Anti-aging mechanism using bacteriphages | experiment

We all have been familiar with many infectious diseases since many centuries ago. Some bacteria have killed millions of our lives, some viruses have great potential to consume many people health and wealth and both are still hugely haunting our humankind. We did discover Penicillin, scientists have developed many antibiotic and antiviral drugs to kill and combat against these bacteria and viruses. This is the war that will have no end.

I have been thinking and studying about these microorganisms since my undergraduate degree emphasizing about the diseases and their basic features. In this study, I wanted to explore many facts about the bacteria and viruses for advantages of our medical sciences and I found out that there had been many researches and discoveries about using the bacteria and viruses for our goodness and amazingly there will be more and many potential for our future medical sciences.

The most interesting thing I have studied is the prokaryotic viruses called Bacteriophage and they really have the very strong potential to be used as a weapon against many infectious diseases including multi drugs resistant bacteria infection and against cancer such as very deadly brain cancers and even the possible cure of many types of cancer by selectively targeting only the cancer cells without affecting the normal ones and I also have studied about the telomerase enzymes that have the potential against human cellular ageing.

OBJECTIVES OF MY INDEPENDENCE STUDY

As we are living on the world interacting with the ecosystems containing different sorts of unicellular and multi cellular organisms, most of our

evolutions and pros and cons are tightly associated with these organisms and the first objective of my study is to know or link the beneficial effects we may obtain from our organisms by understanding them and also understanding ourselves scientifically.

To know and if possible, to propose or to make the steps to develop very effective possible future anti cancer treatment using bacteriophage.

To propose the possible anti-aging mechanism using bacteriphages.

To develop drug which can be effectively used for the many multi drug resistant bacteria infections such as multidrug resistant Tuberculosis using bacteriophages and to identify the possible methods for the drug development and their respective infectious diseases with the delightful and precious help from my supervisor

SCOPE

After studying and emphasizing upon the general main advantages that we get from the bacteria and virus for our medical sciences, I want to focus my study upon the Bacteriophage viruses which can possibly be used as a vector for gene therapy and gene regulation for my desire against aging of human being and in another word against our inevitable part of our human life called death.

Another scope is to use the phage as very specific cancer cell killing agent for many tumors containing specific surface markers or receptors such as brain cancers.

I want to study by reading books and journals and also with my innovative thinking step by step, from general to details and to solve all the questions as much as I can and then to propose the very new techniques using molecular levels and receptors levels.

Schedule

If we want to know something, we must first understand it basically and so, my very first important thing to do is to know about the general important and some very detail characteristics of the bacteria and viruses. Without the general knowledge of them, it is not possible to find out more about them. Many reference books and internet links and help me with this part and to know the many beneficial effects of them for Medical Sciences.

After this, my important plan is to study deeply inside the bacteriophage viruses and their current and future usage for Medicine and then accessing the knowledge with my innovative thinking and advices of my supervisor I hope that I will be able to learn, study and find many things about for Medical Sciences.

2. Bacteria

2. 1: Introduction to bacteria

All prokaryotic organisms are classified as bacteria and they are divided into eubacteria which includes all the bacteria of medical importance and archae-bacteria which is a collection of evolutionarily distinct organisms.

TYPICAL BACTERIA: Most of them have shapes such as rod like, sphere or corkscrew. Their cells are smaller than the eukaryotic cells and all of them except the Mycoplasma have the rigid cell wall surrounding the cell

membrane. Apart from the shapes, the cell wall defines whether the bacteria are Gram Negative or Gram Positive.

Bacteria cells reproduce by binary fission. Atypical Bacteria are the distinct bacteria groups lacking of significant characteristics structural components or metabolic capabilities. They includes Chlamydia, Rickettsia and Mycoplasma etc.

2. 2 ADVANTAGES OF BACTERIA FOR OUR BODY AND MEDICAL SCIENCE

Although bacteria can cause many diseases and health problems to human being, they also have many beneficial effects for our human body and medical sciences.

