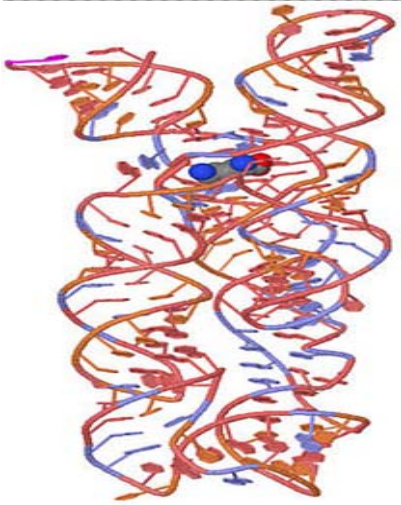

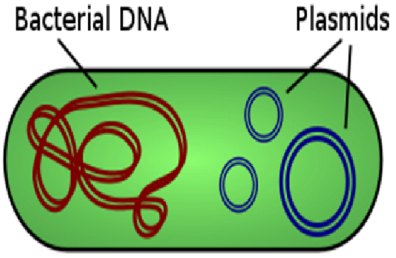

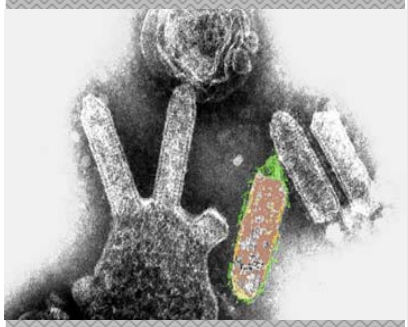

EMGEN Newsletter

Vol. 6, Issue 7

IN THIS ISSUE:

Eastern Mediterranean Health Genomics and Biotechnology Network (EMGEN) was created in 2004 with collaboration of representatives of selected centers 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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NEUROTRANSMITTER

Neurotransmitters (chemical messengers) are innate biochemicals that assist neurotransmission. They transfer indications through a biochemical synapse, for example a neuromuscular intersection, from one neuron to another "objective" neuron, muscle cell, or gland cell. These are secreted from synaptic vesicles in synapses into the synaptic gap, where they are sensed by receivers on the objective cells. Several neurotransmitters are produced from simple and abundant precursors, e.g. amino acids, which are easily accessible from the regime and lonely need a small quantity of biosynthetic stages of alteration. Neurotransmitters have a chief impress in determining daily life and utilities. Their precise amounts are anonymous, but more than 100 chemical messengers have been exclusively recognized. There are two types of neurotransmitters: Inhibitory and Excitatory.

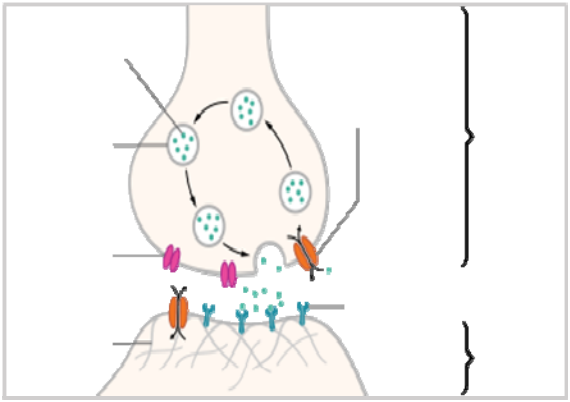

Figure 1: Structure of a typical chemical synapse.

Excitatory biochemicals are not certainly agitating, they are what agitate the brain. Biochemicals that assuage the brain and aid make equivalency are termed inhibitory. Inhibitory neurotransmitters equivalent status and are simply discharged when the excitatory biochemicals are overcharged.

