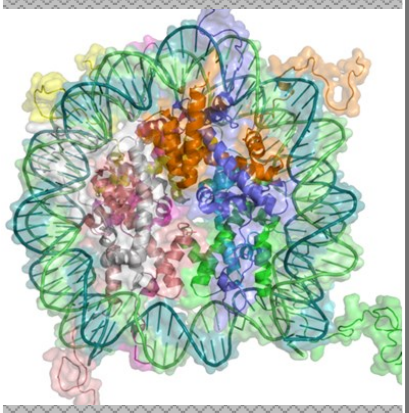

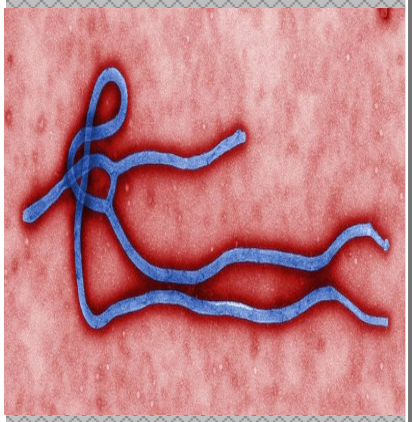

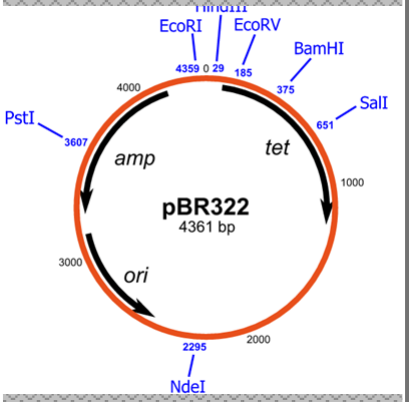

EMGEN Newsletter

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Eastern Mediterranean Health Genomics and Biotechnology Network (EMGEN) was created in 2004 with collaboration of representatives of selected centres of excellence in (health related) molecular biology, biotechnology & genomics in the Eastern Mediterranean region by recommendations and efforts of WHO/ EMRO. Sponsored by Iran Biotechnology Development Council.

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Interview

In this issue, we present the following interesting interview with Dr. Essam F. A. Al-Jumaily from Baghdad University, Iraq (any views or opinions expressed are solely those of the interviewed person and do not necessarily represent those of EMGEN Newsletter).

Dr. Essam F. A. Al-Jumaily

- **Dear Dr. Essam F. A. Al-Jumaily could you please briefly introduce yourself and explain your educational status?**

Essam F. A. Al-Jumaily (Prof.)

Field of specialization:

Major: Biochemistry and Biotechnology; Minor: Enzymology.

Academic Qualification:

B.Sc. degree: 1976. Food Science and Biotechnology Dept., Baghdad University. Iraq. Ranked three on the graduating class.

M.Sc. degree: 1978. Food Science and Biotechnology Dept. (Dairy Chemistry), Baghdad University. Iraq.

Ph.D. degree: 1989, Biochemistry Dept. (Enzymology), Southampton University, U.K.

- **Could you please tell us what your main research area is?**

Microbial Biotechnology,

Enzyme Biotechnology,

Biosafety and Biotechnology,

Purification of Biotechnology materials with downstream production.

- **Do you apply any genomics tools in your researches and please explain how and where?**

Yes, first in My Ph.D. thesis, I published paper about nucleotide sequence for the hemD gene of *E. coli* encoding Uroporphyrinogen III synthase and initial evidence for a hem operon. After that, we published another paper about purification and properties of Uroporphyrinogen III synthase (Co-synthetase) from an overproduction recombinant strain of *E. coli* K-12. All of these works have been done in Southampton University, U.K.

- **What kinds of genomics facilities do you have in your laboratory?**

Very simple experiments, like isolating DNA and using PCR.

- **Are there any diagnosis products that have been made in your country? (i.e. your native researchers involved in the project).**

No.

- **Are there any late stage biological products to be commercialized in your center? Could you please explain.**

No.