NORMAL FLORA: Many different micro-organisms mostly bacteria are continuously inhabiting the human body without giving any harm. Human body is usually sterile when a healthy new born enters the world. But, after birth, the body acquires normal flora from the environment and food. The very important fact is that the species of that flora can not be rigidly defined because they differ from one individual from another as a result of physiological differences, diet, age and geographic habitat.

NORMAL FLORA AGAINST THE INVADING HARMFUL INFECTIONS

The bacteria need receptors and nutrients for their metabolism. The invading infections will face with the competence of normal flora for these essential receptors and nutrients. Some bacteria of the bowel can even produce the antimicrobial substances so that the invading organisms can be killed. But, the substances producing bacteria themselves are immune to their own

substances. These effects can reduce the possibility of the infectious diseases and act amazingly as a defense mechanism against the infections.

GERM FREE ANIMALS: The significant of the normal floral are now well explored by studying the germ free animals which have no normal flora as conventional animals. They are produced by special cesarean sections and then they are maintained in special isolators. Experiments showed that in the germ-free animals, the alimentary lamina propria is underdeveloped, the motility of the GI tract is reduced and the intestinal epithelial renewal rate is just half of the normal conventional animals.

In studies with antibiotic treated animals also suggest that the normal flora can protect our bodies from the pathogens. The researchers first treated the animals with Streptomycin to reduce the normal flora and then made them infected with the Streptomycin resistant Salmonella bacteria. In normal condition, about 10000000 Salmonella were needed to cause the establish infection but in Streptomycin pre treated ones, only 10 organisms were needed to cause infection.

NORMAL FLORA FOR OUR IMMUNE SYSTEMS

Bacteria colonization of a new born infant is the very powerful stimulus for the development of immune system. The studies showed that the antibodies concentration after infections is significantly reduced in germ-free animals indicating the defect in acquired immune system.

Bacteria are also the important providers of important nutrients such as Vitamin K and they also help with digestion and absorption of nutrients.

REFERENCES

LIPPINCOTT’s ILLUSTRATED REVIEWS of MICROBIOLOGY 2007 EDITION

INTRODUCTION TO BACTERIA , page 1 -6 Normal Flora Page , 7 – 10

KAPLAN USMLE TEXT BOOK (MICROBIOLOGY)2009 EDITION

HARRISON’S PRINCIPLES OF INTERNAL MEDICINE 2006

3. VIRUSES

3. 1 INTRODUCTION TO VIRUSES

A virus is an infectious agent containing genome which is either RNA or DNA and a protein capsid designed to protect the genome. Many viruses have additional structure like envelope which is protein containing lipid bi-layer. The sort of nucleic acid in the virus is the most fundamental and important of properties of virus. The nucleic acid may be single stranded (ss RNA ss DNA) or double stranded (ds DNA or ds RNA).

The Single stranded RNA genome are subdivided into the positive (+) polarity which is, of messenger RNA sense that can be used as template for protein synthesis. Negative (-) polarity or antisense which is complementary to the mRNA sense and so they can not be used as temperate for protein synthesis directly.

3. 2 THE REPLICATION CYCLES OF VIRUSES

The cycle begins with the attachment of the virus to the host cell called adsorption phase,

1. ADSORPTION:

The initial attachment of a virus to the host cell is with the interaction between specific molecular structure on the surface of the virus and receptor molecules in the host membrane that can recognize the structure. The receptor molecules on the host cell membrane are specific for the family of the viruses and they are the molecular structures that usually carry out normal cell functions. The receptors for the viruses are present only on specific cells or are unique for one animal species. So, the absence or presence of the host cell receptors is so important determination for the susceptibility or resistance of a species to a given virus. If we can genetically manipulate the specific receptor affinity for the viruses, we will be able to attack or kill or change the desired targeted cells.

