radiographic and molecular response were 77% and 71%, respectively. The median overall survival and median progression-free survivals were 14 and 11.8 months, respectively.[3]

Improved Survival Rates: The FDA-approved Pluvicto™ (lutetium Lu 177 vipivotide tetraxetan) for the treatment of PSMA-positive metastatic castration-resistant prostate cancer (mCRPC) has shown a statistically significant reduction in the risk of death. [2]

Anti-Tumor Activity: Combination of radioligand therapy and Pembrolizumab, significant anti-tumor activity was observed with 56% of participants having a positive response. [3]

Better Efficacy with Minimal Toxicity: Compared to other systemic cancer therapies, RLT has shown better efficacy with minimal toxicity.[3]

Potent Option for Managing Certain Types of Cancers: RLT combines the specificity of molecular targeting agents with the therapeutic efficacy of radiation, making it a potent option for managing certain types of cancers. [3]

There are several ongoing clinical trials related to Radioligand Therapy (RLT):

Salivary Gland Cancers, Renal Cell Carcinoma, High Grade Glioma, and Soft Tissue Sarcoma: There are early reports in small case series and relevant ongoing early clinical trials for these types of cancers .[4.]

Differentiated Thyroid Carcinoma and Tumors of the Sympathoadrenal Axis:

Radiotheranostic agents such as radioiodine for differentiated thyroid carcinoma and Iodine-131-labeled meta-iodobenzylguanidine therapy of tumors of the sympathoadrenal axis are being used. [5.] Gastroenteropancreatic Neuroendocrine Tumors and Lymphoma: RLT has been shown to be safe and effective in a variety of disease states, including gastroenteropancreatic neuroendocrine tumors and lymphoma.[6.]

Conclusion

One of the fascinating aspects of RLT is the potential to combine different kinds of radioactive atoms, and targeting molecules, into different combinations unique for a particular type of tumor. There is an expanding role of radiotheranostics as a safe and effective therapy option in the management of oncology patients. There is increasing interest in developing novel radiotheranostics agents to fully exploit the huge potentials of radiotheranostics as a viable form of personalized cancer care.

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Fostemsavir: Aiming at a Novel Target

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Introduction

Fostemsavir is a novel HIV-1 attachment inhibitor approved by the FDA for treating heavily treatment-experienced (HTE) adults with multidrug-resistant HIV-1 infection. It has been thoroughly studied in clinical trials to evaluate its efficacy and safety in this specific patient population.

Mechanism of Action

Fostemsavir works by inhibiting the gp120 subunit within the gp160 envelope glycoprotein, a crucial step in the HIV-1 replication cycle. This inhibition prevents the virus from attaching to and entering host cells, thereby reducing the viral load and slowing disease progression. Fostemsavir is effective in reducing viral load and improving CD4 cell count in individuals with multidrug-resistant HIV-1. Its unique mechanism of action allows it to overcome resistance developed by HIV-1 to other antiretroviral therapies (ARTs), making it a valuable addition to the antiretroviral therapy arsenal. Additionally, fostemsavir interacts with other antiretroviral medications, enhancing their efficacy when used in combination therapy regimens. The drug has a favourable pharmacokinetic profile with a half-life of approximately 12 hours.[1]

Efficacy

The efficacy of fostemsavir was evaluated in the phase 3 BRIGHTE study, which compared outcomes in individuals receiving fostemsavir or placebo combined with a failing background regimen for 8 days. The study demonstrated significant improvements in viral load suppression and CD4 cell count increases in the fostemsavir group compared to the placebo group. At week 96, 54.5% of participants achieved HIV-1 RNA levels of less than 40 copies per mL. [2]

Clinical Trials

1. **Phase IIa Study:** This study assessed the antiviral activity of fostemsavir in an 8-day monotherapy in 50 participants across five different dosing arms. The study included both ART-naive and ART-experienced patients. The maximum median decline in HIV RNA viral load from baseline varied from 1.21 log10 copies/mL in the 1200 mg fostemsavir BID arm to 1.73 log10 copies/mL in the 1200 mg fostemsavir plus 100 mg ritonavir BID arm. Despite the use of ritonavir, the decline in viral load was consistent.
2. **Phase IIb Study:** In this trial, treatment-experienced patients were randomized to receive different doses of fostemsavir or atazanavir/ritonavir, all with optimized background therapy. The primary endpoint was the proportion of subjects with HIV RNA viral load <50 copies/mL at week 24.
3. **Phase III BRIGHTE Study:** This pivotal trial enrolled 372 HTE participants with multidrug-resistant HIV-1 infection. It included a randomized cohort (n=272) with at least one fully active agent in less than two antiretroviral classes and a nonrandomized cohort (n=99) without any remaining antiretroviral options.

Safety and Side Effects

Serious side effects of fostemsavir include:

- **Immune Reconstitution Inflammatory Syndrome (IRIS):** An inflammatory response to indolent or residual opportunistic infections that may require further evaluation and treatment.
- **Hypersensitivity Reactions:** Symptoms include swelling of the face, lips, tongue, or throat, fast/irregular heartbeat, severe dizziness, and fainting.
- **Serious Eye Symptoms:** Sudden vision loss, blurred vision, tunnel vision, eye pain or swelling, or seeing halos around lights.
- **Serious Heart Symptoms:** Fast, irregular, or pounding heartbeats; fluttering in the chest; shortness of breath; sudden dizziness, light-headedness, or passing out.

The long-term safety of fostemsavir was evaluated in the BRIGHTE study, which showed that the drug maintained its safety profile over a 240-week treatment period. Common adverse events at Week 240 included nausea, diarrhoea, headache, abdominal pain, indigestion/heartburn, fatigue, rash, sleep disturbance, IRIS, drowsiness, and vomiting. Serious drug reactions occurred in 3% of participants at Week 96 and 4% at Week 240, including severe IRIS in 3 cases.