- **Are there significant genomics centers in your country?**

Yes, there is one center for DNA in Niharin University and one in Basrah Univeristy.

- **Are there any academic training courses in genomics and molecular biology in your country?**

Yes.

- **If yes, to above question, in which level and how many students are trained annually?**

There are PCR and DNA extraction training courses, the B.Sc. and M.Sc. students level, and about 20-30 students are trained annually.

- **Are you familiar with EMRO countries and EMGEN (Eastern Mediterranean Health Genomics and Biotechnology Network)? Would you please tell us how you know the EMGEN?**

Yes, I got to know about EMGEN and Biotechnology Network by one of EMGEN staff.

- **Would you please explain your cooperation with EMRO countries, in the field of biotechnology and health genomics?**

There is no cooperation with EMRO countries, especially with my field of biotechnology.

- **Do you have any suggestions for establishing/extending collaborations with EMRO countries?**

We want several training courses with EMRO countries.

- **Are there any possibilities for young researchers from EMRO countries to participate in training courses in your genomics centers?**

No.

- **What kinds of difficulties do you face, in research and commercialization of medical genetics in your country and the region?**

There are many difficulties in apparatus and materials especially primer kit for genetics research.

- **Do you have any training courses or workshops in your research center?**

Yes.

Thank you Dr. Essam F. A. Al-Jumaily for sharing information and your opinion with us. In addition, we are grateful for your kind and useful cooperation.

PATENTING IN BIOTECHNOLOGY

One of the main objectives in biotechnology is financial benefits of products. However, no company will initiate research in long-time and expensive procedure without assurance that the consequences of its effort can be legally protected from others. On the other hand, new researches, methods and materials are the basic fundamentals for advancement of science and technology. A strategy that face both of these purposes is for governments and legislative systems to grant inventors exclusive right to the novel products or processes that they develop. For biotechnology, patents are most important type of intellectual property that design to save the inventors rights and in the same time give them chance to introduce their products, processes and the objective of the works. Patent is a legitimate evidence that gives the patent holder monopolized rights to expand invention commercially. Moreover, according to the claims of patents, the patent holder can develop other products that directly derived from the original invention with exclusive rights. While, competitors would must to acquire official permission to use the invention or other products that are directly derived. In other word, commercially making, utilizing, distributing, importing, or selling of an invention without the patent holder permission is inhibited. Also, patent is a public document that contain a detailed description of the invention and can give comprehensive information about invention itself, limits and potentials.

The term period of patent, or the period that patent maintain in force, generally is 20 years, from filling application form or maybe date of granting patent depends on countries laws. For example, in the USA the duration of patent protection is twenty years from the time of granting the patent. Unfortunately, patent has not a global organization that it is caused U.S patent grant; for example, it is effective only within the united state and its territories. There are three types of patents which consist of utility patents, design patents and plant patents. Utility patent territory contains any qualified invention, discovering, article of manufacture, composition of matter or any improvement. Design patent may grant to anyone who invents a new, original and ornamental design for an article of production as patent office claimed. The final type of patents, the plant patent, may be granted to someone who invents or discover new and distinct variety of plants, but their reproduce must be in asexuality form generally. There are some principle requirements that determinate an invention or discovering, any new and beneficial process, machine, manufacture, or combination of matter would

be patentable or not, which includes novelty, inventiveness or discovering, utility and external existence; also this is important that the subject be eligible for patent protection. Patent must contain new things that no one else reported them before. There is simple ration behind this step that is protection of priority rights and prevention of background art being patentable again. The patent cannot be granted for something which is obvious or the person having ordinary skill in the art. In other word, invention should be sufficiently inventive. This is non-obviousness principle and determines whether the invention is adequately distinct from pervious works or not. In the utility step, the important issue is usefulness of plan and also the operative of machines. Machines must to work to be useful and an invention must to have a purpose to do to be useful. A mere idea or suggestion is not sufficient to obtain patent. A complete description of a new actual machine is needed for patent application form. Moreover, the patent-eligible subject matter determines which subject is capable of granting as patent and this vary from country to country. For example, according to patent office in USA, "The Atomic Energy Act of 1954 excepts the patenting of inventions beneficial particularly in the application of special nuclear material or atomic energy in an atomic weapon."