Fig: HIV virus adhering to the cell, attachment is accomplished by the SU fragment of the env gene product on the surface of the HIV which binds to the CD4 molecule. So, the HIV viruses can only infect the helper T cells, monocytes and dendritic cells which contain the CD4 protein in their cell membrane.

2 PENETRATION:

The two mechanisms the virons enter the cells crossing the cell membrane are the receptor-mediated endocytosis: the viron binds the cell surface receptor and the cell membrane invaginates enclosing the virion in and endocytotic vesicle (endosome). The virion then enters the cytoplasm by various mechanisms depending upon the viruses. It is facilitated by one or

more viral molecules in general. C: Documents and SettingsuDesktopendoem. jpg f

Membrane Fusion: Some enveloped viruses enter the cell by fusion with their envelopes with the membranes of host cells. Glycoproteins of the envelope can promote this and viral membrane then still remains associated with the plasma membrane of the cell and just the nucleocapsid is released into the cells. HIV viruses enter the cells by this fashion.

3 UNCOATING:

This is the stepwise process of disassembly of the viron that enables the expression of the viral genes that carry out viral replications. Most of the steps occur inside the cells and depend on cellular enzymes and in rare occasions, newly synthesized viral proteins are needed to complete the process. The loss of one or more structural components of the viron will lead into the loss of ability to infect another cells reflecting as the eclipse period of the growth curve.

4 REPLICATION:

DNA virus replication: There is a wide macromolecular event variation between families of viruses for the replication processes depending primarily upon the viral genome sizes. The smaller the viral genome, the more the virus must depend on the host cell to replicate. Also the mechanisms of replications for ss DNA viruses and ds DNA viruses are different.

RNA virus replications

Type 1: RNA viruses with a single stranded genome of (+) polarity that replicates with complementary (-) strand intermediate. In this, the infecting parental RNA serves as both mRNA and later as a template for synthesis of the complementary (-) strand.

Type 2: Viruses with ssRNA genome of (-) polarity which replicate with a complementary (+) strand intermediate. (-) polarity genomes have two functions, one is to provide information for protein synthesis and the second is to serve as template for replication. But they can not accomplish without prior construction of complementary (+) strand intermediate.

Type 3: Viruses with ds RNA genome: dsRNA genome is segmented, with each segment coding for one polypeptide. But, the eukaryotic cells do not have the enzyme to transcribe dsRNA. So, mRNA transcripts are produced by virus-coded, RNA dependent RNA polymerase (transcriptase) located in the sub viral core particle. This particle contains dsRNA genome and associated viral protein, including the transcriptase. In replications, the (+) RNA transcripts are not only used for translation, but also as templates for complementary (-) strand synthesis, resulting in the formation of dsRNA progeny.

Type 4: Viruses with a genome of ssRNA of (+) polarity that is replicated with with a DNA intermediate: the conversion of a (+) strand RNA to a double-stranded DNA is accomplished by an RNA-dependent DNA polymerase, commonly known as “ reverse transcriptase”, which is contained in the virion. The resulting dsDNA becomes integrated into the cell genome by a

viral integrase’s action. Viral mRNA abd progeny (+) strand RNA genomes are transcribed srom this integrated DNA by the host cell RNA polymerase.

4 ASSEMBLY AND RELEASE OF PROGENY VIRUSES:

The assembly of the nucleocapsids generally occurs in the cytoplasm for most RNA viruses and in the nucleus for most DNA viruses where the viral nucleic acid replications take place.

REFERENCES

LIPPINCOTT’s ILLUSTRATED REVIEWS of MICROBIOLOGY 2007 EDITION , Unit-Viruses , 233-243

KAPLAN USMLE TEXT BOOK (MICROBIOLOGY) 2009 EDITION

HARRISON’S PRINCIPLES OF INTERNAL MEDICINE 2006 EITION

BACTERIOPHAGE

Introduction to Bacteriphages

Bacteriophages are the viruses that replicate inside the bacterial cells. It contains nucleic acid encapsulated by the protective protein coat. The nucleic acid may be DNA or RNA depending on the phage and may be single stranded and some are double stranded ranging from the length of 3000 bases to 200, 000 bases.