Indications and Administration

Fostemsavir is an antiretroviral medication used in combination with other antiretroviral drugs to treat HIV-1 infection. It is specifically indicated for:

1. **HTE Adults:** Heavily treatment-experienced adults with multidrug-resistant HIV-1 infection.
2. **Multidrug-Resistant HIV-1 Infection:** Patients who have failed previous antiretroviral therapies due to resistance, intolerance, or contraindications to other medications.

Regimens and Administration

Indications

Fostemsavir is prescribed for adults with HIV-1 who have a history of extensive antiretroviral treatment and are dealing with multidrug-resistant strains of the virus. This medication is crucial for those who have not responded adequately to standard treatments and need an alternative to manage their condition effectively. [3]

Dosage

The recommended dosage for Fostemsavir is:

- **600 mg taken orally twice daily.**
- It must be taken in combination with other antiretroviral drugs to ensure effectiveness.

Administration

- **Oral Intake:** Fostemsavir tablets should be swallowed whole, not chewed, crushed, or split.
- **Consistent Schedule:** It's important to take Fostemsavir at the same times each day to maintain consistent levels of the medication in the bloodstream.
- **With or Without Food:** Fostemsavir can be taken with or without food, making it flexible for patients' routines.

Conclusion

Fostemsavir is a significant addition to the antiretroviral therapy arsenal due to its novel mechanism of action, efficacy, and safety profile. Its ability to overcome resistance developed by HIV-1 to other ARTs makes it an essential treatment option for heavily treatment-experienced adults with multidrug-resistant HIV-1 infection. The BRIGHTE study demonstrated its long-term efficacy and safety, maintaining a high proportion of participants with virologic suppression over a 240-week period.

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R21/Matrix-M™ Malaria Vaccine

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Malaria remains one of the leading causes of morbidity and mortality worldwide.[1] Human malaria is caused by five *Plasmodia* species, of which *P. falciparum* is the most common and the most deadly. *P. vivax* is also an important cause of morbidity and mortality worldwide. Malaria parasites are members of the genus *Plasmodium*, a class of unicellular eukaryotes that are obligate parasites of multiple species of insects and vertebrae, including birds and mammals.[2] *Plasmodium falciparum* is a complex pathogen with numerous immune evasion mechanisms. Development of an efficacious vaccine against this parasite has remained elusive for many decades.[1]

The leading malaria vaccine candidate, RTS,S/AS01, induces partial efficacy through induction of antibodies against the central repeat (Asn-Ala-Asn-Pro [NANP]) of the circumsporozoite protein (CSP).[3] RTS,S/AS01 was not prequalified for use by WHO due to increased incidence of meningitis, cerebral malaria cases and increased female mortality seen in many studies, but instead a malaria vaccine implementation programme was launched in three countries over the course of 2019.[4] RTS,S vaccine was later on approved in October 2021 by the World Health Organization (WHO). Four doses of RTS,S vaccine reduce clinical malaria cases by 39% and severe malaria by 30%. Given the extreme burden malaria puts on families, communities and economies across the world, this is not insignificant, and the vaccine has already been given to one million children in pilot roll-outs since 2019.[2]

R21/Matrix-M™ is a newly developed malaria vaccine which has been recommended for use by the World Health Organization's Strategic Advisory Group of Experts (SAGE) and the Malaria Policy Advisory Group (MPAG). R21 is a novel pre-erythrocytic candidate malaria vaccine. R21 and RTS,S both include HBsAg fused to the C-terminus and central repeats of the CSP, which self-assemble into virus-like particles in yeast. R21 lacks the excess HBsAg found in RTS,S. R21 comprises only fusion protein moieties, in contrast to RTS,S, which comprises 20% with the remaining 80% being HBsAg monomers expressed alone, thereby likely diminishing CSP coverage of the virus-like particle surface.[5,6] The highly effective vaccine developed by the University of Oxford and the Serum Institute of India, leveraging Novavax's adjuvant is critical to reducing over half a million malaria-related deaths annually. This was declared by Serum Institute of India Pvt. Ltd., Pune, India in a Press Release on the 2nd of October 2023.

R21/Matrix-M™ malaria vaccine has demonstrated high efficacy with a reassuring safety profile. It is an easily deployable vaccine that can be manufactured at mass scale and modest cost, enabling as many as hundreds of millions of doses to be supplied to countries which are suffering a significant malaria burden. The Serum Institute of India has already established production capacity for 100 million doses per annum, which will be

doubled over the next two years. The World Health Organization's recommendation today is required for UNICEF to procure and GAVI to purchase the vaccine, paving the way for vaccination of children in populations most at risk. R21/Matrix-M™ malaria vaccine marks the culmination of 30 years of malaria vaccine research at the University of Oxford's Jenner Institute.

It has been recommended for use by the World Health Organization (WHO) after meeting required safety, quality and effectiveness standards. Following a rigorous, detailed scientific review by the WHO's independent advisory body, the Strategic Advisory Group of Experts (SAGE) and the Malaria Policy Advisory Group (MPAG), the R21/Matrix-M™ malaria vaccine has been recommended for use. The recommendation was based on pre-clinical and clinical trial data which showed good safety and high efficacy in four countries, at sites with both seasonal and perennial malaria transmission, making it the world's second-ever WHO recommended vaccine for preventing malaria in children.

The vaccine was developed by the Jenner Institute at Oxford University and Serum Institute of India with support from the European and Developing Countries Clinical Trials Partnership ('EDCTP'), the Wellcome Trust, and the European Investment Bank ('EIB'). To date the R21/Matrix-M™ malaria vaccine has been licensed for use in Ghana, Nigeria and Burkina Faso. Ghana was the first country to approve this vaccine in April 2023. In combination with public health measures such as the use of insecticide-treated bed nets, this vaccine can help save and improve the lives of millions of children and their families.

