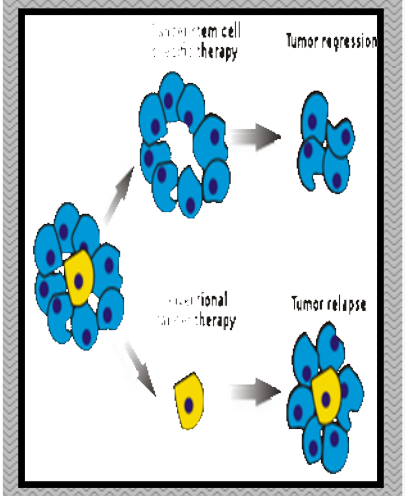

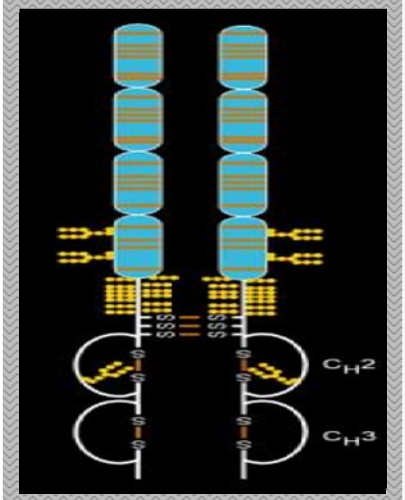

EMGEN Newsletter

Vol. 3 Issue 6, October 2009

INSIDE THIS ISSUE:

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

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What we must know about swine flu

What is an influenza virus?

Influenza A virus strains are categorized according to two proteins found on the surface of the virus: haemagglutinin (H) and neuraminidase (N). All influenza viruses contain haemagglutinin and neuraminidase. The structures of these proteins differ from strain to strain e.g., swine flu belongs to the H1N1 type, avian flu to H5N1 (emerged in 2004) and the currently dominant seasonal flu belongs to the H3N2 type. These proteins on the surface attract the human immune system. Some forms of both seasonal flu and swine flu are designated H1N1 because of their related, but differing surface proteins. The newest, much-publicized strain of H1N1 swine flu is believed to have caused deaths and hospitalizations because victims' immune systems did not recognize the latest variations in these surface proteins. Neuraminidase structure of the 2009 H1N1 influenza A virus has undergone broad surface mutations compared to closely related strains such as the H5N1 avian flu virus or other H1N1 strains comprising the 1918 Spanish flu; Neuraminidase of the 2009 H1N1 influenza A virus strain is more similar to the H5N1 avian flu than to the historic 1918 H1N1 strain (Spanish flu).

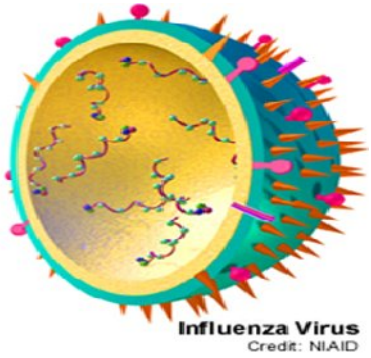

Figure 1: Model of Influenza Virus from NIH1

What is swine flu?

Swine flu is a contagious respiratory disease of pigs caused by type A influenza viruses. There are many different types of swine flu and the current cases involve the H1N1 strain of type A influenza virus.

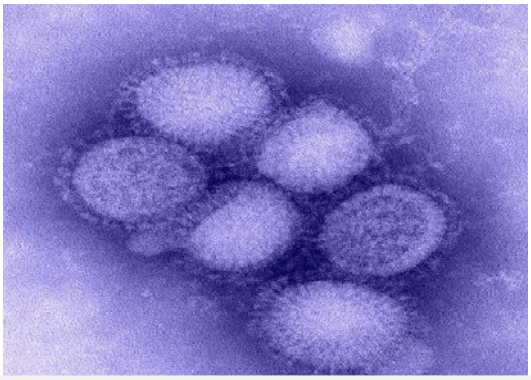

Figure 2: Electron microscope image of the reasserted H1N1 influenza virus photographed at the CDC Influenza Laboratory. The viruses are 80–120 nanometers in diameter.