The replication starts with the attachment of the virus to the receptors of the cell surface of bacteria. Then the phage injects the nucleic acid into the cell leaving all or most of the protein outside the cell. This is the obvious difference between the virus that infects the vertebrates and the virus that

infect the bacteria. In former case, the virus is entirely taken up by the cell and its nucleic acid is released inside the cell. (1)

The phage nucleic acid takes over the biosynthetic machinery of the cell to replicate its won genetic materials and to synthesize phage specific proteins. When new phage proteins and new phage DNAs have accumulated, they self-assembly into mature phage particles, the phage specific enzyme (lysozyme) that dissolves the bacterial cell wall and the phage is released from the bacteria. A single phage can produce millions of progeny at the expense of bacteria cells in culture. (1) (2)

4. 2 Virulent phage

Phage are classified as virulent or temperate depending on the nature of their relationship to the host bacterium. Infection of a bacterium by the virulent phage results in the lysis of the bacterium and death releasing newly replicated phage particles. One phage can produce hundreds of progeny within twenty minutes under optimal condition. The interesting thing about that virulent phage is that the phage that attack one bacterial species do not attack other species. (1)(2)

That is a huge advantage to use phage as an antibiotic because the phage against E coli bacteria will only kill that species and will not affect the others including the normal floral of our human body. So, they will be the most specific antibacterial agent. (1) (2)

4. 3 Temperate Phage

The temperate phages are different from the virulent one in that they have two possible fates after infecting the bacterium. Some cause the lysis and

death of the bacterium just like the virulent phages do but they do have another alternative outcome. After entering the cell, the phage DNA integrates with the chromosome of the host cell. During this state (prophage) the gene expression of the phage is continuously by a protein (repressor) encoded by the phage genome and therefore no new phage particles are produced, the host cell survives and the phage DNA replicate as part of the host cell. (1)(2)

4. 4 LYSOGENIC BACTERIA

The bacteria which carry the prophage are called lysogenic bacteria and this phenomenon is called LYSOGENY. The association of the phage and the bacteria is very stable unless the host DNA damage or the exposure to the ultraviolet light occurs. When the DNA damage occurs, the repression of phage gene is lifted and the lysis occurs and the host cells die. (1) (2)

4. 5 MOLECULAR DETAIL OF LYSOGENY

In Lysogenic mechanism, the genes for the lytic process will have to be turned off and this process is caused by the phage coded repressor gene. This may be proteins or sometimes anti sense RNA. The repressor genes can turn off almost all the transcriptional initiation and so most of the gene transcriptions including the essential ones for the lytic mechanism are inhibited. But the repressor gene acts only onto the few promoter genes and the gene for lysis mechanisms in late part of the processes are only indirectly inhibited by the lack of early gene transcriptions tuned off by the repressor proteins or anti sense RNAs.

The early gene products are needed to activate the subsequent gene expressions and their absence make the whole lysis process inhibited. The repressors also promote their own transcriptions to ensure their functions. The lysogenic state is very stable and only one in 100000 cell divisions may undergoes lysis by spontaneous activation. There are also many ways to stop the lysogenic state in experimental such as heating in which the repressor proteins become denature, treating with the UV ultraviolet light in which the specific system called SOS system of the bacteria is activated. The SOS system is the global regulatory system which responds to DNA damage. The breakdown products such as oligonucleotides activate the Rec A protein’s co-protease activity and this protein in turn inactivate the main protease protein called LexA and then repressors and the lysogeny state is ended. (1) (2)

There is also a type of protein called anti-repressor protein and they inhibit the repressors’s activities and this anti-repressor synthesis is turned off in the lysogenic cells by the maintenance protein called Mnt protein.