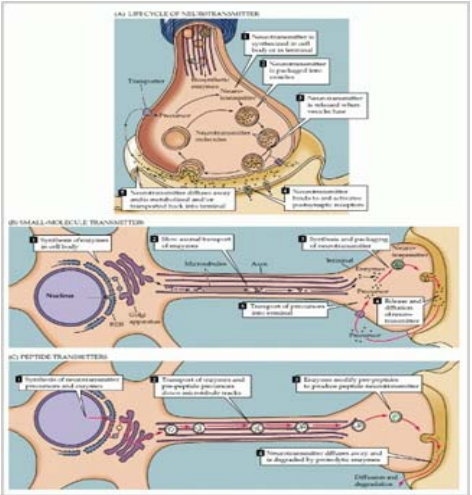

Figure 2: The synthesis, packaging, secretion, and removal of neurotransmitters.

Inhibitory neurotransmitters

Serotonin is a repressor neurotransmitter, which consequently it does not motivate the brain. Sufficient quantities of serotonin are essential for a steady attitude and to equilibrium any extreme excitatory neurotransmitter discharge in the brain. If you consume stimulating drugs or caffeine in your regular regime, it can origin a reduction of serotonin during the time. Serotonin furthermore controls numerous other routes; for example, carbohydrate consumption, sleep, pain rein and suitable ingestion. Small serotonin levels are moreover related to reduce immune system action. GABA is a repressor neurotransmitter that is usually mentioned to as “nature’s Valium-comparable material”.

When GABA is produced consumedly, it is probable that an excitatory neurotransmitter is producing too in the brain. GABA will be directed out to equilibrate this exciting over-producing. Dopamine is a distinct neurotransmitter since it is assumed to be both excitatory and inhibitory. Dopamine aids with dejection in addition to focus.

Excitatory neurotransmitters

Once dopamine is either decreased or reduced – for example, not recollecting where we left our keys, misremembering what a passage explained when we ended reading it or ordinary castle building and not being capable to do a job. Dopamine is moreover accountable for our energy or wish to get affairs done - or incentive. Motivates such as medicines for ADD/ADHD and caffeine force dopamine to be discharged into the synapse, consequently attention is enhanced. Regrettably, inspiring dopamine constantly can cause a reduction of dopamine over time. Norepinephrine is an excitatory neurotransmitter that is in charge for excitatory routes in the body. Norepinephrine aids to produce epinephrine too. This neurotransmitter can cause anguish at raising levels in addition to some “temper reducing” possessions. Little amounts of norepinephrine are related to short energy, reduced attention aptitude and sleep difficulties.

Epinephrine is an excitatory neurotransmitter that is inverting of stress. This biochemical can be raised when ADHD like indications are existing. Long term pressure or sleeplessness can decrease the levels of epinephrine. Epinephrine additionally controls heart rate and blood pressure.

There are four key principles for recognizing neurotransmitters:

1. The chemical must be created in the neuron or be existing in it.

2. When the neuron is vigorous, the chemical must be discharged and induce a reaction in some targets.

3. The similar reply must be gained when the chemical is empirically used on the target.

4. A procedure must be available for eliminating the chemical from its place of triggering after its object is completed.

Nevertheless, the word "neurotransmitter" can be used to chemicals that:

1. Transport messages between neurons via an effect on the postsynaptic membrane.

2. Have slight or none influence on membrane voltage, but have a mutual transport utility, such as altering the construction of the synapse.

3. Communicate by directing inverse-path messages that affect the discharge or reabsorption of transmitters.

Neurotransmitter imbalance

Neurotransmitter imbalances are the reason of numerous illnesses. These comprise Parkinson's, dejection, sleeplessness, attention deficit hyperactivity disorder (ADHD), anguish, memory damage, severe alterations in weight and habits. They all are related to amino acids, which build neurotransmitters. Amino acids are shaped proteins and cells are not organized correctly in lacking an adequate quantity of this, consequently not operating correctly. Long-lasting pressure is the main cause of neurotransmitter imbalance. Bodily and emotional stress from an occupation or a relationship origins neurons to consume a great quantity of neurotransmitters with the purpose of managing the current stress. After a period, stress rub off the nervous system and reduces neurotransmitter source. Heredity has a major role in neurotransmitter imbalance. Some persons are born with neurotransmitter shortages or the excrescence. Experts are trying to support the shortages by using drugs; adding amino acids into the body. Drugs that instantly counter with serotonin and norepinephrine are approved for patients with illnesses such as dejection and anxiety complaints.