There was some waning of efficacy over the first year of follow-up at both seasonal and perennial transmission sites, but a booster dose restored efficacy at the seasonal sites with a vaccine efficacy over 18 months of 74% (70-77; p<0.001). Significantly higher vaccine-induced antibody titres were observed in the 5–17-month age group compared with 18–36-month-olds (p<0.0001). The younger age group, in whom this vaccine is most likely to be widely deployed, showed the highest 12-month vaccine efficacy at both seasonal, 79% (73-84, p<0.001), and standard sites, 75% (65-83, p<0.001).[7]

In a previous Phase IIb clinical trial conducted in Burkina Faso, Oxford researchers and their partners reported 2 year efficacy and showed that that a booster dose of R21/Matrix-M™ maintained high efficacy against malaria and continued to meet the World Health Organization's Malaria Vaccine Technology Road map goal of a vaccine with at least 75% efficacy. This followed earlier results from the same trial reporting 1 year efficacy of 77%.[1] The Phase III results improve understanding of how vaccine efficacy varies with age and across regions in relation to transmission intensity and seasonality. Further studies are also exploring optimal dosing schedules and tracking long-term immune response.

When the anopheles mosquito that carries the malaria parasite bites a person, it sends the parasite through the bloodstream, where it shape shifts through stages of its life cycle. The complexity of the malaria parasite's life cycle has meant vaccine development has been hampered for years. The R21/Matrix-M™ vaccine targets the plasmodium 'sporozoite', which is the first form of the malaria parasite entering the human body. Only a few (10–100) sporozoites are injected by infected mosquitoes before the parasite multiplies, making them the ideal target for a vaccine. R21 is a subunit vaccine that delivers parts of a protein secreted by the sporozoite that are bundled up with a part of the hepatitis B virus that is known to trigger a strong immune response. The vaccine also contains Novavax's Matrix-M, an "adjuvant" which boosts the immune system response to make it more powerful and long-lasting. Vaccines work by putting the antigen, which is the piece of the virus or bacteria that our system recognises and responds to, in front of our immune cells. This technology – that was used in Novavax's COVID-19 vaccine – induces the influx of antigen-presenting cells at the injection site and enhances antigen presentation in local lymph nodes, which means that the immune system is triggered as strongly as possible.

Thus, the R21/Matrix-M™ vaccine comes as a true ray of hope along with RTS,S vaccine to

fight against the serious burden of malaria across the world, specially in the poor developing countries of Africa and Asia.

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New small molecule offers hope in combating antibiotic resistance

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Researchers from the University of Oxford have developed a new small molecule that can suppress the evolution of antibiotic resistance in bacteria and make resistant bacteria more susceptible to antibiotics.

The global rise in antibiotic-resistant bacteria is one of the top global public health and development threats, with many common infections becoming increasingly difficult to treat. It is estimated that drug-resistant bacteria are already directly responsible for around 1.27 million global deaths each year and contribute to a further 4.95 million deaths. Without the rapid development of new antibiotics and antimicrobials, this figure is set to rise significantly.

A new study led by researchers at the Ineos Oxford Institute for antimicrobial research (IOI) and the Department of Pharmacology at Oxford University offers hope in the discovery of a small molecule that works alongside antibiotics to suppress the evolution of drug-resistance in bacteria.

One of the ways that bacteria become resistant to antibiotics is due to new mutations in their genetic code. Some antibiotics (such as fluoroquinolones) work by damaging bacterial DNA, causing the cells to die. However, this DNA damage can trigger a process known as the 'SOS response' in the affected bacteria. The SOS response repairs the damaged DNA in bacteria and increases the rate of genetic mutations, which can accelerate the development of resistance to the antibiotics. In the new study, the Oxford scientists identified a molecule capable of suppressing the SOS response, ultimately increasing the effectiveness of antibiotics against these bacteria.

The researchers studied a series of molecules previously reported to increase the sensitivity of methicillin-resistant *Staphylococcus aureus* (MRSA) to antibiotics, and to prevent the MRSA SOS response. MRSA is a type of bacteria that usually lives harmlessly on the skin. But if it gets inside the body, it can cause a serious infection that needs immediate treatment with antibiotics.

MRSA is resistant to all beta-lactam antibiotics such as penicillins and cephalosporins. Researchers modified the structure of different parts of the molecule and tested their action against MRSA when given with ciprofloxacin, a fluoroquinolone antibiotic. This identified the most potent SOS inhibitor molecule reported to date, called OXF-077. When combined with a range of antibiotics from different classes, OXF-077 made these more effective in preventing the visible growth of MRSA bacteria.

In a key result, the team then tested the susceptibility of bacteria treated with ciprofloxacin over a series of days to determine how quickly resistance to the antibiotic was developing, either with or without OXF-077. They found that the

emergence of resistance to ciprofloxacin was significantly suppressed in bacteria treated with OXF-077, compared to those not treated with OXF-077.

This is the first study to demonstrate that an inhibitor of the SOS response can suppress the evolution of antibiotic resistance in bacteria. Moreover, when resistant bacteria previously exposed to ciprofloxacin were treated with OXF-077, it restored their sensitivity to the antibiotic to the same level as bacteria that had not developed resistance.

Dr Thomas Lanyon-Hogg, Principal Investigator at Oxford's Department of Pharmacology said: 'This is a great example of what can be achieved through interdisciplinary collaboration between microbiologists in the IOI and chemical biologists in Pharmacology. The AMR crisis presents technical obstacles innumerous areas, and if the challenges we face as scientists are not confined to a single scientific discipline, then the solutions will not be either.'

Source:

University of Oxford

Journal reference:

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Liquid Biopsy- A Harbinger of Hope in The Diagnosis And Treatment of Diseases

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A biopsy is a procedure by which a piece of tissue or a portion of cells are removed from the body to identify a disease. This process is used to identify cancers or any other mass lesions. The traditional method of tissue biopsies usually employs invasive procedures. The procedures can be painful and cumbersome, often decreasing patient compliance.