Patent established the right to exclude others from commercial benefits of an invention by legal, and to maintain a granted patent in force, patent holder must pay maintenance fees or renewal fees. Not all patent laws require maintenance fees and the payment and period regularity of maintenance fees are different from country to country. For example, maintenance costs for utility patents in the United States are payable 3½, 7½ and 11½ years after licensing the patent. There is need to attention that, the rights given by a government to patent is accredited only throughout the government territory and patent standards vary in different countries.

Patent in biotechnology has specific stage. In present, sequence of modified DNA, modified RNA, cDNA or modified proteins has potential to be patentable. But until recently, natural biological substances themselves could be patented and gene sequence was not an exception. So, thousands of patent applications for sequences have been approved by patent offices in worldwide and almost 20% human genes write-in as patent. Some of these sequences apply to produce therapeutic proteins such as recombinant erythropoietin that motivate red blood cell formation.

Many of the other sequences have potential to apply as diagnostic probes for disease detection and rarely, some sequences show unique properties. In the USA the key requirement for patent eligibility in case of DNA sequences was demonstration of "specific and substantial credible utility", but according to the U.S. Supreme Court rule on June 13th 2013, isolated but otherwise unmodified genes produce by nature has not eligibility for patent subject matter. This is important to note that, sequence patentability, true or false, is a controversial issue and there are many opposite claims and ideas about it, but it seems that the big argument is about organisms and specially multicellular organism patentability.

As a rule of Supreme Court of U.S. in 1980, a created bacterium by genetic manipulation could to be patentable and under umbrella of this landmark decision and next ones; by now, several bacteria, animals and plants received patent in U.S.A..

The oncomouse or Harvard mouse has place in history as a first complex animal achieved to get patent in the U.S. This mouse designed by Philip Leder and Timothy A. Stewart of Harvard university and carry an v-Ha-ras gene under the control of the promoter of mouse mammary tumor virus. This active oncogene enhance aptitude of the mouse to carcinoma and made them suitable for cancer researches. Viewpoint about multicellular organism patentability in all countries is not same; for example, in some countries such as Canada, transgenic mice are not patentable at all. A kind of climbing, ever-blooming rose got a patent as the first plant in 1931. Granting patent to multicellular organism, true or false, need to put through ethic landscape and answer to some moral questions is necessary. Today, Biotechnology arrived to a critic point, we have power to manipulate many organisms, include humans, but the big question is, should we do this? The other questions that rise about this issue are: Can we predict every single consequence of our decisions? The manipulation of life forms, even for our benefits, is our rights? Where is the bands and where we should to stop? The answer to these questions and other issues help us to make a sensible decision about the road we are going to pass through and according to that, determines which works are true, and in the field, which things could be patentable, and vice versa.

As previously mentioned, patent preserves the commercial rights. The "Cohen/Boyer patents" that invented by Stanley Cohen and Herbert Boyer covered inventions for splicing genes to make recombinant proteins. Stanford university managed the patents and licensed them non-exclusively and broadly, earning over $200 million for the universities. Axel Patents that invented by Richard Axel et al. of Columbia University covered co-transformation. Columbia University licensed these patents nonexclusively and broadly and earned about $790 million in general. These and many other examples obviously show that this is a successful procedure for preserve exclusive commercial rights of patent holder. This is important to note that only 2-3% of all patented products find their own way to market.

The biggest drawback of patent is that, typically it is not difficult to legally design a product like pervious patent products and there are no “patent police” out there and maybe your idea got stolen.

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6. https://en.wikipedia.org/wiki/Novelty_(patent)

SYNTHETIC BLOOD

Introduction

Blood consists of white cells, red cells, platelets, and plasma. It plays a vital role in our body. Plasma is made up of water, salts, and proteins that, along with platelets, endorse blood to clot. The white blood cells are responsible for the immune system.