Drug effects

Realizing the effects of medicines on neurotransmitters is an important question in the field of neuroscience. Most researchers in this arena believe that such determinations may later develop our comprehension of the factors liable for many neurological ailments and complaints, in addition to methods to successfully treat and someday probably avoid or remedy such ailments. Medications can affect performance by changing neurotransmitter activity. For example, medications can reduce the speed of production of neurotransmitters by motivating the synthetic enzyme(s) for that neurotransmitter. When neurotransmitter production is stanched, the quantity of accessible neurotransmitters becomes considerably lower, causing a reduction in neurotransmitter activity. Some medications stop or excite the discharge of precise neurotransmitters. On the other hand, medications can avoid neurotransmitter storing in synaptic pouches by triggering the synaptic pouch membranes to exude. Medications that avert a neurotransmitter from attaching to its receptor are termed receptor antagonists. For instance, medications utilized to cure patients with schizophrenia; e.g. chlorpromazine, clozapine, and haloperidol are antagonists at receptors in the brain to dopamine. Other medications perform by attaching to a receptor and simulating the standard neurotransmitter. Such medications are termed receptor agonists.

Other medications intervene with disabling a neurotransmitter after it has been produced, thus extending the action of a neurotransmitter. This can be done by choking re-uptake or preventing destructive enzymes. Finally, medications can likewise avoid an action from happening, blocking the neuronal action via the central and marginal nervous system. Medications such as tetrodotoxin that choke neural activity are naturally deadly. Medications aiming the neurotransmitter of the main systems affect the entire system, which can clarify the intricacy of the act of some medications. As dopamine stays in the synapse lengthier, the neurotransmitter endures to attach to the receptors on the postsynaptic neuron, provoking an enjoyable emotive reply.

Diseases and disorders

Sicknesses and complaints may furthermore distress precise neurotransmitter systems. For instance, difficulties in creating dopamine can cause Parkinson's ailment, a complaint that disturbs a person's capability to act as they want to, causing rigidity or shaking, and other indications. Some investigations propose that having too slight dopamine or difficulties utilizing dopamine in the thinking and sensation areas of the brain may play a role in complaints like schizophrenia or attention shortage hyperactivity complaint. Additionally, difficulties in glutamate usage have been related to numerous cerebral complaints, counting autism, obsessive compulsive disorder (OCD), schizophrenia, and depression.

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ELECTROPORATION

Electroporation is a practice in which an electrical ground is utilized to upsurge the penetrability of the cell membrane, permitting chemicals, medicines, or DNA to be transferred into the cell. In microbiology, the procedure of electroporation is usually utilized to transform bacteria, yeast, or plant protoplasts by transferring novel coding DNA. If bacteria and plasmids are blended together, the plasmids can be moved into the bacteria after electroporation, however reliant on what is being moved, cell-incisive peptides could furthermore be applied. It works by transiting some hundred volts through a space of several millimeters are normally utilized in this procedure. Subsequently, the cells have to be treated sensitively until they have had a chance to amplify, creating novel cells that comprise copied plasmids. This procedure is nearly ten times more operative than chemical conversion. Electroporation is extremely effectual for transferring oversea genes to tissue culture cells, particularly mammalian cells. For instance, it is applied in the procedure of creating knockout mice, in addition to cancer therapy, gene therapy, and cell-based therapy. The procedure of transferring oversea DNA into eukaryotic cells is recognized as a transfection. Electroporation is extremely operative for transfecting cells in suspension by electroporation cuvettes. Electroporation has confirmed the effectiveness for usage on tissues *in vivo*, for *in utero* submissions in addition to *in ovo* transfection. Cohort cells can additionally be transfected by electroporation, supplying scholars with a substitute to trypsinizing their cells before transfection.

Advantages and Disadvantages of Electroporation

Numerous approaches other than electroporation are utilized to transfer polar molecules like DNA into host cells. These approaches comprise microprecipitates, microinjection, liposomes, and biological shuttles.

A) Advantages:

1. Flexibility: Electroporation is operative with almost all cell and species kinds.

2. Effectiveness: A big majority of cells receives the objective DNA or molecule. In a work on electrotransformation of *E. coli*, for instance, 80% of the cells received the oversea DNA.