CII gene: In order to achieve the stable lysogenic state, both the establishment of the repression of the lytic gene and the integration into the chromosome of the cell are needed. CII is a transcriptional activator which is coordinated with the lysogeny. Within the CII gene, the gene called CI gene which transcription needs the CII-dependent promoter establish the repression of the lytic genes. This promoter is activated only for a short period during lysogenization and after the repression has been established, the CII gene is repressed itself.

The CI gene is then transcribed only from the pM gene which is the maintenance promoter gene. The another protein called Integrase which is essential in integrating of the phage nucleic acid with the chromosome is also transcribed from the CII dependent promoter called PI. The pAQ which is also the CII dependent promoter makes an antisense transcript that opposes the Q gene expression. Q gene's products stimulate the late gene expression and late gene products which could kill and lyse the cell and they are not made by the CII expressing cells and so the CII gene is so essential for the lysogenic state and only these cells expressing CII gene effectively become lysogenic cells. (1) (2)

REFERENCES

LIPPINCOTT's ILLUSTRATED REVIEWS of MICROBIOLOGY 2007 EDITION Bacteriophage in chapter 7 Bacteria genetic , gene transfer , Page 60-61

RICHARD CALENDAR THE OXFORD TEXT BOOK OF " THE BACTERIOPHAGE" 2nd EDITION 2006 part II, Life of Phages, Page 66-104

BACTERIOPHAGE AS AN ANTIBIOTIC

5. 1 WHAT PROPERTIES NEEDED AS AN ANTIBIOTIC?

The antibiotic must be effective in the treatment of infection because of their selective toxicity. That means the drug should kill or effect against the invading desired organism without harming the cells of the host. In most of the cases, this toxicity is just relative rather than absolute, requiring that the concentration of the drug be carefully controlled to attack the microorganism while still being tolerated by the host. (1)

5. 2 WHY PHAGES AS ANTIBIOTIC?

As the PHAGE viruses can infect and kill the bacteria, they can be used as a drug targets against the Bacteria. Phage Therapy: Phage therapy is the use of lytic phages to kill specific bacteria as an alternative to antibiotic.

The lytic mechanism of the Bacteriophages ensures the effective antibiotic mechanism of the Phages. The other useful thing is that the specific type of Bacteriophage attacks only the corresponding bacteria and so the other normal bacteria will not be affected by the specific Phage Therapy targeted to the aimed bacteria. So, the Phages have more specificity than all antibiotics in attacking the bacteria.

5. 3 Host Vs Phages

The phages are immunogenic and could initiate the immune responses. This effect may limit the uses of Phages because the Bacteriophages may be destroyed by our immune system even before attacking the desired target bacteria and also the strong immune responses may trigger the allergic reactions and also the human immune system produces antibodies against the Phages.

Despite these matters, the good news is that their clinical uses reveal only very few side effects or allergic reaction. The best way to avoid the sensitization is to use the Phages only when it is necessary as in the case of multidrug resistant infection and using the Intra Venous IV Administration method.

5. 4 BACTERIOPHAGE AGAINST TB

Tuberculosis, one of the oldest diseases known to affect humans, is caused by bacteria belonging to the Mycobacterium tuberculosis complex. The disease usually affects the lungs, although in up to one-third of cases other organs are involved. If properly treated, tuberculosis caused by drug-susceptible strains is curable in virtually all cases. If untreated, the disease may be fatal within 5 years in more than half of cases. Transmission usually takes place through the airborne spread of droplet nuclei produces by patients with infectious pulmonary tuberculosis.

MULTIDRUG RESISTANT TUBERCULOSIS: This condition arises when the Bacteria undergo point mutation in their genome which occurs at low but predictable rates. There are two types of drug resistant

Primary drug resistant: This occurs when the strain infects the one who has never been treated before and

Acquired drug resistant: In which, the resistant develops during treatment with inappropriate regimen.