This has led to the introduction of a groundbreaking technique for the detection and monitoring of cancer. This technique is known as liquid biopsy. Liquid Biopsy can detect cancer early, keep tabs on the real-time treatment and spot any minimally recurrent sickness. The procedures are less invasive, increasing patient compliance while monitoring disease progress and treatment efficacy. Understanding the evolution and genetics behind different cancers through liquid biopsy can help develop personalized medicine. [1] [2]

Different biological fluids like blood, urine and cerebrospinal fluid can be used to detect and interpret biomarkers. The biomarkers play an important role in cancer diagnosis and management of cancers like Lung, Breast, Prostate and Colorectal cancers. The common biomarkers seen in liquid biopsies are Circulating tumour DNA, Circulating Tumour Cells, Exosomes and MicroRNAs. [1] [2]

Circulating Tumour DNA:

These are small fragments of tumour DNA produced by necrotic or apoptotic cells. They keep moving freely in the bloodstream, can help in detecting cancer early and keep a track on the treatment provided. Digital PCR can be used for measuring Circulating Tumour DNA with high sensitivity and specificity. Cell free DNA that can emerge from Circulating Tumour DNA also help to know the various genes associated with the disease.[1] [2] [3]

Circulating Tumour Cells:

These cells break away from the primary tumour. They move into the blood unharmed and can be used to check for characteristics of the tumour, tendency to metastasise and treatment response. Molecular profiling and genetic changes like mutations, amplifications and deletions would result in use of targeted medicines that can go a great way in creating personalized treatment regimens. The cells are separated from blood samples by immunomagnetic separation, microfluidic devices, and filtration procedures. Increase in Circulating tumour cells count can lead to higher chances of metastasis and poor prognosis.[1] [2] [3]

Exosomes:

Extracellular vesicles are produced by the tumour cells that are found in body fluids like blood,

urine and saliva. They are called exosomes. The exosomes contain proteins, lipids and nucleic acids that can reach different cells altering their normal processes. These biomarkers can give an insight to the tumour microenvironment that will help greatly in treatment.[1] [2] [3]

MicroRNAs:

These are small non-coding RNA molecules. They are stable in body fluids like blood, urine and saliva which makes them preferable candidates for diagnosis and prognosis. miR-21 is found to be increased in breast, lung and colorectal cancer while miR-200 is important for the suppression of metastasis. miR-155 has been associated with resistance to chemotherapy in breast and lung cancer. [1] [2] [3]

The mutations seen in the different biomarkers can have a great role in the treatment of different diseases.

Lung Cancer:

Mutations in the Epidermal Growth Factor Receptor and Anaplastic Lymphoma Kinase from Circulating Tumour DNA analysis can help in choosing appropriate tyrosine kinase inhibitors for treatment. The most common mechanism of resistance to first and second-generation EGFR Tyrosine Kinase Inhibitors is the mutation of EGFR T790M. Third Generation EGFR Tyrosine Kinase Inhibitor, Osimertinib can be used in treatment of these cases. [1] [4] [5]

Breast Cancer:

Circulating Tumour Cells or DNA can be used to identify mutations in phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA), human epidermal growth factor receptor 2 (HER2), and breast cancer gene 1/2 (BRCA1/2) which can provide information for targeted treatment strategies. The phosphatidylinositol -4,5-bisphosphate 3- kinase α inhibitor Alpelisibwas approved for Metastatic Breast Cancer patients with PIK3CA mutations detected in ctDNA. [1] [2] [6]

Colorectal Cancer:

Gene mutations like Kirsten rat sarcomaviral oncogene homolog (KRAS), neuroblastomaras viral oncogene homolog (NRAS), and v-raf murinesarcoma viral oncogene homolog B1 (BRAF) can be detected. Patients who were positive for Circulating Tumour DNA after surgery were administered adjuvant chemotherapy of 5-fluoropyrimidine oroxaliplatin-based chemotherapy in the DYNAMIC trial. The researchers found an increase in survival benefit in patients with stage II colon cancer having detectable Circulating TumourDNA after surgery.[1] [2] [7]

Prostate Cancer:

Liquid biopsies can detect gene mutations like transmembrane protease, serine 2, gene-erythroblast transformation-specific-relatedgene (TMPRSS2-ERG), androgen receptor (AR), and phosphatase and tensin (PTEN). [1] [2] [8]

Ovarian Cancer:

Liquid biopsy can treat Circulating Tumour DNA with BRCA1 and BRCA2 mutations. All cases with reversions had become resistant to platinum or PARP-inhibitors at the time of blood collection as per Christie et. al. [1] [2] [9]

Neurological Diseases:

The neural-derived exosome biomarker data demonstrates certain cargo proteins as therapeutic targets. The blocking of astrocyte complement-mediated neurotoxicity and restoring growth and regenerative factors ofthe small, but widespread, set of chondroitin sulfate proteoglycan type 4 (CSPG4) cells can be helpful in Alzheimer's Disease. The alteration of various kinases and proteases activities; and restoring levels of excitatory synaptic proteins may also be useful efforts, but lack of specificity is proving to be an obstacle. In cerebrovascular disease, there are favourable efforts to block complement-mediated endothelial toxicity. Enhancing eNOS activity in endothelial cells by suppressing the level of NOSTRIN and enhancing angiogenesis of

collateral vessels by increasing endothelial P-YAP-1 transcriptional activityis a source of encouragement.[1] [2] [10]

Concluding, we can say that liquid biopsies can revolutionize the way diseases are diagnosed and treated. Through non-invasive, continuous, and thorough molecular profiling it can open avenues forearly cancer detection, individualized therapy selection, and treatment response tracking. With further development, standardization and regulatory clearances liquid biopsies can play an important role in boosting fast diagnosis and early cure in different diseases. The doctors, pharmaceutical industries, governments and the regulatory agencies can come together to achieve a significant milestone in the future.