How this virus is transferred?

Being in close contact with pigs.

From person to person, this has happened in the latest outbreak.

Coughing and sneezing.

You cannot catch it through eating pork.

What is the difference between seasonal and swine flu?

Seasonal influenza is caused by viruses that are adapted to spread in humans. Humans have some natural immunity to the strains that are in common circulation, and this immunity can be boosted by immunization with a vaccine. Avian influenza is caused by influenza viruses adapted for infection in birds. Similarly, swine influenza is caused by influenza viruses adapted for infection in pigs. These illnesses all cause the same respiratory symptoms in sufferers and can be passed between one another.

How many people have died of swine flu?

Now, More than 150 people have died and thousands made ill. If the flu spreads over a wide geographic area and affects a large proportion of the population it goes beyond an epidemic and becomes a pandemic.

What is our definition for pandemic flu?

According to the Health Protection Agency, an influenza pandemic is defined as a new or novel influenza virus that spreads easily between humans. When new influenza viruses are introduced into the environment, humans do not have any natural immunity to protect against them. Therefore, there is a risk that new influenza viruses could develop into a pandemic if the virus passes easily from human-to-human.

What are swine flu symptoms?

Symptoms of swine flu are like regular flu symptoms and include:

Fever, cough, sore throat, runny nose, body aches, headache, chills, and fatigue, diarrhea and vomiting. Neurologic symptoms in children as also observed in seasonal. Although it is rare, but it can be very severe and often lethal. These symptoms is associated with Reye's syndrome regularly arises in children with a viral illness who have taken aspirin.

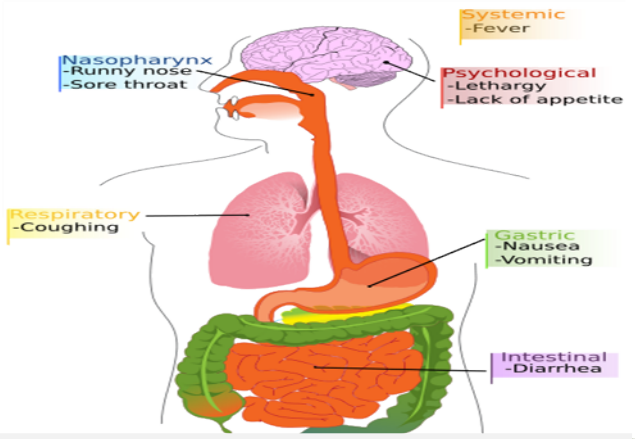

Figure 4: Main symptoms of swine flue in humans

Almost everyone is predicted to have at least two of the symptoms. It should be considered in mind that many conditions may create such symptoms and the doctors are also not able to recognize swine flu unless they offer some swine flu tests, although a negative result doesn't essentially mean you don't have the flu.

What is recommended to prevent the infection?

For reducing transmission of all viruses, it is highly advised to people to follow general infection control practices and good hygiene to reduce transmission of all viruses. These include:

Covering their nose and mouth when coughing or sneezing

Disposing of dirty tissues promptly and carefully

Washing hands frequently with soap and water

Cleaning surfaces which are regularly touched

What has happened in past pandemics of influenza?

There is a common belief that the current pandemic influenza is arisen from the past pandemic in 1918-19. Some believe that there is a pattern between the last mild wave of disease and the current epidemic flu. But Dr. Morens and its colleagues from National Institute of Allergy and Infectious Diseases (NIAID), have another opinion as titled **"**Understanding influenza backward" published in *Journal of the American Medical Association" August 13.* Theses authorities of this center say that there is no sufficient data to confirm such pattern. Also their investigation during the past 50 years disclose that the last pandemic have no relation with current outbreak. Although in terms of severity, a similarity may exist. So, it is difficult to predict the future course of H1N1 due to the last variable track of the flu pandemics. The two past flu pandemic in 1957 and 1968 was no such pathogenic in early years of its circulation But there is a hope among scientists because of the modest transition efficacy of the H1N1 virus and also some people have a pre existing immunity from past flu pandemics. Thus, a more indolent pandemic course and fewer deaths than in many past pandemics are predicted.

