DOWNLOAD PDF MOLECULAR VIROLOGY

Chapter 1 : Institute for Molecular Virology

Molecular virology is the study of viruses on a molecular level. Viruses are submicroscopic parasites that replicate inside host cells. They are able to successfully infect and parasitize all kinds of life forms- from microorganisms to plants and animals- and as a result viruses have more biological diversity than the rest of the bacterial, plant, and animal kingdoms combined.

Viral replication[edit] Viruses rely on their host to replicate and multiply. This is because viruses are unable to go through cell division, as they are acellularâ€"meaning they lack the genetic information that encode the necessary tools for protein synthesis or generation of metabolic energy; hence they rely on their host to replicate and multiply. According to this system, viruses are classified into seven classes based on their replication strategy: Depending on the location of genome replication, this class can be subdivided into two groups: These viruses only replicate in the nucleus. The viruses in this class have segmented genomes. Each segment is transcribed individually to produce a monochromatic mRNA that codes for only one protein. Single-stranded RNA - Positive-sense. These viruses can be subdivided into two groups depending on their translation process: Single-stranded RNA - Negative-sense. Retroviruses are the most well-known family among this class. The genome of these viruses are gapped, double-stranded, and subsequently become filled to form cccDNA covalently closed circular DNA. This group also use the reverse transcription during the process of maturation. The host range of a virus is determined by the specificity of the binding. Due to their rigid cellulose -made chitin in case of fungal cells cell walls, plants and fungal cells get infected differently than animal cells. Often, a cell wall trauma is required for the virus to enter the cell. The capsid could have been degraded by either host or viral enzymes, releasing the viral genome into the cell. The process includes the transcription of mRNA, synthesis, and assembly of viral proteins and is regulated by protein expression. On the other hand, enveloped viruses become released by a process called budding in which a viruse obtain its lipid membrane as it buds out of the cell through membrane or intracellular vesicle. There is a specialized field of study in virology called viral pathogenesis in which it studies how viruses infect their hosts at the molecular and cellular level. First, the virus has to enter the body and implant itself into a tissue e. Second, the virus has to reproduce extracellular after invading in order to make ample copies of itself. Third, the synthesized viruses must spread throughout the body via circulatory systems or nerve cells. This image shows a non-specific interstitial pneumonia pattern with no giant cells present. With regards to viral diseases it is essential to look at two aspects: The course and severity of all viral infections are determined by the dynamic between the virus and the host. Common symptoms of virus infections are fever, body aches, inflammation, and skin rashes. The shape of adherent cellsâ€" cells that attach themselves to other cells or artificial substratesâ€" may change from flat to round. The cell damage is due to partial degradation of cytoskeleton. In this case the entire cell breaks down because of the absorption of extracellular fluid and swelling. It should be noted that not all viruses cause lysis. These cells have a short lifespan compared to other cells. Viruses can increase the membrane permeability which allows many extracellular ions e. This kind of infection occurs when a virus successfully invades a host cell but is unable to complete its full replication cycle and produce more infectious viruses. Created by GC microbiologist Cynthia Goldsmith, this colorized transmission electron micrograph TEM revealed some of the ultrastructural morphology displayed by an Ebola virus virion. Many common viral infections fallow this pattern. Acute infections are brief since they are often completely eliminated by the immune system. Acute infection is frequently associated with epidemics since most of virus replication happens before the onset of symptoms. These infections have a prolonged course and are hard to eliminate since the virus stays in the host for a significant period. There is a delicate balance between the host and the virus in this pattern. The virus adjusts its replication and pathogenecitiy levels to keep the host alive for its own benefit. While it is possible for the virus to live and replicate inside the host for its entire lifetime, oftentimes the host eventually eliminates the virus. Being the ultimate infection, the latent virus infections tend to exist inside the host for its entire lifetime. A well-known example of such infection is the herpes simplex virus in humans. These vaccines can prevent or lower the intensity of viral illness. Developing

vaccines against smallpox, polio, and hepatitis B over the past 50 years has had a significant impact on world health and thus on global population. Nevertheless, there have been ongoing viral outbreaks such as the Ebola and Zika viruses in the past few years affecting millions of people all around the globe. The specificity of an antiviral drug is the key to its success. These drugs are toxic to both the virus and the host but in order to minimize their damage they are developed in such a way as to be more toxic to the virus than to the host. The efficiency of an antiviral drug is measured by the chemotherapeutic index, given by: In clinical practice, this index is used to produce a safe and clinically useful drug. A Very Short Introduction. Principles of Molecular Virology. Introduction to Modern Virology. Mahy, Brian and Collier, Leslie.