3. Small scale: The quantity of DNA required is lesser than for other approaches.

4. *In vivo*: The process can be done with whole tissue.

B) Disadvantages:

1. Cell destruction: If the beats are of the incorrect length or strength, some pores may convert too big or fail to close after membrane discharge producing cell injury or breach.

2. Nonspecific carriage: The carriage of substances into and out of the cell through the time of electropermeability is comparatively nonspecific. This may cause an ion inconsistency that could later produce unsuitable cell function and cell death.

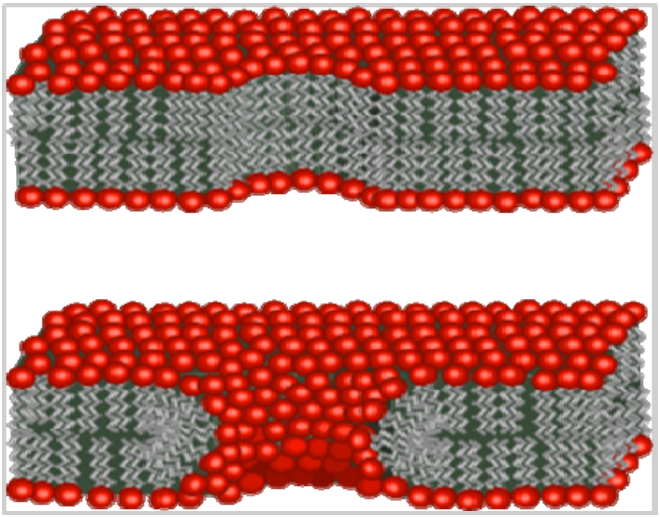

Figure 1: Schematic representation of the theoretical arrangement of lipids in a hydrophobic pore (top) and a hydrophilic pore (bottom).

Physical mechanism

Electroporation lets cellular transfer of big extremely charged particles, e.g. DNA, which would never inactively transfer across the hydrophobic bilayer core. This aspect designates that the process is the formation of tiny-scale water-occupied holes in the membrane. Though electroporation and dielectric collapse both come from submission of an electrical ground, the appliances used are basically dissimilar. In dielectric collapse the obstacle material is ionized, generating a conductive path.

The material modification is therefore chemically in the environment. Dissimilarly, through electroporation the lipid molecules are not chemically modified, but solely change location, opening up a pore which performs as the conductive path over the bilayer as it is occupied with water. Electroporation is a dynamic aspect that is influenced by the local transmembrane voltage at each point on the cell membrane. It is commonly recognized that for a given pulse period and form, a definite transmembrane voltage onset occurs for the exhibition of the electroporation phenomenon (from 0.5 V to 1 V). This causes the description of an electric field dignity onset for electroporation (Eth).

Applications

Electroporation is extensively applied in several areas of molecular biology study and in the medical arena. Some submissions of electroporation comprise:

1. DNA transfection or transformation: This is the most extensive application of electroporation. Definite genes can be cloned into a plasmid and then this plasmid transferred to host cells so as to examine gene and protein construction and function.

2. Straight transmission of plasmids between cells: Bacterial cells previously comprising a plasmid may be hatched with an additional strain that does not comprise plasmids but that has some other desirable properties. The voltage of electroporation will generate pores, permitting some plasmids to exit one cell and enter another. The chosen cells may then be nominated by antibiotic resistance or alternative approaches.

This kind of transmission may moreover be achieved between species. Therefore, greater quantities of plasmids can be grown quickly by reproducing bacterial colonies and then transported to yeast cells by electroporation for study.

3. Prompted cell fusion: The distraction of the membrane that happens with the rapid pulse of electricity in the electroporation process has moreover been shown to prompt fusion of cells.

4. Transdermal drug delivery: As electroporation origins passing pores to form in plasma membranes, comparable pores form in lipid bilayers of the cortex corneum- the outmost dead layer of skin. These pores could permit medications to pass through to the skin to an objective tissue. This technique of drug delivery would be more agreeable than inoculation for the patient and could evade the difficulties of unsuitable absorption or degradation of oral medicine in the gastric system.