Why H1N1 is more pathogenic?

An international team of researchers led by UW-Madison virologist Yoshihiro Kawaoka , believe that a new greatly detailed study of the H1N1 flu virus demonstrates that the pathogen is more virulent than earlier thought. They reported their studies in *Nature*, July 13, 2009.

It is because this virus penetrates to deeper cells in pulmonary system than seasonal flu viruses. In other words, lower parts of respiratory system are infected by H1N1 which cause pneumonia and in severe cases death whereas the seasonal flu infects the upper respiratory system.

This virus also can be more pathogenic as its course goes ahead and it will obtain more features .

How this virus is spreading throughout the world?

This virus is in southern hemisphere and is predicted to return to the northern hemisphere in future fall and winter flu season.

Is a vaccine available? How they are produced?

There are different methods to produce vaccine. But the foremost approach is by embryonic chicken eggs that the seed virus is injected to them. After harvesting they are purified.

Today there are two technologies: Inactivated vaccines and live attenuated vaccines that are used for 90% and 10% vaccine production respectively. The first one is originated from killed viruses and the latter from weakened form of the virus.

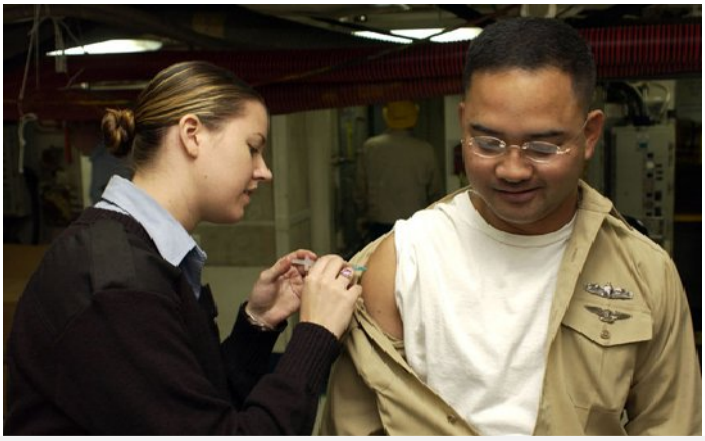

Figure 5 : U.S. Navy personnel receiving influenza vaccination.

How many different vaccine candidates will be available for H1N1

For answer to these questions, it's better to refer to Dr**.** Marie-Paule Kieny who is director of the Initiative for Vaccine Research at the World Health Organization (WHO). She points out that "About 30 vaccines are available including:

What are the differences between such vaccines?

1. They are produced and purified in different ways.
2. Whether adjuvant is added or not may make some differences. (Adjuvant maybe only used in killed vaccines).
3. The type of immunity they produce.(For example in attenuated vaccine the local immunity is created in the nose as they are administered in nose to cover the entry of the nose which accounts for the entry of the virus.)

Even though the last methods are the dominated approaches to produce vaccine, but researchers throughout the world are searching to design better vaccine with higher efficiency and less immunogenicity.

What are the new strategies for vaccine design?

A group of researchers at the bio-defense center for Immune Modeling at the University of Rochester Medical Center including immunologists, mathematical modelers, statisticians and software developers created a new model over three years for treatment design and preparation ahead of future pandemics. High simulation tools are emergently required to say us how much every influenza strain is able to cause infection and which parts of our immune system is involved in contributing against the viruses. As using the accurate and fast modeling we would be able to keep our speed as the same as the virus evolution which in real world is not possible. The new model predicts how rapidly the T and B cells respond to influenza type A virus infection**.** In this modeling the innate immunity is excluded but researchers are planning to involve it in future simulation. Depending on the pathogen and weather the patient has been exposed to virus in past or not, either T or B cells could have more important role in clearing the virus.