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Autophagy and Intermittent Fasting

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Autophagy, a cellular process for degrading and recycling cellular components, plays a crucial role in maintaining cellular homeostasis, responding to stress, and promoting survival during nutrient deprivation. The term "autophagy" comes from the Greek words "auto," meaning self, and "phagy," meaning eating. This self-digesting process allows cells to remove damaged organelles and proteins, thus preventing the accumulation of cellular debris and promoting cellular renewal.

Mechanisms of Autophagy

Autophagy begins with the formation of a double-membraned structure called the phagophore, which engulfs the targeted cellular components. The phagophore then matures into an autophagosome, which subsequently fuses with a lysosome to form an autolysosome. In the autolysosome, the engulfed material is degraded by lysosomal enzymes[1].

The breakdown products, such as amino acids and fatty acids, are then released back into the cytoplasm for reuse by the cell. The regulation of autophagy involves various signalling pathways, with the mammalian target of rapamycin (mTOR) pathway being one of the most significant[2]. mTOR acts as a nutrient and energy sensor, inhibiting autophagy when nutrients are plentiful and promoting it during nutrient scarcity. Another key regulator is the AMP-activated protein kinase (AMPK), which activates autophagy in response to low energy levels.

Benefits of Autophagy

Autophagy has numerous health benefits, including[3]:

1. **Cellular Quality Control:** By removing damaged organelles and misfolded proteins, autophagy helps maintain cellular integrity and function.
2. **Adaptation to Stress:** During periods of stress, such as nutrient deprivation, autophagy provides an internal source of nutrients and energy, enhancing cell survival.
3. **Immune Response:** Autophagy plays a role in defending against infections by degrading intracellular pathogens.
4. **Cancer Prevention:** By removing damaged components that could potentially lead to cancer, autophagy contributes to the suppression of tumour development.
5. **Longevity:** Studies in various organisms have shown that autophagy contributes to increased lifespan, likely due to its role in maintaining cellular health and preventing age-related diseases[4, 5].

Intermittent Fasting and Its Impact on Autophagy

Intermittent fasting (IF) is an eating pattern that cycles between periods of eating and fasting[6]. Unlike traditional diets that focus on what to eat, IF focuses on when to eat. Common methods include the 16/8 method (fasting for 16 hours and eating during an 8-hour window), the 5:2 diet (eat-

ing normally for five days and restricting calories for two non-consecutive days), and alternate-day fasting[7].

Mechanisms of Intermittent Fasting

During fasting periods, the body experiences a shift in its energy metabolism. Glycogen stores in the liver are depleted, leading to increased fat oxidation and the production of ketone bodies. These metabolic changes mimic a state of nutrient scarcity, thereby activating autophagy pathways, particularly through the inhibition of the mTOR pathway and activation of AMPK[8].

Health Benefits of Intermittent Fasting[9]

1. **Weight Loss and Metabolic Health:** IF can help reduce body weight and improve metabolic parameters such as insulin sensitivity, blood sugar levels, and lipid profiles.
2. **Cellular Repair and Longevity:** By promoting autophagy, IF supports cellular repair mechanisms, which can contribute to increased lifespan and reduced risk of age-related diseases.
3. **Brain Health:** IF has been shown to enhance brain function and protect against neurodegenerative diseases by reducing oxidative stress, inflammation, and promoting autophagy.
4. **Reduced Inflammation:** IF helps decrease inflammation and oxidative stress, which are linked to many chronic diseases.
5. **Cancer Protection:** By enhancing autophagy and reducing insulin levels, IF may reduce the risk of certain cancers.

Intermittent Fasting and Autophagy: A Synergistic Relationship

The connection between intermittent fasting and autophagy highlights a synergistic relationship where IF induces autophagy, and in turn, autophagy mediates many of the health benefits associated with fasting. This relationship underscores the potential of IF as a non-pharmacological intervention for improving health and longevity.

Practical Considerations and Challenges

While the benefits of autophagy and intermittent fasting are compelling, there are practical considerations and challenges to keep in mind[10]:

1. **Individual Variability:** The effectiveness and tolerability of IF can vary widely among individuals. Factors such as age, sex, baseline metabolic health, and lifestyle can influence the outcomes.
2. **Sustainability:** Adherence to IF can be challenging, especially in social and cultural contexts where meal patterns are deeply ingrained.
3. **Potential Risks:** IF may not be suitable for everyone, particularly for individuals with certain medical conditions, eating disorders, or those who are pregnant or breastfeeding. It's essential to consult a healthcare provider before starting IF.

Conclusion

Autophagy is a vital cellular process that promotes health and longevity by maintaining cellular homeostasis, adapting to stress, and preventing disease. Intermittent fasting, by mimicking nutrient deprivation, activates autophagy and confers numerous health benefits, including weight loss, improved metabolic health, and enhanced brain function. While IF holds promise as a powerful tool for promoting health, it is important to consider individual variability and potential risks. As research continues to unravel the complex interplay between autophagy and intermittent fasting, these insights may pave the way for novel interventions in disease prevention and health promotion.

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Pharmacology and Hollywood

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Pharmacology and Hollywood have intersected in various ways, often with significant influence on public perception and understanding of drugs and medical treatments. Here are some notable aspects of this relationship:

1. Depiction of Drugs in Movies and TV Shows

- **Accuracy**: Hollywood's portrayal of drugs and their effects is often dramatized or inaccurate. Pharmacology helps to correct misconceptions created by these portrayals.
- **Examples**: Films like "*Requiem for a Dream*" and "*Trainspotting"* depict the severe consequences of drug addiction, while TV shows like "*Breaking Bad"* explore the illegal drug trade and methamphetamine production.