5. Tumor electro-chemotherapy: Researchers are examining the possibility of electroporation to upsurge the usefulness of chemotherapy. As in electroporation for DNA transformation, the used electrical pulse would disturb the membrane of the tumor cell and upsurge the quantity of medicine supplied to the site.

6. Gene therapy: Electroporation skills can permit vectors comprising vital genes to be transported through the skin and into the objective tissue. When combined into the cells, the protein created from this gene could substitute a faulty one and thus cure a genetic complaint.

Drug and gene delivery

Electroporation can be utilized to aid carry medicines or genes into the cell by putting short and strong electric pulses that rapidly permeabilize the cell membrane, so permitting the carriage of molecules could not convey by a cellular membrane. This process is stated to as electro-chemotherapy when the particles to be conveyed are chemotherapeutic agents or gene electrotransfer when the molecule to be conveyed is DNA.

Researchers practice electroporation of exosomes to transport siRNAs, antisense oligonucleotides, chemotherapeutic agents and proteins exactly to neurons after inoculating them systemically (in blood). Since these exosomes are talented to cross the blood brain blockage this procedure could resolve the problem of weak distribution of drugs to the CNS and cure Alzheimer's and Parkinson's ailments and brain tumor between other illnesses.

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UNCOVERING THE MYSTERY OF DNA REPLICATION

Lately, a set of enzymes was revealed named Thg1-similar proteins (TLPs), which were recognized to add nucleotides in the opposite path. Instances of adding nucleotides in this way are uncommon. TLPs are the exclusion and increase nucleotides in the opposite path to overhaul the "opposite end" of broken RNAs. In this study, researchers applied X-ray crystallography to expose the construction of the TLP/RNA composite. This provided them a vision of the intricate mechanism that TLPs hire to add nucleotides in the opposite path. Their fundamental examination discovered a two-step procedure: energy-providing molecules are employed and then nucleotide is added. The second phase has moreover been observed in the forward reaction. What was inimitable to the opposite reaction was the employing energy at the start. The enzyme seemingly uses this energy employment to change the path from forward to backward. The team considers that the reverse-path enzyme is not utilized in DNA duplication since it needs a basically complex procedure. "By associating the molecular appliances of forward and backward reactions in more aspect, we would be able to completely comprehend the evolutionary background of DNA duplication," says Yao, chief scientist.

Reference: https://www.sciencedaily.com/releases/2016/07/160713102725.htm

DISCOVERY OF A NEW DEFENSE SYSTEM AGAINST MICROBIAL PATHOGENS

For the first time, scientists found a humanoid immune receptor, which senses the assault of pathogenic microbes. They thus prospered in recognizing an up to now unidentified host protection mechanism. These outcomes will help to upcoming progresses in the therapy and avoidance of infectious illnesses. The scientists in Japan currently completed the finding that definite varieties of microbes dodge the immune system by generating protein-piercing enzymes (protease), which slice and thus deactivate antibodies that activate immune answers in the host. They additionally discovered an up to now unidentified receptor inside the host that identifies the sliced antibodies and contest the immune dodging mechanisms of pathogenic microbes. The scientists identified these receptors (LILRA2) when they examined humanoid cell strains diseased with *Mycoplasma*, which are exceedingly small microbes having no cell walls.

As with *Mycoplasma*, other pathogenic microbes, e.g. *Legionella*, *pneumococcus* and *Haemophilus influenzae* in addition to *Candida* similarly generate protease that slices antibodies. About *Legionella*, which contaminate and reproduce inside immune cells, results display that their development is repressed when LILRA2 identify the sliced antibodies. Likewise, LILRA2-indicating cells were triggered in other spaces infected with microbes too, e.g. tympanitis, inflammatory atheroma, and cellulitis.