Apart from the resistant, some of the patients are not appropriate to give the usual dose of conventional treatment due to their co existing diseases like renal failure, hepatitis or liver failure. (1)(6)

MYCOBACTERIOPHAGE

Mycobacteriophages are the bacteriophages that infect against mycobacteria, the bacteria causing Tuberculosis and many other diseases like Leprosy. Mycobacteriophages were first discovered by the in 1946. They

are the double stranded DNA viruses with non contractile tail belonging to the Siphoviridae family of the Bacteriophage. They also infect the pathogenic bacilli of the Mycobacterium Tuberculosis complex and now more than 250 mycobacteriophages have been indentified. They are either lytic or temperate. Some mycobacteriophages like DS6A can exclusively infect the Mycobacterium tuberculosis alone. Phages like 13, D 29, TM4, Bxz2 and Chel 2 infect both Mycobacterium tuberculosis and other Mycobacterium bacteria. Their morphological variation is limited but their genomes show extra ordinary genetic variability. The implications of phages in mycobacterial diseases may be greater than previously realized. (1) (2) (3)(7)

5. 6 PHAGE THERAPY

We can use lytic phages to kill specifically pathogenic bacteria as an alternative to antibiotics treatment especially for the multidrug resistant Tuberculosis. Lack of knowledge of bacteriophage biology and the quality monitoring during the preparation of therapeutic stocks had made the therapy difficult though the first known therapeutic use was in 1919. The M. Tuberculosis infections are hard to treat because the bacteria are naturally resistant to many antibiotic. The bacilli may remain in the latent or dormant state avoiding the action of drugs that require replication of the bacteria. So, the treatment of Tuberculosis requires multiple drugs for extended periods of time to effectively cure and avoid the drug resistant. The minimal duration for the treatment is four months with four drugs and then two months with two drugs. The most important thing is the emergence of multi drugs resistant strains and that makes the Phage Therapy more interested. (1) (2) (3)

Dr Margaret Chan, the director-general of the World Health Organization said," The situation is already alarming, and poised to grow much worse very quickly". She and Bill Gates also stated that they only had little help from the modern drugs for the disease that is affecting 9 millions people each year killing nearly 2 millions of them. The conventional drugs are useless against some strains of tuberculosis and they addressed the situation OUT OF CONTROL and A POTENTIALLY EXPLOSIVE (5)

TIM JOHNSON, Mc Clatchy Newspapers

Animal study: One of the Mycobacteriophage, DS6A, showed reduction in the observed in the lesions in spleen, lungs and livers of guinea pigs infected with (Challenged with) Mycobacterium tuberculosis and the study showed that the anti bacterial effect of the phages is at least as good as Isoniazid monotherapy. The results are promising in the treatment of tuberculosis using phages.

5. 7 MYCOBACTERIM INSIDE THE MACROPHAGES: Mycobacterium can reside in the macrophage cells of our immune system. They can even persist inside the phagolysosome where many bacteria and pathogens are killed. It was uncertain whether the mycobacteriophages can survive and replicate inside the hostile intra-cellular environment with reduced PH. (8)(9)

5. 8 MYCOBACTERIUM SMEGMATIS, THE VEHICLE INTO THE MACROPHAGES: The above problem can be solved by using the vector bacterium Mycobacterium smegmatis. The technology was introduced in 2002. In this technology, the non-virulent bacteria Mycobacterium smegmatis act like a carrier into the macrophages.

Macrophages infected with the Mycobacterium Tuberculosis or Mycobacterium avium were treated with the additional Mycobacterium smegmatis infected with Mycobacteriophage TM4. After they are ingested and destructed by the macrophages, the TM4 phages were released within the macrophages infecting and destroying the pathogenic bacteria even within the macrophages. The experiments showed the significant reduction of both the Mycobacterium tuberculosis and Mycobacterium avium. (9)

5. 9 D29bacteriophages: This D29 are capable of entering the Macrophages without the need of any carrier and they can infect the mycobacterium and kill them effectively.