2. Influence on Public Perception

- **Positive and Negative Influences**: Movies and TV shows can raise awareness about drug issues (e.g., addiction, mental health) but can also glamorize drug use or spread misinformation.
- **Examples**: "*Limitless*" portrays the fictional drug NZT-48, which enhances cognitive abilities, sparking public interest in nootropics and cognitive enhancers.

3. Role in Promoting Awareness

- **Awareness Campaigns**: Some films and documentaries aim to educate the public about drug abuse, mental health, and the importance of medication adherence.
- **Examples**: Documentaries like "*The Pharmacist*" highlight the opioid crisis and the role of pharmacists in combating it. [1]

4. Celebrity Influence

- **Impact of Celebrity Endorsements**: Celebrities discussing their experiences with medications or mental health issues can significantly impact public opinion and destigmatize drug use for medical purposes.
- **Examples**: Celebrities like Carrie Fisher and Demi Lovato have openly discussed their struggles with bipolar disorder and addiction, promoting understanding and empathy.

5. Medical Dramas and Realism

- **Authenticity**: Shows like *"House," "ER," and "Grey's Anatomy*" attempt to portray medical scenarios realistically, often consulting medical professionals to ensure accuracy.
- **Pharmacological Aspects**: These shows sometimes feature pharmacological treatments and their effects, although they may still take creative liberties.

6. Biopics and Historical Films

- **Depiction of Real-Life Stories**: Films about real-life scientists and medical professionals, such as "*The Theory of Everything" (Stephen Hawking) and "A Beautiful Mind" (John Nash*), often touch on pharmacological treatments for diseases.
- **Examples**: "*Dallas Buyers Club*" highlights the struggle for access to experimental HIV/AIDS drugs in the 1980s.

7. Fictional Drugs

- **Invented Substances**: Hollywood frequently creates fictional drugs with exaggerated effects for storytelling purposes, such as the aforementioned NZT-48 in "*Limitless*" or the drug "soma" in "*Brave New World."*
- **Pharmacological Insights**: While fictional, these portrayals can spark discussions about real pharmacological research and the potential for future drug developments.

8. Sci-Fi and Futuristic Medicine

- **Speculative Pharmacology**: Science fiction often explores futuristic drugs and medical technologies, such as the "Red Pill" and "Blue Pill" in "*The Matrix"* or the use of advanced psychotropics in "*Altered Carbon*."
- **Pharmacological Concepts**: These depictions can inspire real-world pharmacological research and innovation, even if the science is currently speculative.

9. Legal and Ethical Issues

- **Dramatizing Controversies**: Hollywood films often dramatize legal and ethical issues surrounding drug development and pharmaceutical companies, such as "*The Constant Gardener" and "Love and Other Drugs".* [2]
- **Pharmacology's Role**: These films bring attention to important issues like drug testing ethics, pricing, and access to medications.

10. Educational Impact

- **Teaching Tools**: Some educational programs use clips from movies and TV shows to teach pharmacology, illustrating both good and bad practices in medication use and medical ethics.
- **Engaging Students**: These visual aids can make complex pharmacological concepts more accessible and engaging for students.

11. Pop Culture and Drug Trends

- **Impact on Trends**: Hollywood's portrayal of drug use can influence real-world trends, both positively and negatively, by normalizing or stigmatizing certain behaviors.
- **Examples**: The portrayal of cocaine use in the 1980s and 1990s in films like "*Scarface" and "Blow*" impacted public perception and usage trends.[3]

12. Pharmacists in Media

Representation: Pharmacists are sometimes featured in movies and TV shows, highlighting their role in healthcare beyond just dispensing medications.

- **Examples**: Shows like "*Pharmacist" and movies like "The Pharmacist*" (2020) explore the crucial role of pharmacists in the healthcare system and their impact on patient care.

Conclusion

The relationship between pharmacology and Hollywood is multifaceted, influencing public perception, awareness, and understanding of drugs and medical treatments. While Hollywood often dramatizes and takes creative liberties, pharmacology provides a scientific foundation that can help educate and correct misconceptions.

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The Future Scope of Pharmacology: Advancements and Potential

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Pharmacology has seen significant advancements over the past few decades. As we move further into the 21st century, the field is poised for even more remarkable developments. The future scope of pharmacology promises to be transformative, driven by technological innovations, personalized medicine, and a deeper understanding of human biology.

Personalized Medicine

One of the most exciting prospects in pharmacology is the advent of personalized medicine. With the integration of genomics, pharmacogenomics, and bioinformatics, treatments can be tailored to individual genetic profiles. This approach not only increases the efficacy of drugs but also minimizes adverse effects. Personalized medicine is set to revolutionize how we treat diseases, moving away from the one-size-fits-all model to more customized therapies.[1]

Advances in Drug Delivery Systems

Innovations in drug delivery systems are another critical area of development. Nanotechnology, for instance, has opened new frontiers in delivering drugs more precisely to target tissues. This technology allows for controlled release, improving the therapeutic index of drugs while reducing side effects.[2] Additionally, advances in biotechnology have led to the development of biologics, such as monoclonal antibodies and gene therapies, which offer new treatment options for previously untreatable conditions .[3]

Artificial Intelligence and Machine Learning

Artificial intelligence (AI) and machine learning (ML) are set to play a pivotal role in pharmacology. These technologies can accelerate drug discovery by analyzing vast datasets to identify potential drug candidates, predict their interactions, and optimize clinical trials. AI-driven algorithms can also help in predicting patient responses to drugs, leading to more efficient and effective treatment plans.[4]

Regenerative Medicine and Pharmacology

The intersection of regenerative medicine and pharmacology holds immense potential. Stem cell therapies and tissue engineering are advancing rapidly, offering new avenues for treating degenerative diseases and injuries. Pharmacological research in this area focuses on finding drugs that can enhance the regenerative capacity of cells and tissues, thereby improving outcomes for patients with chronic conditions. [5]