Reference: https://www.sciencedaily.com/releases/2016/07/160712110758.htm

NEW PROTOCOL ENABLES ANALYSIS OF METABOLIC PRODUCTS FROM FIXED TISSUES

In the biomedical study, operating tissue samples is crucial since it authorizes visions into the biological reality of patients, for instance, along with those acquired from Petri dishes and computer models. The tissue is typically fixed in formalin and entrenched in paraffin wax so as to retain the tissue, as long as probable, in its unique state for further examines. It was formerly expected that in substances that had been preserved in this way an examination of metabolites, in comparison to DNA or proteins, would be hardly probable for technical details. A team of academics has now got rich in refusing this opinion. Scientists established a procedure which creates it feasible - in one day - to define the structure of the tissues by a mass spectrometry method, and to create it evident in tissue pieces. Comparatively slight quantities of material are essential for this, as said by the authors. This technique allows the examination of tiny cultures and even tissue microarrays, creation of it is chiefly exciting for molecular study and diagnostics. To confirm that the gauged data was not untrue by the fixation procedure, the scholars related it with the gauged quantities for the similar testers that were not fixed but were shocked frosty. Furthermore to simple treatment and high repeatability, the likelihood to manage high quality work is a vital improvement of the novel technique, based on the researchers. In particular, it is currently thinkable to investigate the spatial dispersal of particles in the tissue clearly and with high accuracy.

Reference: https://www.sciencedaily.com/releases/2016/07/160715112942.htm

Book Alert

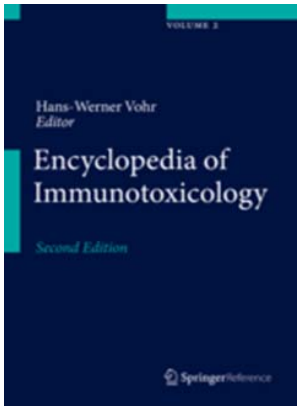
ENCYCLOPEDIA OF IMMUNOTOXICOLOGY

Publisher: Springer international publishing

Author: H.W. Vohr

Publication Date: 2016

ISBN: 978-3-642-54595-5



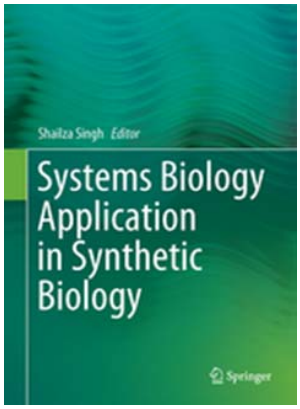
SYSTEMS BIOLOGY APPLICATION IN SYNTHETIC BIOLOGY

Publisher: Springer international publishing

Author: S. Singh

Publication Date: 2016

ISBN: 978-81-322-2807-3



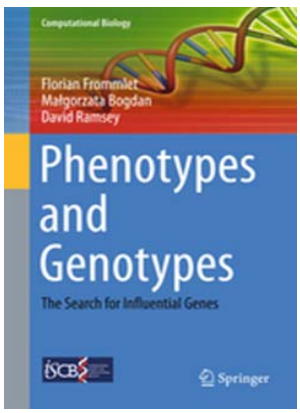
PHENOTYPES AND GENOTYPES

Publisher: Springer international publishing

Author: F. Frommlet, M. Bogdan and D. Ramsey

Publication Date: 2016

ISBN: 978-1-4471-5310-8

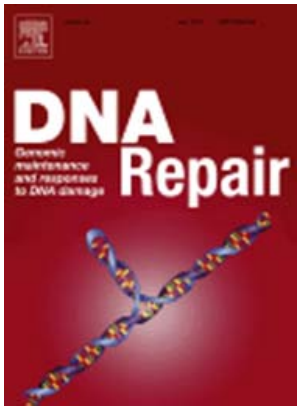


DNA REPAIR

Scope: Genetic, cellular, biochemical, structural and molecular aspects of DNA repair, mutagenesis, cell cycle regulation, apoptosis and other biological related issues.