Chapter 2 : Influenza: Molecular Virology

The Molecular Virology Program at Yale University is a campus-wide, interdepartmental program designed to coordinate and facilitate the study of viruses and viral diseases. The mission of the Molecular Virology Program at Yale is to facilitate the acquisition of new insights into virus biology and.

Martinus Beijerinck in his laboratory in The word virus appeared in and originally meant "venom". It involved the application of materials from smallpox sufferers in order to immunize others. In Lady Mary Wortley Montagu observed the practice in Istanbul and attempted to popularize it in Britain, but encountered considerable resistance. In Edward Jenner developed a much safer method, using cowpox to successfully immunize a young boy against smallpox, and this practice was widely adopted. Vaccinations against other viral diseases followed, including the successful rabies vaccination by Louis Pasteur in The nature of viruses however was not clear to these researchers. In , the Russian biologist Dmitry Ivanovsky used a Chamberland filter to try to isolate the bacteria that caused tobacco mosaic disease. His experiments showed that crushed leaf extracts from infected tobacco plants remained infectious after filtration. Ivanovsky reported a minuscule infectious agent or toxin , capable of passing the filter, may be being produced by a bacterium. He called it contagium vivum fluidum. In it was suggested for the first time that transduction by viruses might cause cancer. In Bang and Ellerman showed that a filterable virus could transmit chicken leukemia , data largely ignored till the s when leukemia became regarded as cancerous. Several other cancer-causing retroviruses have since been described. As bacteria could be grown easily in culture, this led to an explosion of virology research. The cause of the devastating Spanish flu pandemic of was initially unclear. While plant viruses and bacteriophages can be grown comparatively easily, animal viruses normally require a living host animal, which complicates their study immensely. In it was shown that influenza virus could be grown in fertilized chicken eggs, a method that is still used today to produce vaccines. In , Max Theiler managed to grow the yellow fever virus in chicken eggs and produced a vaccine from an attenuated virus strain; this vaccine saved millions of lives and is still being used today. The Hersheyâ€"Chase experiment in showed that only DNA and not protein enters a bacterial cell upon infection with bacteriophage T2. Transduction of bacteria by bacteriophages was first described in the same year. In John F. Enders , Thomas Weller and Frederick Robbins reported growth of poliovirus in cultured human embryonal cells, the first significant example of an animal virus grown outside of animals or chicken eggs. This work aided Jonas Salk in deriving a polio vaccine from deactivated polio viruses; this vaccine was shown to be effective in The first virus that could be crystalized and whose structure could therefore be elucidated in detail was tobacco mosaic virus TMV , the virus that had been studied earlier by Ivanovski and Beijerink. In , Wendell Stanley achieved its crystallization for electron microscopy and showed that it remains active even after crystallization. Clear X-ray diffraction pictures of the crystallized virus were obtained by Bernal and Fankuchen in Based on such pictures, Rosalind Franklin proposed the full structure of the tobacco mosaic virus in Southam , a leading virologist and cancer researcher, injected cancer patients, healthy individuals, and prison inmates from the Ohio Penitentiary with HeLa cancer cells in order to observe if cancer could be transmitted. Additionally, in hopes of creating a vaccine for cancer, he observed if the subjects could become immune to cancer by developing an acquired immune response. This experiment was highly controversial, as the cancer patient subjects were unaware that they were being injected with cancer cells. In , Howard Temin described the first retrovirus: The viral enzyme reverse transcriptase , which along with integrase is a distinguishing trait of retroviruses, was first described in , independently by Howard Temin and David Baltimore. The first retrovirus infecting humans was identified by Robert Gallo in Later it was found that reverse transcriptase is not specific to retroviruses; retrotransposons which code for reverse transcriptase are abundant in the genomes of all eukaryotes. In the functioning of oncoviruses was clarified considerably. Michael Bishop and Harold Varmus showed that the oncogene of Rous sarcoma virus is in fact not specific to the virus but is contained in the genome of healthy animals of many species. The oncovirus can switch this pre-existing benign proto-oncogene on, turning it into a true oncogene that causes cancer. In , Frederick Sanger achieved the first complete sequencing of the genome of