Global Health and Emerging Diseases

The COVID-19 pandemic has underscored the importance of pharmacology in addressing global health challenges. Future pharmacological research will likely focus on developing antiviral drugs, vaccines, and treatments for emerging infectious diseases. This includes a better understanding of zoonotic diseases and the development of broad-spectrum antivirals that can combat multiple pathogens. [6]

Ethical and Regulatory Considerations

As pharmacology advances, ethical and regulatory considerations will become increasingly important. The development of new drugs and therapies must be balanced with patient safety, ethical research practices, and equitable access. Regulatory bodies will need to adapt to the fast-paced advancements in the field to ensure that new treatments are both safe and effective.[7]

The Role of Pharmacologists

The role of pharmacologists will continue to evolve, requiring a multidisciplinary approach to research and practice. Pharmacologists will need to collaborate with geneticists, biotechnologists, data scientists, and clinicians to drive innovation. Education and training programs will also need to adapt to equip future pharmacologists with the skills necessary to navigate this rapidly changing landscape.[8]

Conclusion

The future scope of pharmacology is incredibly promising, with potential breakthroughs that could significantly improve human health and well-being. Personalized medicine, advanced drug delivery systems, AI and ML, regenerative medicine, and a focus on global health are just a few areas where pharmacology is set to make transformative strides. As we embrace these advancements, it is crucial to consider the ethical and regulatory frameworks that will ensure these innovations benefit all of humanity. The journey ahead is exciting, and the possibilities are endless as we explore the future of pharmacology.

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Regenerative Medicine: It's Goals and Applications

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Over the centuries, scientists have been concerned to understand how can amphibians and reptilians regenerate their amputated limbs. [1] The regenerative capacity is seen in many animal species such as zebra fish who regenerate internal organs like injured heart muscles or hepatic tissues. [2,3] Although several adult mammalian organs like the heart, brain, and liver are incapable of functional self-recovery following injury, so understanding the mechanisms which allow reptilian fish to regenerate will start an evolutionary era in medicine that will save millions of lives of patients suffering from congestive heart failure and myocardial infarction (MI) due to the limited number of donors for heart transplantation. [4,5] However, despite the enormous size of available data aiming to understand such regenerative mechanisms, limited outcomes have been achieved from the pilot studies about their application in mammals. With the evolution of interdisciplinary medical sciences in the last decades, a new branch of medicine occurred namely regenerative medicine (RM).[6]

WHAT IS REGENERATIVE MEDICINE?

Regenerative medicine is the "process of replacing or regenerating human cells, tissues or organs to restore or establish normal function". [7] It is the most recent and emerging branch of medical science which deals with functional restoration of specific tissue and/or organ of the patients suffering with severe injuries or chronic disease conditions, in the state where bodies own regenerative responses do not suffice. [7] The field of regenerative medicine encompasses numerous strategies, including the use of materials and de novo generated cells, as well as various combinations thereof, to take the place of missing tissue, effectively replacing it both structurally and functionally, or to contribute to tissue healing.[8] The current therapyof transplantation of intact organs and tissues to treat organ and tissue failures and loss suffers from limited donor supply and often severe immune complications, but these obstacles may potentially be bypassed through the use of regenerative medicine strategies.[9]

WHAT ARE THE GOALS OF REGENERATIVE MEDICINE?

Many common chronic diseases begin with harmful cell depletion. For example, Alzheimer's disease is associated with a loss of brain cells,

heart disease is often marked by a loss of healthy heart muscle, and type 1 diabetes occurs when cells in the pancreas fail to produce insulin. [10] The Institute for Stem Cell and Regenerative Medicine (ISCRM) at the University of Washington is a leader in biomedical research that uses stem cells to develop therapies and cure for human diseases and disorders. It's approach to regenerative medicine includes basic and clinical research, tissue engineering, and stem cell-based therapies. At this institute researchers are studying how to jump start the growth of cells in the brain, heart, pancreas, liver, kidney, eyes, ears, and muscles. Ultimately, the goal of regenerative medicine is to improve the daily well being of patients with debilitating chronic diseases by developing a new generation of therapies that go beyond treating symptoms.[10] A number of therapies have received Food and Drug Administration (FDA) approval and are commercially available and shown in Table 1. [11]

Table 1. Regenerative medicine FDA-approved products

Category	Name	Biological agent	Approved use
Biologics	laViv	Autologous fibroblasts	Improving nasolabial fold appearance
	Carticel	Autologous chondrocytes	Cartilage defects from acute or repetitive trauma
	Apligraf, GINTUIT	Allogeneic cultured keratinocytes and fibroblasts in bovine collagen	Topical mucogingival conditions, leg and diabetic foot ulcers
	Cord blood	Hematopoietic stem and progenitor cells	Hematopoietic and immunological reconstitution after myeloablative treatment
Cell-based medical devices	Dermagraft	Allogenic fibroblasts	Diabetic foot ulcer
	Celution	Cell extraction	Transfer of autologous adipose stem cells
Biopharmaceuticals	GEM 125	PDGF-BB, tricalcium phosphate	Periodontal defects
	Regranex	PDGF-BB	Lower extremity diabetic ulcers
	Infuse, Infuse bone graft, Inductos	BMP-2	Tibia fracture and nonunion, and lower spine fusion
	Osteogenic protein-1	BMP-7	Tibia nonunion

Table -1 Regenerative medicine FDA – approved products

HOW ARE STEM CELLS USED IN REGENERATIVE MEDICINE?