The role of humeral immunity against swine flu

One of the roles of antibodies is, when we are faced to a worst pandemic of swine flu. We can provoke the immune system of high risk individuals (health care providers) by injecting the sera of patients encountered to virus and recently have been improved. The sera are full of antibodies that can cause immunity against virus. Since the antiviral therapy is useful in within 48 hours of infection and vaccines takes several weeks to come to effect, as using the sera, such leaving gap can be filled efficiently. Because the genetic material of the swine flu is new, little is known about the distribution of pre existing immunity to current H1N1 "swine" flu across populations, the immune response to the virus or the efficacy of available vaccines. The researchers in Rochester are willing to contribute to the building of models that simulate swine flu infection across the entire U.S. population to better predict its course. Bioinformatics researchers in Singapore have reported analysis of a critical protein in H1N1 virus called neuraminidase by use of a computational 3-dimensional (3D) structural model of the protein. With using the 3D model, the researchers could draw the map of the regions of the protein and therefore the mutated regions were recognized and then they could evaluate if the current drugs or vaccines were effective or not.

How is swine flu treated?

FDA has approved Relenza (Zanamivir) and Tamiflu (Oseltamivir) as antiviral products, and rRT-PCR as diagnostic test.

Now, Relenza and Tamiflu inhibit the key proteins that virus needs to reproduce.

Relenza is approved to treat acute unsophisticated illnesses attributed to influenza in adults and children 7 years and older that have been symptomatic for less than two days and for the prevention of influenza in adults and children 5 years and older.

Tamiflu is approved for the treatment and prevention of influenza in patients 1 year and older. The EUAs allow for Tamiflu also to be used to treat and prevent influenza in children under 1 year, and to give alternate dosing recommendations for children older than 1 year.

Under the EUAs, both medications may be distributed to large numbers of the population without complying with the label requisites otherwise applicable to dispensed drugs, and accompanied by written information due to the emergency use. They may also be distributed by a broader range of health care workers, concluding some public health officials and volunteers, in accordance with applicable state and local laws and/or public health emergency responses. According to researchers in Stanford University" *Relenza and Tamiflu* both are *equally effective in prevention of symptoms of flu virus before infection*." But the sufficient data to support the effectiveness of these both drugs in vulnerable groups such as the very young and people with compromised immune systems is not clear When the viruses reproduce, they undergo some mutations that make them resistant to drugs. The scientists in Japan have developed a drug that is able to prevent cells from infection by blocking the virus in early steps. The whole story is brought in an article titled" *Inhibition of Influenza Virus Infections by Sialylgalactose-Binding Peptides Selected from a Phage Library"* in *Journal of Medicinal Chemistry in July 23(2009).*

Sources:

1- Teruhiko Matsubara et al., Inhibition of Influenza Virus Infections by Sialylgalactose-Binding Peptides Selected from a Phage Library: Journal of the Medicinal Chemistry (2009). Vol. 54(14):4247-56.
2- S. Maurer-Stroh et al., Mapping the sequence mutations of the 2009 H1N1 influenza A virus neuraminidase relative to drug and antibody binding sites: Biology Direct (2009). Vol. 4 (1): 18.
3- DM. Morens and JK. Taubenberger. Understanding influenza backward. *Journal of the American Medical Association* (2009). Vol. 302: 679-680.
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5- http://en.wikipedia.org/wiki/Swine_influenza
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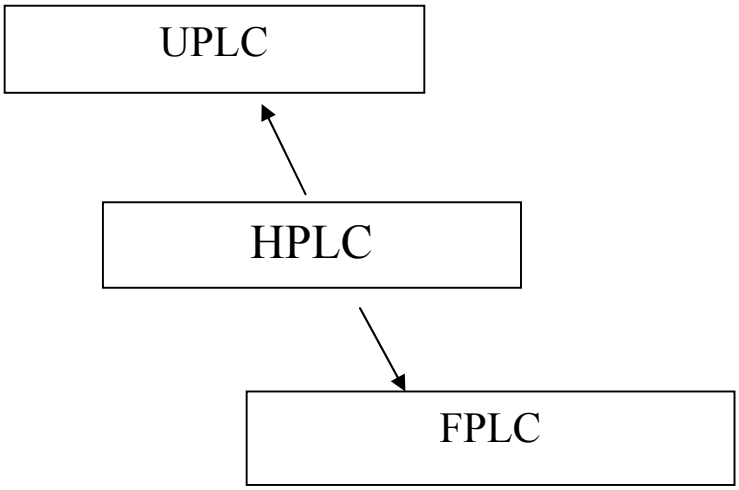
Fast protein liquid chromatography (FPLC)