Impact Factor: 3.929

ISSN: 1568-7864

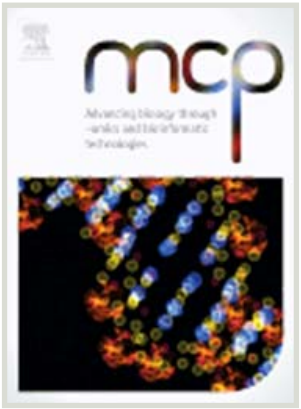


MCP

Scope: Molecular biology, cell biology, biochemistry, immunology, physiology, epidemiology, ecology, virology, microbiology, parasitology, genetics, evolutionary biology, genomics, bioinformatics, proteomics, metabolomics, glycomics, and lipidomics.

Impact Factor: 5.912

ISSN: 0890-8508

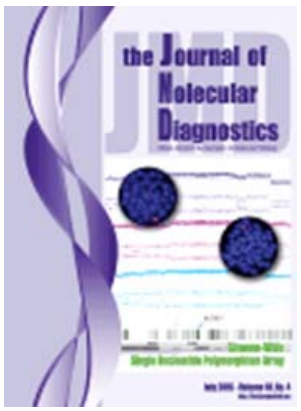


THE JOURNAL OF MOLECULAR DIAGNOSTICS

Scope: Molecular discoveries in medicine, clinical diagnostic settings, molecular diagnostic medicine.

Impact Factor: 5.201

ISSN: 1525-1578



Announcements

www.biotherapeuticsanalyticalsummit.com

http://www.icbfs.org/

http://www.sexualhealthconference.com.au/ehome/index.php?eventid=169685&

https://eutranslationalmedicine.org/eustm-2016/

RIBOSWITCH

In molecular biology, a riboswitch is a tuning particle of an mRNA molecule that attaches a small molecule, causing an alteration in the creation of the proteins determined by the mRNA. Therefore, an mRNA that comprises a riboswitch is straightly involved in tuning its own action, in reply to the quantity of its effector particle. The finding that contemporary creatures utilize RNA to attach small molecules, and distinguish beside strictly associated equivalents, extended the recognized natural capabilities of RNA further than its aptitude to code for proteins, catalyze reactions, or to attach other RNA or protein molecules. The main explanation of the word "riboswitch" shows that they straightly sense small-molecule metabolite concentrations. Most recognized riboswitches happen in bacteria, but one kind of these have been found in plants and definite fungi.

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

PLASMID

A plasmid is a small DNA fragment inside a cell that is actually unrelated to a chromosomal DNA and can duplicate autonomously. They are most frequently available in bacteria as small circular, double-stranded DNA particles; while, plasmids are occasionally existing in archaea and eukaryotic creatures. In nature, plasmids usually transmit genes that may advantage the existence of the creature, e.g. antibiotic resistance. Though chromosomes are big and comprise all the vital genetic material for living in regular circumstances, plasmids typically are very tiny and comprise merely extra genes that could be valuable for the creature in definite circumstances. Synthetic plasmids are extensively applied as carriers in molecular replication, helping to effort the duplication of recombinant DNA structures inside host creatures. Plasmids are assumed replicons, a unit of DNA capable of duplicating separately inside a proper host. Nevertheless, plasmids, similar to viruses, are not usually categorized as life. Plasmids can be diffused from one bacterium to another by three key mechanisms: transformation, transduction, and conjugation. This host-to-host transferal of genetic material is termed horizontal gene transmission.

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

LYSSAVIRUS

Lyssavirus is an RNA virus, in the family Rhabdoviridae. Hominids, mammals, and vertebrates are its usual hosts. There are 14 species in this genus comprising the *Rabies virus*. Viruses in *Lyssavirus* are coated, with bullet formed structure. These viruses have nearby 75 nm wide and 180 nm long. *Lyssaviruses* have helical symmetry, so their infectious units are roughly cylinder-shaped. This is a usual plant-infecting virus.

Human-infecting viruses more frequently have cubic symmetry and yield forms similar to regular polyhedral. The particle contains a specific outer coat, a central area comprising matrix protein M, and an internal ribonucleocapsid complex, comprising the genome connected with other proteins. *Lyssavirus* genome contains a negative-sense, single-stranded RNA particle that codes five viral proteins: polymerase L, matrix protein M, phosphoprotein P, nucleoprotein N, and glycoprotein G. Genomes are linear, around 11kb in length.

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