any organism, the bacteriophage Phi X In the same year, Richard Roberts and Phillip Sharp independently showed that the genes of adenovirus contain introns and therefore require gene splicing. It was later realized that almost all genes of eukaryotes have introns as well. A worldwide vaccination campaign led by the UN World Health Organization resulted in the eradication of smallpox in In , Stanley Prusiner discovered prions and showed that they cause scrapie. Subsequent tremendous research efforts turned HIV into the best studied virus. Several antiretroviral drugs were developed in the late s, decreasing AIDS mortality dramatically in developed countries. They contained the foreign gene but did not contain the viral genome and therefore could not reproduce. Tests in mice were followed by tests in humans , beginning in The first human studies attempted to correct the genetic disease severe combined immunodeficiency SCID , but clinical success was limited. In the period from to , gene therapy was tried on several other diseases and with different viral vectors, but it became clear that the initially high expectations were overstated. In a further setback occurred when year-old Jesse Gelsinger died in a gene therapy trial. He suffered a severe immune response after having received an adenovirus vector. In a faster method was shown to assemble the base genome of the bacteriophage Phi X in 2 weeks. The giant mimivirus , in some sense an intermediate between tiny prokaryotes and ordinary viruses, was described in and sequenced in The strain of Influenza A virus subtype H1N1 that killed up to 50 million people during the Spanish flu pandemic in was reconstructed in Sequence information was pieced together from preserved tissue samples of flu victims; viable virus was then synthesized from this sequence. By , Harald zur Hausen had shown that two strains of Human papillomavirus HPV cause most cases of cervical cancer. Two vaccines protecting against these strains were released in In and it was reported that introducing a small number of specific transcription factor genes into normal skin cells of mice or humans can turn these cells into pluripotent stem cells , known as induced pluripotent stem cells. Sputnik reproduces in amoeba infected by mamavirus , a relative of the mimivirus mentioned above and the largest known virus to date. It is estimated that about 9 percent of the human genome have their origin in ERVs. In it was shown that proteins from an ERV are actively expressed in 3-day-old human embryos and appear to play a role in embryonal development and protect embryos from infection by other viruses.

Chapter 3 : Molecular Virology group home

The Institute for Molecular Virology is a research institute located in Bock Labs and administered by the Office of the Vice Chancellor for Reasearch and Graduate Education (OVCRGE).