Stem cells are powerful tools of discovery used by researchers hoping to understand how regenerative medicine could be used to treat patients. Right now, ISCRM researchers are using stem cells to study how heart diseases develop, testing stem cell-based therapies that could regenerate damaged or lost heart tissue, and even launching heart tissue into space to study the effects of microgravity on cardiovascular health. Many ISCRM scientists use stem cells to create 3D organ models, known as organoids, that allow them to study diseases and test regenerative treatments without involving animals or human subjects.[11]

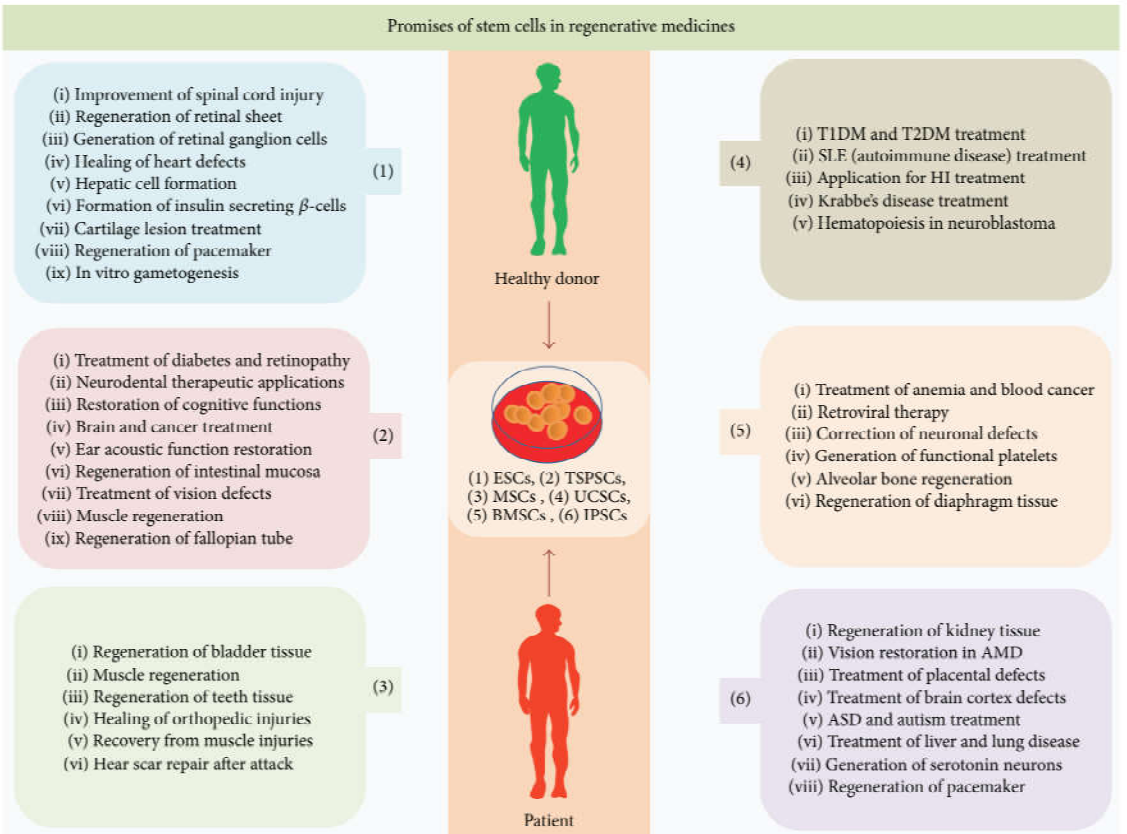

FIGURE 1: Promises of stem cells in regenerative medicine: the six classes of stem cells, that is, embryonic stem cells (ESCs), tissue specific progenitor stem cells (TSPSCs), mesenchymal stem cells (MSCs), umbilical cord stem cells (UCSCs), bone marrow stem cells (BMSCs), and induced pluripotent stem cells (iPSCs), have many promises in regenerative medicine and disease therapeutics.

WHAT ARE EXAMPLES OF REGENERATIVE MEDICINE RESEARCH AT ISCRM?

Heart Regeneration

In 2018, a study led by ISCRM Director Dr. Charles Murry demonstrated that stem cell-derived cardiomyocytes have the potential to regenerate heart tissue in large non-human primates, a major step toward human clinical trials. In another investigation, ISCRM faculty members Jen Davis, PhD and Farid Moussavi-Harami, MD are developing new tools to help cardiologists design personalized treatments for certain heart diseases. [11]

Diabetes

ISCRM researchers are studying the mechanisms that regulate the development and function of beta cells in the pancreas that produce insulin. Vincenzo Cirulli MD, PhD, is screening for biological factors that could promote the growth of beta cells necessary for insulin production. Dr. Cirulli's ISCRM colleague Laura Crisa MD, PhD is using a "disease-in-a-dish" model to study how islet cells falter and whether they can be regenerated, and eventually transplanted, into patients. [11]

Vision Disorders

Researchers at ISCRM are using stem cell-derived retinal organoids to study how diseases of the retina form and how they can be treated. Organoids closely approximate human tissue without many of the ethical questions and supply limitations that complicate the use of fetal tissue.[11] In an October 2021 study published in the journal Cell Reports, Reh and his team used proteins (known

as transcription factors) that regulate the activity of genes to induce glial cells in the retina to produce neurons. The effort demonstrates that gene therapy could someday be used in clinics to help repair damaged retinas and restore vision. [10]

In a groundbreaking medical achievement, Chinese scientists have reportedly cured a patient's diabetes using an innovative cell therapy. This pioneering treatment is developed by a team from Shanghai Changzheng Hospital, the Centre for Excellence in Molecular Cell Science under the Chinese Academy of Sciences, and Renji Hospital.

The patient, a 59-year-old man who had been living with type 2 diabetes for 25 years, was at serious risk of complications from the disease. He had a kidney transplant in 2017, but had lost most of his pancreatic islet function, and relied on multiple insulin injections every day.

The patient received the innovative cell transplant in July 2021. Eleven weeks after the transplant, he was free of the need for external insulin, and the dose of oral medication to control blood sugar levels was gradually reduced and completely stopped one year later.

The patient has now been insulin-free for 33 months and is not on any other medication. [12]

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