The red cells have a key role in transportation of gases, O_2 and CO_2, throughout the body with the help of hemoglobin which is encased in red blood cells. There are also different kinds of proteins on the membrane of these cells which are responsible for different blood types.

Researchers are investigating on an artificial blood which can be utilized as a substitute for the function of red blood cells; hence, we can also name these products oxygen carriers. There are a few blood substitutes which are also known as oxygen therapeutics and hemoglobin-based oxygen carriers, but these substitutes are not sufficiently safe.

The study, headed by Charles Natanson, a major scientist at the U.S. National Institutes of Health (NIH), showed a threefold increase in the risk of rupture of heart in patients who used the alternatives, compared with the control group who used donor blood. Depending on the type of artificial blood, it can be synthesized in different ways using synthetic production, chemical isolation, or recombinant biochemical technology.

Recently, scientists of NHS Blood & Transplant used stem cells from adult and umbilical cord blood as a potential route to produce a small volume of manufactured red blood cells. By 2017, this manufactured blood will be exerted to a group of 20 volunteers by a small volume transfusion of between five and ten mls. Synthetic blood has made an opportunity to specialist patients with blood disorders such as sickle cell anemia and thalassemia who need regular transfusions and for whom it is hard to find matchable donors.

Some advantages of artificial blood include not requiring to check blood types before transfusion as it is the universal blood group, O negative. It also has a longer shelf-life than donor blood which can only be stored for a maximum of 42 days before use.

History

In fact, the first human trials of lab-produced blood, dates back to the early 1600s, and the first successful human blood transfusions were done in 1667. Unfortunately, the following trials on men was prevented due to subsequent transfusions death. During the 1800s various materials such as milk, saline solutions, hemoglobin and animal plasma were tried as a substitute for blood. Hemoglobin and animal plasma were hampered due to difficulties of isolation and the presence of toxic materials.

Ringer's solution, a solution combined of sodium, potassium, and calcium salts, was created in 1883, however, it is still used today as a blood-volume expander, it can not replace the function of red blood cells, so it is not a real blood substitute. Karl Landsteiner, the father of immunology, was primarily interested in danger of blood transfusion as the donor's blood frequently clotted in the patient.

After performing different experiments Landsteiner found out that human beings could be classified into blood groups according to the capacity of their red cells to clot in the presence of different serums. He named his blood classification groups A, B, and O. The AB group was discovered the following year.

The severe requirement to donate blood was encouraged in World War II. Plasma donated from humans was commonly used to substitute blood and to save soldiers from exsanguinations and as a result, this led to the organization of blood banks by the American Red Cross in 1947.

Again the limited storage of the blood bank system were appeared during the Vietnam conflict and this provoked some researchers to begin looking for hemoglobin solutions and other synthetic oxygen carriers. The HIV and hepatitis crisis in the 1980s triggered research into artificial blood.

Perflurocarbon-based (PFC) products

There are two main products which are under investigation as blood substitutes. They differ from each other according to their oxygen transportation. PFC are biologically immobile materials that can be solve about 50 times more oxygen than blood plasma. They are inexpensive and capable of producing free from any biological materials. This can prevent spreading an infectious disease through a blood transfusion. But they have two serious problems. First, they are insoluble in water, which means they need to be merged with emulsifiers before use like fatty compounds called lipids that are able to suspend small particles of perfluoro-chemicals in the blood. Second, they do not have the capacity to carry oxygen as much as hemoglobin-based products do. Due to such problems its commercial use has not been thriven.

Hemoglobin-based products

Hemoglobin transports oxygen from the lungs to the body tissues and transports CO_2 from body tissues to the lungs. Artificial blood based on hemoglobin can perform a natural function. Oxygen covalently attaches to hemoglobin. These hemoglobin are not encased in a membrane so the problem of blood typing is obliterated.