Fast protein liquid chromatography is categorized in liquid chromatography like high-performance liquid chromatography using in separating and purifying from mixtures. FPLC system possesses some capabilities that make it a good candidate for usage in lab scale for segregating proteins and other biomolecules. In this method the mobile phase is liquid and the stationary phase can be either mobile or stationary phase. In FPLC the pumps are used to control the speed of mobile phase and in such way the constant flow rate of solvents is controlled. FPLC is equipped to different tubes to transfer solvents to system along with various columns depending on types of separation Depending on the types of separation preferred, various columns are used. FPLC is generally used in biochemistry and enzymology. In1982 Pharmacia introduced this new chromatographic to market.



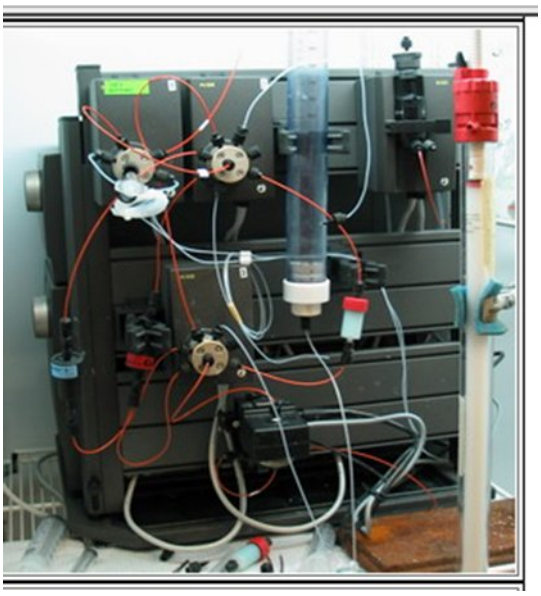


Figure 1: this picture shows a typical FPLC

FPLC is basically a "protein friendly" HPLC system

What is the difference between HPLC and FPLC?

1. FPLC is an intermediate between classical column chromatography and HPLC.
2. The columns used for FPLC can only be used up to maximum pressure of 3-4 MPa.
3. Stainless steel components replaced with glass and plastic.
4. Stainless steel was thought to denature proteins .
5. many ion-exchange separations of proteins involve salt gradients; thought that these conditions could results in attack of stainless steel systems .
6. FPLC can also be used to separate other biologically active molecules, such as nucleic acids.
7. FPLC pump delivers a solvent flow rate in the range of 1-499ml/hr while for HPLC pump= 0.010-10ml/min.

8. FPLC operating pressure: 0-40 bar while for HPLC = 1-400bar.
9. Since lower pressures are used in FPLC than in HPLC, a wider range of column supports are possible.

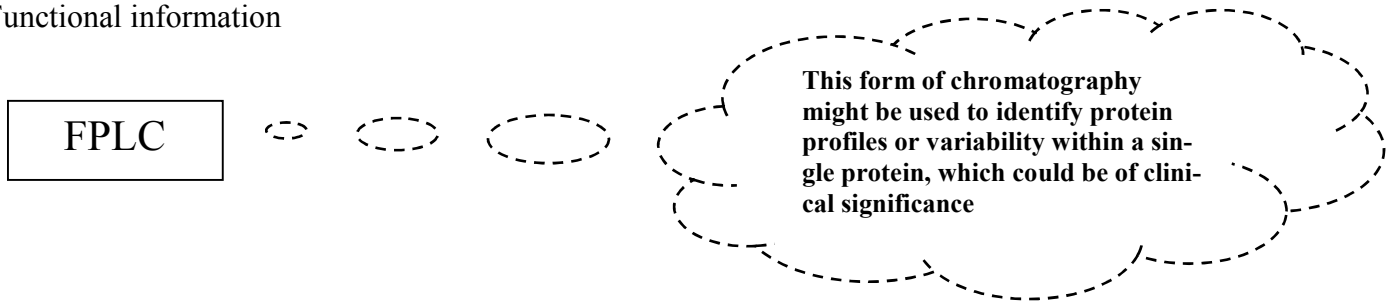
The properties of columns in FPLC:
Large [mm id] tube that contain small [µ] particles or gel beads that are known as stationary phase.
The chromatographic bed is composed by the gel beads inside the column
The sample is introduced into the injector and carried into the column by the flowing solvent.