So, the mechanisms of action of mycobacteriophages are completely different from the conventional drugs and will be so important in the multi-drug resistant cases. The Phage therapy also dose not need repeat dosing because the viruses do increase within the target bacteria and new virions are released on lysis. The endotoxin may be released into the body after the bacteria has been lysed and this could trigger the immune reactions but till now the clinical use of bacteriophages revealed only very few cases of side effects or allergic reaction indicating that our human body can really tolerate them. The other advantage is that they are cheaper and easier to produce than antibiotics. (10)

REFERENCES

LIPPINCOTT’s ILLUSTRATED REVIEWS of MICROBIOLOGY 2007 EDITION

HORACE T. ADAMS CONTEMPORARY TRENDS IN BACTERIOPHAGE RESEARCH 2009 EDITION

RICHARD CALENDAR THE OXFORD TEXT BOOK OF “ THE BACTERIOPHAGE” 2nd EDITION 2006

http://www. microphage. com/technology/phageBiology. cfm

WHO, world health organization, Global Tuberculosis control Geneva

Harrison text book of Practice of Medicine , USA 6th edition

Fuller, KJ and Hatfull GF 1997 Mycobacteriophage L5 infection of Mycobacterium bovis BCG implications for phage genetic in the slow-growing mycobacteria Mol Microbiaol 26 755-766

Kaufmann SH 2002 Protection against Tuberculosis cytokines T cells and macrophages Ann Rheum Dis 61 Sulll 2 ii54-58

BroxmeyerL Sonsowaka DMiltner 2002 killing of Mycobacterium by a mycobacteriophage delivered by non virulent mycobacterium , model for phage therapy of intracellular bacterial pathogen, J infect Dis 1155-1160

Trollip A Albert H and Maskell 2001 Bacteriophage based technology for the rapid diagnosis and drug susceptibility testing of tuberculosis Am Clin Lab 20: 39-42

Phage as cancer curing agent

6. 1 PHAGE DISPLAYis a process by which a peptide or a protein is expressed as an exterior fusion to a surface protein of a phage particle. The peptide or protein sequence can be deduced from its encoding DNA sequence that resides in the phage particle or in a transductant. Amplification of the DNA of

interest can take place by phage/transductant propagation or by polymerase chain reaction PCR. By producing large amount of phage particles, each expressing a unique peptide or protein peptide and protein libraries can be obtained. The peptides or proteins interacting with defined molecular targets (most often proteins) can be isolated from such libraries by enrichments through repeated cycles of panning. So, the phage display can be regarded as a search engine of protein-target interaction. (1)

Phages are bacterial viruses that have no native affinity to mammalian cells. But we can amazingly genetically reengineered to display peptides fusions to coat proteins that can recognize and bind to our mammalian cells. Oligonucleotide sequences encoding for foreign peptides are cloned into phage coat protein genes resulting in combinatorial libraries of billions of different phage clones displaying encoded peptides on their surfaces. This phage display libraries can be easily screened against various biological targets including the intact mammalian cells to give binding molecules with desired target-specific characteristics. Even the cell-specific peptides indentified through phage display can be used as delivery moieties for construction of gene therapy vectors, liposomes, or targeted drugs to diseased cells in many sorts of disorder including the cancer. (2)(3)

6. 2 PHAGES AGAINST BRAIN TUMORS

Malignant brain tumors are very difficult to treat because they are heterogenous, migrate far into adjacent essential brain normal tissues, are resistant to chemotherapy and radiotherapy and also protected by the blood brain barrier. (1) (4)

The phage display might be so much effective against this fatal condition by following means.

Phages can optimize the targeted delivery platforms to malignant brain cells using the cell specific peptides.

The emerging of phage probes for profiling of brain tumors in individual patients and then making the personalized treatment based on the profiles of these tumors.

To identify