It has to be considered that raw hemoglobin cannot be applied; because it would break down into compounds which are toxic to the body and etc.. For the production of a hemoglobin-based artificial blood, a raw hemoglobin molecule must be modified. To stabilize hemoglobin, different techniques such as chemically cross-linking molecules or recombinant DNA technology is using to produce modified proteins similar to stabilized hemoglobin solutions, polymers encapsulated hemoglobin, polymerized hemoglobin solutions, conjugated hemoglobin solutions.

Artificial blood can be made in several ways using synthetic production, recombinant biochemical technology or chemical isolation. Synthetic hemoglobin-based productions are made from hemoglobin collected from an *E. coli* bacteria. Conjugation of hemoglobin enlarges its molecular size and decreases antigenicity, which in turn causes a slow rate of removal from the circulation and reduced "visibility" to the reticulo-endothelial system. Unique features of conjugated hemoglobins are their viscosity and their high oncotic pressure, which causes them to be very potent plasma-volume expanders. Intramolecular cross-linked hemoglobins are not crucially enlarged in molecular weight but have specific chemical cross-links between polypeptide chains which prevent splitting to dimers or monomers. Such improved hemoglobins are more stable and dissolvable in it have a higher capability to carry oxygen than normal red blood cells.

Production process

Different kinds of raw materials must be used according to the type of artificial blood. Hemoglobin-based productions can be apply either isolated or synthetically produced hemoglobin. To synthesize hemoglobin, amino acids and specific type of bacteria are required.

The hemoglobin can also be isolated from human blood. It is mainly provided through donated blood that has expired. Other resources of hemoglobin come from animal blood and must be modified before being used. The main steps for the production of hemoglobin-based products involve isolation or synthesization of hemoglobin, molecular modification and then rebuilding in an artificial blood formula.

Hemoglobin synthesis

For the production of hemoglobin, a specific strain of *E. coli* is used. This strain is capable of synthesizing human hemoglobin. (After an interval of 3 days, the protein is collected and the bacteria will be expunged). To start the fermentation procedure, a specimen of the genuine bacteria culture is transferred to a test tube which contains a suitable growth media.

After bacterial proliferation, they will be moved to a seed tank which is a large stainless steel tank that gives a favorable environment for bacterial growth. This tank have warm water, food, and an ammonia source which all are necessary for the production of hemoglobin. Growth factors such as vitamins, amino acids, and minor nutrients also can be added. The bacterial solution inside the seed tank is continuously bathed with compressed air along with mixing. After an interval of time, the contents of the seed tank is moved to the fermentation tank.

The fermentation tank is also filled with a growth media which is required for the bacterial growth and hemoglobin production. The control of pH is necessary for optimal growth; hence, ammonia water should be added to the tank. Once the required amount of hemoglobin has been synthesized, the tank will be vacanted.

In this stage isolation begins. It employs a centrifugal separator that can isolate much of the hemoglobin. Later it can be segregated and purified with the help of Fractional Distillation. Fractional Distillation is a method which consists of boiling a liquid to separate one or more components and passing that through vertical structures called fractionating columns. Through this column, the hemoglobin is conducted to a final processing tank.

This is the last step where hemoglobin is mixed with water and other electrolytes to complete the production of the artificial blood. Eventually, the artificial blood should be pasteurized and put into a favorable packaging. The quality of compounds must be checked regularly. Frequent checks must be performed on the bacterial culture. All physical and chemical properties of the final product must be checked. These include pH, melting point, moisture content, and etc. This production technique has been proved to be able to produce batches as large as 10,000 L.

Blood Pharming

There is a new method to grow human red blood cells from cells that are extracted from umbilical cord. This method is known as blood pharming.

Here, the first step is isolation of hematopoietic stem cells from an umbilical cord. “We then culture those on our Nanex technology, which is a polymer nanofiber substrate that expands the stem cells much more rapidly than normal cell culture techniques”, Sorkin explains. “In 10 days we get a 300 to 350-fold increase in cells and over a month we can get hundreds of thousands, or a million-fold increase”.

The second step is to rebuild the differentiation process *in vitro*, with the help of special cocktail of growth factors to make a favorable environment same as what exists in the body. Scientists circumspectly lead most of these stem cells to form red blood cells that have the ability to function same as the red blood cells that the men would produce natively.