How the compounds are separated in FPLC?
As a result of different components adhering to or diffusing into the gel, the sample mixture gets separated.

What criteria are involved in columns for separation process?
Size
Charge distribution (ion exchange),
Hydrophobicity, reverse-phase
Biorecognition (as with affinity chromatography)
Not only FPLC/HPLC systems can be used to isolate and purify proteins, but they can be coupled to other instruments for further analysis like:

- UV/VIS
- Mass Spectrometer

This instrument interfacing can allow for the determination of:
Protein amino acid sequence
Structural information
Functional information



What is Ultra Performance Liquid Chromatography?
Further advances in column technology and chromatography instrumentation introduced UPLC in 2004:

- Utilized even smaller packing particle sizes (1.7µm)
- Higher pressures (15000psi)
- Allowed for significant increases in LC speed, reproducibility, and sensitivity.
- New research utilizing particle sizes as small as 1µm and pressures up to 100,000psi

Optimizing Protein Purification by FPLC

In order to purify a mixture, combinations of chromatography methods are utilized. Developing a common protocol for purification by HPLC can be an important goal. The purification process should be done in such way that ultimately enough volume of the purified protein be achieved while keeping its all biological activity with proper folding. The type and starting material are two main keys that would considerably be important in purification development and affect the final product. Therefore purification process should be regulated fast and quickly with satisfactory results. Purity depends on our objectives but every more purity, the structure analysis will be better. Purity process should be in such circumstances that not only biological activity be reserved but also not any additive substances exist in our protein. The term "yield" is defined as the proportion of the final product to starting material. So we can use yield as a parameter to count the amount of essential starting material to reach the separation goal when the starting material is restricted and full optimization of purification protocol cannot be performed. Therefore, minimum adjustment and optimization steps are required to design a safe standard protocol. This might not be best possible with respect to experimental time, yield and economy but it will be as close to the purification goal. On the other hand, when enough amount of starting material is available, reaching to optimal separation goal depends on the accessible sample information and target molecule features.

The properties of a standard purification

First step in a standard purification protocol begins with IEC (Ion Exchange Chromatography).
The medium employed are Fast Flow, HR (a type of column use in HPLC).
For high flow rates, Short and wide column are preferred.
HIC (Hydrophobic Interaction Chromatography) is exploited as the first middle step.
Column characteristics are smaller and longer to allow elution with high resolving low gradients.
Selectivity in HIC is independent of running pH and downward salt gradients are used. Adding ammonium sulphate to match the buffer A concentration.
If HIC is used before IEC, the ionic strength would have to be lowered to fit that of buffer A for IEC step by dilution, dialysis or buffer exchange on gel filtration.
Polishing is carried out on gel filtration column for complete purification.
Although this is the standard purification protocol for proteins, the conditions are selected to include wide range of target proteins.
Extra intermediate purification step is added or optimization of the different steps is performed for improving inadequate purity.

Extra step commonly involves extra IEC step under utterly diverse situations.

Different Modules and their Operation

A standard FPLC comprises a control unit, a column, a detection system (UV spectrophotometer), one or two high-precision pumps and a fraction collector. In the standard arrangement, the sample is served via a sample loop. The loops sizes can be changed depending on the sample volumes. The samples are loaded manually by injecting through FP (Fabry– Perot) type gradient technique. It involves injection needle and threading of injection fill port into valve port.