Influenza In the last years there have been three major influenza pandemics: These claimed the lives of approximately 50 million, 2 million and 1 million people respectively. Added to this is the annual death toll of , to , people worldwide with a further 3 to 4 million people suffering severe illness. These statistics make influenza an extremely important pathogen. However the battle against influenza is going to be difficult. Recently another subtype, H1N1, has emerged. This subtype causes a relatively mild infection in humans, however is highly transmittable between people and a new influenza pandemic was declared by the World Health Organization. If this virus were to acquire some of the lethal capabilities of H5N1, then the ensuing pandemic could be devastating. In this timely book, internationally renowned scientists critically review the current research and the most important discoveries in this highly topical field. Subjects covered include the NS1 protein of influenza A virus, the structure of influenza NS1, influenza B hemagglutinin, influenza A nucleoprotein, influenza A hemagglutinin glycoproteins, the M2 channel, virulence genes of the pandemic influenza, influenza virus polymerase, gene diagnostic microarrays, and computer-assisted vaccine design. Highly informative and well referenced, this book is essential reading for all influenza specialists and is recommended reading for all virologists, immunologists, molecular biologists, public health scientists and research scientists in pharmaceutical companies. Reviews "This is a good quality, concise book on the basic nature of influenza viruses that comprehensively covers the current work on influenza. Appropriate audiences for the book would be final-year virology students and influenza researchers. Today Table of contents 1. Krug The NS1 protein of influenza A viruses is a small amino acid , multi-functional dimeric protein that participates in both protein-RNA and protein-protein interactions. It is comprised of two functional domains: Here we focus on several of the best-characterized functional interactions of the NS1 protein. A major role of the NS1 protein is to counter host cell antiviral responses. A region of the effector domain binds the protein kinase PKR, thereby preventing its activation that would otherwise lead to the shutdown of both viral and host protein synthesis. The NS1 protein also has other functions that are not directly involved in countering host antiviral responses. The C-termini of pathogenic influenza A viruses have a PDZ-binding motif that has been implicated in pathogenicity. Finally, the NS1 protein functionally interacts with the viral polymerase complex in infected cells and likely has a role in the regulation of viral RNA synthesis. Bornholdt, Berenice Carrillo and B. Venkataram Prasad The non-structural protein 1 NS1 of influenza virus is a potent antagonist of the cellular antiviral interferon IFN response. Although, initially sequestration of dsRNA was considered the primary mechanism for countering IFN, subsequent studies have shown that the interactions of ED with various cellular proteins are likely involved. NS1 is shown to be a virulence determinant, especially in the highly pathogenic H5N1 viruses that are currently a threat for another influenza pandemic. Among various influenza virus strains, NS1 is relatively well conserved with major differences occurring in the linker region and the C-terminus, where several NS1 proteins contain truncations. How these differences contribute to virulence remains unknown but these differences seem to have an effect on NS1 function that may be strain specific. In recent years, substantial progress has been made toward understanding of the structural aspects of this two-domain protein. Here we review this progress and discuss the structural basis of various activities of NS1. Influenza Type B Virus Hemagglutinin: Antigenicity, Receptor binding and Membrane Fusion Qinghua Wang Influenza B virus infection remains a significant cause of morbidity and mortality worldwide, with particularly severe impacts on the young and the elderly. However, compared to influenza A virus, influenza B virus was very poorly studied. Most recently, a series of research have been published that drastically deepened our understanding of influenza B virus. In this review, I will summarize the recent advances on influenza B virus hemagglutinin from aspects of antigenicity, receptor binding and membrane fusion. In addition, I will discuss some of the remaining challenges in influenza B virology. The nucleoprotein NP , the major protein component of RNPs, binds along the entire length of each genomic RNA segment at a nt

interval, forming the double-helical RNP structures found in mature viruses. As one of the most abundant proteins made in infected cells, influenza virus NP has essential roles in many important viral processes, including intracellular trafficking of the viral genome, viral RNA replication, viral genome packaging, and virus assembly. Site-directed mutagenesis and RNA binding assays have confirmed that a positively charged groove plays an important role in NP: These new findings have led to a more detailed model for RNP structure and assembly. Steinhauer The influenza A virus hemagglutinin glycoprotein HA is the principle mediator of viral entry into host cells. It is responsible for attachment of virions to sialic acid-containing receptors on the host cell surface, and for inducing membrane fusion between viral envelopes and cellular endosomal membranes following endocytosis. HA serves a classic example of a type I membrane glycoprotein, with a cleaved N-terminal signal sequence, a membrane anchor domain near the C-terminus, and post-translational modifications resulting from the addition of N-linked oligosaccharide side chains to the ectodomain, and acylation of cysteine residues in the cytoplasmic tail region. HA spikes on the viral surface are also the major target for neutralizing antibodies, and as such, the antigenic properties of the HA are of fundamental significance for the design of influenza vaccines. The depth of knowledge relating to high resolution atomic structures of HA in various forms have made it a prototype for the investigation of viral glycoproteins in general, and this chapter outlines some of the special features that have derived from structure-function studies on HA. Chou and Jason R. Schnell Viral ion channels have minimalist architecture. Despite their relatively simple structure, viral channels can achieve highly specific gating and selection of ions, and the particular mechanisms appear to be different from those of prokaryotes and eukaryotes. The unique structural and functional properties of viral channels make them ideal targets for antiviral therapy because the molecules that inhibit viral ion channels may not interact with human ion channels. The M2 proton channel of influenza A virus is a model viral ion channel. This small channel, whose pore is formed by four equivalent transmembrane helices, is the target of two widely used anti-influenza A drugs, amantadine and rimantadine, both belonging to the adamantane class of compounds. However, resistance of influenza A to adamantane is now widespread. Naturally-occurring resistants mutants have been observed in as many as six different positions in the transmembrane segment of M2. How could there be so many different resistance-conferring mutations along a transmembrane helix of 25 amino acids? The recently-determined high-resolution structures of M2 in complex with adamantane allow us to begin answering this question. The extinct virus caused severe pathology in both the upper and lower respiratory tract, resulting in fatal respiratory complications and bacterial pneumonia. Using reverse genetics, the pandemic virus has been studied in different animal models in an attempt to determine which viral genes contribute to the increased virulence. Studies to date point to the role of the hemagglutinin, neuraminidase, and the polymerase basic protein 1 genes as the virulence genes responsible for the high pathogenicity seen with the influenza virus. Its critical roles in the influenza virus life cycle and high sequence conservation suggest it should be a major target for therapeutic intervention. However, until very recently, functional studies and drug discovery targeting the influenza polymerase have been hampered by the lack of three-dimensional structural information. In this chapter, we will review the recent progress in the structure and function of the influenza polymerase, and discuss prospects for the development of anti-influenza therapeutics. Dawson and Kathy L. Rowlen Rapid and accurate diagnostic methods for typing and subtyping influenza viruses are needed for improved worldwide surveillance. We have developed a low-density microarray MChip and accompanying pattern recognition algorithm combined with a reverse transcription PCR based assay and that allows for the identification and subtyping of influenza A viruses in approximately seven hours. MChip is unique in that it is based solely on the matrix M gene segment which has enough genetic diversity for subtype analysis but sufficient genetic stability to circumvent the need for continual redesign of primers and microarray probes. In addition, we present data indicating that the MChip performs well relative to gold standard methods for identification of influenza A. It is our hope that improved diagnostic assays coupled with improvements in microarray detection methodology will enable better worldwide surveillance and diagnosis of influenza viral infections. Pophale and Michael W. Deem We define a new parameter to quantify the antigenic distance between two H3N2 influenza strains: For the data between and , the measure of antigenic distance correlates better with efficacy in humans of the H3N2