At the last step, cells must be filtered and placed in plasma or fluid before direct blood transfusion. Recent method of artificial blood production through stem cells is as follows: First step is to take out blood cells from a human donor with the universal blood group O negative. Next is to rewound blood cells into a stem cell-like state, creating induced pluripotent stem cells (iPS). iPS cells are then cultured for one month, turning into red blood cells. Eventually, mature red blood cells are produced and disserted from immature cells in a centrifuge. These red blood cells are ready for transfusion.

Conclusion

Due to sophisticated medical and surgical processes such as cardiovascular and transplant surgery, trauma care and therapy for cancer and blood disorders such as sickle cell anemia and thalassemia, the need for blood is increasing day by day, but there is a shortage of blood supply.

That is why scientists are trying to produce a suitable substitute for blood. In addition, artificial blood can be stored for long periods of time, in contrast to human blood that must be used within a few weeks of being stored.

Artificial blood can be stored at room temperature, whereas human blood must be kept refrigerated. Also, with the help of man-made blood there is no risk of a transfusion reaction caused by mismatched blood type. Synthetic blood are sterilized and hence, there is no risk for different kinds of infections caused by blood transfusions.

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FIGURE OUT STABLE MODIFIED DNA BASE

DNA structure was discovered more than 60 years ago and as we know well, it comprised of four bases: G, A. T and C. the way of they ordering determined the function of genome. Temporary modification of these bases (adding small molecules to them) is a way to regulation of genome. 5-formylcytosine is a modified DNA base first discovered in 2011. TET enzymes with adding oxygen to methylated DNA form this naturally modification. Before the new report that published in the journal of Nature Chemical Biology, scientist thought this is transitional state of cytosine base in DNA. But, Researchers from the Babraham Institute and the University of Cambridge figure out that 5-formylcytosine (5fC) appears to be stable in all tissues in mammalian. This is a big step that candidate the 5fC as fifth base in DNA. This is very rare modification that occur around 10 per million in brain where it is most common and 1-5 per million in other tissues. The researchers believe that this modification maybe alter protein recognition way for DNA. “While work is ongoing in specifying the detailed function of this ‘extra’ base, its position in the genome suggests that it has a key role in the regulation of gene expression” said Professor Shankar Balasubramanian, Department of Chemistry and Cancer Research, Cambridge Institute, UK. Researchers use measuring of carbon and hydrogen isotope uptake to 5fC that fed to mice and cells to detect percentage of stable and transient state of the molecule.

Reference: http://www.cam.ac.uk/research/news/

NEW INSIGHT INTO THE PRION DISEASES CURE

As we knew previously some heterogenisity state in proteins and genes help to resistance against some diseases like malaria. In the case of neurodegenerative diseases, it seems that such mechanism work as well, the scientist report in nature. Misfolded cellular Prion Protein (PrP) assemblies is responsible for lethal neurodegenerative diseases such as Kuru or Creutzfeldt–Jakob Disease (CJD). Mammalian Prions are transmissible agents and as they are proteins, they have variants and work under evolution force. A novel PrP variant that was under positive evolutionary selection during the epidemic of Kuru in heterozygous state can estimate strong protection against both Kuru and classical Creutzfeldt–Jakob disease. As coauthor John Collinge a neurologist and molecular biologist at University College of London says “We’ve never seen anything before that is completely protective” and it express the importance of the discovery.

Also, understanding the mechanism behind of this event can help us to develop new ways to cure of Parkinson and Alzheimer and many other neurological diseases that aggregation of proteins are cause of them.

Reference: http://www.ncbi.nlm.nih.gov/pubmed/23764833

OBSERVING of DNA REPROGRAMMING in GERM CELLS for the FIRST TIME

The codes of life are embedded in our DNA molecule in cells as genes. The genes turned on or off according to cell situation and growth stages. One mechanism for this regulation is based on epigenetic switches. One well known example of these switches is adding methyl molecules to DNA to set-out gene expression. The patterns of methylation in DNA are caused by interaction with environment or spontaneous procedures almost in all conditions occur in germ lines before transmission to next generation. According to a study by professor Surani and colleagues in Welcome Trust/Cancer Research, UK Gurdon Institute, University of Cambridge, the reprogramming of epigenetic pattern, to inhibition of epigenetic error accumulation in generations, initiate in primordial germ cells that generate germ cells, located in embryo in week two and continues through to around week nine. In this step around 95% of our DNA reprogrammed. The rest of DNA regions or escapee regions resistant to reprogramming which are active in neural cells particularly and maybe their role in development of cells caused this exception. It seems that some epigenetic information could pass down to several future generations and some regions are same in human and mice. Retroelements made of almost more than 50% of our genome. They have entered to genome mainly by foreign invaders such as bacteria and plants DNA and depend on condition, may have advantages and particularly in case of jumping ones, disadvantages that they could interrupt genes structures. Researcher found that in human genome notable fraction of the retroelements considered as escapees. It is proposed that maybe some epigenetic information in development path is for protection of us from potentially detrimental effects.

Reference: http://www.cam.ac.uk/research/news/reprogramming-of-dna-observed-in-human-germ-cells-for-first-time

Announcements

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http://www.icbbt.org/

http://cse2016.org/bioen/index.html

Announcements

http://www.icbfs.org/

http://www.icbpe.org/

http://www.icbsp.org/

Book Alert

- **ALTERED GENES, TWISTED TRUTH**

Publisher: Clear River Press

Author: Steven Druker

ISBN: 978-0985616908

- **MOLECULAR BIOLOGY OF THE GENE, 7/E**

Publisher: Benjamin Cummings

Authors: James D. Watson, Cold Spring Harbor Laboratory

Tania A. Baker, Massachusetts Institute of Technology

Stephen P. Bell, Massachusetts Institute of Technology

Alexander Gann, Cold Spring Harbor Laboratory

Michael Levine, University of California, Berkeley

Richard Losick, Harvard University

ISBN: 9780321762436

- **EPIGENETICS: CURRENT RESEARCH AND EMERGING TRENDS**

Publisher: Caister Academic Press

Editor: Brian P. Chadwick, Department of Biological Science, Florida State University, USA

ISBN: 978-1-910190-07

Title: Nucleosome 1KX5 2

Nucleosome is an structural unit of DNA in eukaryotes that provide more condensed DNA in the cells. The DNA wrap tightly around eight histones molecules. Histones are basic proteins which could bind to DNA and pack them. The scheme is a cartoon representation of the nucleosome structure which DNA shown as blue and green while histone octamer shown as ribbon coils.

Reference: https://commons.wikimedia.org/wiki/File:Nucleosome_1KX5_2.png

Title: Ebola virus virion

Ebola is a kind of virus within the family *Filoviridae*, genus *Ebolavirus* cause of a sever and often fatal hemorrhagic fever. The virus could to infect human or nonhuman primates. The first discovery of Ebola was in 1976 near the Ebola river. Ebola viruses carries a negative-sense RNA genome and the virions are cylindrical/tubular that their length could to reach up to 1000 nm.

Reference: https://commons.wikimedia.org/wiki/File:Ebola_virus_virion.jpg

Title: pBR 322 PLASMID

pBR322 plasmid is an extra chromosomal DNA molecule in bacteria which widely used in *E. coli* cloning vectors. It created in 1977 in the laboratory of Herbert Boyer, University of California, USA. It was named after the creators of plasmid; Bolivar and Rodrigez. The p refers to "plasmid".

pBR322 has 4361 base pairs in length and contains the origin of replication (OriC) of plasmid pMB1. pBR322 also comprises the ampR gene, encoding the ampicillin resistance protein and the tetR gene, encoding the tetracycline resistance protein. The plasmid has distinctive restriction sites for more than forty restriction enzymes which can be used to entering a foreign gene into the plasmid.

Reference: https://en.wikipedia.org/wiki/PBR322/