influenza A annual vaccine than do current state of the art measures of antigenic distance such as phylogenetic sequence analysis or ferret antisera inhibition assays. We suggest that this measure of antigenic distance could be used to guide the design of the annual flu vaccine. We combine the measure of antigenic distance with a multiple-strain avian influenza transmission model to study the threat of simultaneous introduction of multiple avian influenza strains. We find that a multiple-component avian influenza vaccine is helpful to control a simultaneous multiple introduction of bird-flu strains. We introduce Population at Risk PaR to quantify the risk of a flu pandemic, and calculate by this metric the improvement that a multiple vaccine offers.

Chapter 4 : Richard Sutton, MD/PhD > Molecular Virology | Yale School of Medicine

Aspects regarding the molecular evolution of hepatitis viruses including their genetic diversities with implications for vaccine development are treated in the second chapter. Metabolic disorders that are a consequence of hepatitis C virus infection are discussed in the succeeding chapter.

Chapter 5 : Molecular virology - Wikipedia

Molecular Virology Understanding the molecular basis of viral interactions with their hosts requires a more complete picture of virus structure and regulation at the molecular level.

Chapter 6 : Molecular Virology | Microbiology & Molecular Genetics | University of Pittsburgh

The Molecular Virology Research Group is based at the University of Liverpool and is led by Prof. James Stewart. We employ and integrative and molecular approach to study the immunity to and pathogenesis of virus infections of man and animals.

Chapter 7 : Job Openings - Molecular Virology

The Saint Louis University Institute for Molecular Virology was established in to provide a unique faculty and special facilities for research and teaching in molecular virology, viral oncology and cancer biology.

Chapter 8 : Molecular Virology and Microbiology | Baylor College of Medicine | Houston, Texas

Education and Training Programs. The Department of Molecular Virology and Microbiology offers a program leading to the doctorate degree, with specialization in molecular virology or molecular microbiology.

Chapter 9 : Virology - Wikipedia

Molecular biology techniques include molecular cloning, gel electrophoresis, nucleotide sequencing, macromolecule blotting and probing, polymerase chain reactions, and microarrays. These powerful technologies have revolutionized virology and have shifted the attention away from the virus particle onto the virus genome.