Sources:

1- Comparison of fast protein liquid chromatography (FPLC) with HPLC, electrophoresis & microcolumn chromatography techniques for the diagnosis of β-thalassaemia: Indian J Med Res (2009). Vol. 129(3): 242-8.
2- http://www.waters.com/WatersDivision/flash/hplc_primer/hplcsys_primer.html
3- http://en.wikipedia.org/wiki/Fast_protein_liquid_chromatography

Announcement

9th Annual UK Meeting on Genetics & Molecular Mechanisms in Archaea

January 7th-8th 2010

As usual most of the program will consist of offered papers. Contributions from younger scientists are strongly encouraged.
We are very happy to announce that Dr Sonja-Verena Albers from the Max Planck Institute for Terrestrial Microbiology in Marburg will give a plenary lecture as part of the program.
Registration can be done online.

For details, please refer to the links below.
Enquiries to archaea2010@gmail.com
(0)121 414 5583

Current status and future trends in monoclonal antibodies: A brief history

The history of monoclonal antibody gets back to about one century ago when human used the sera of animals that were immunized by a pathogen and the same pathogen could cause disease in human. For example the serum therapy for treatment of diphtheria. It was about in 1901 that Behring could win the Nobel Prize in medicine because he was successful in serum therapy as he had found out bacteria itself can not do anything and the related toxin is responsible for causing disease and he discovered the first antitoxin for neutralizing the toxin of diphtheria. The introduction of therapeutic monoclonal antibodies was not possible without the understanding of this concept that microorganisms and toxin they produce do exist and they can cause disease.

When was the first turning point that therapeutic monoclonal antibodies could be marketed?

As the initial successes in the late 1800s, sera from humans or animals including polyclonal antibodies were extensively used for prophylaxis and therapy of viral and bacterial diseases. Although serum therapy has been successful in clinical, but there are some limitations associated with polyclonal antibodies such as uncertain dosing and toxicity related side effects like allergic reactions that arise from animal origin of such polyclonal antibodies. On the other hand, the total antibody in sera was not useful and only a small proportion (1%) were beneficial to our related disease and the rest of antibodies could be toxic and high immunogenic. Another limitation was due to low specificity of such antibody that until 1970 was not achievable. The second turning point in therapeutic monoclonal antibodies began when hybridoma technology was described as a method in 1975 that can produce limitless amount of MABs with desired specificity. Even though one of the most challenges was that this technology couldn't produce human antibody. Therefore following administration, immune response is stimulated and allergic reactions potentially can take place.

State of art in pharmaceutical biotechnology

Nevertheless, the arrival of a number of molecular biology techniques, typically recombinant DNA technology and the improved understanding of the antibody structure and function resulted in the development of different types of antibodies technically and structurally. The following diagram shows the development process in monoclonal production in summery.

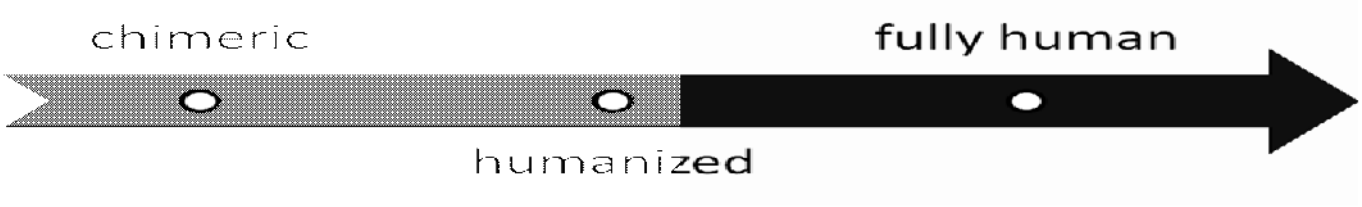


Figure 1: Development process in monoclonal antibody production

With development of phage display technique and transgenic animals, fully human monoclonal antibodies came to market. All these changes in monoclonal antibody production happened in 2-3 decades from 1970s to 1990s. As the changes in the past decades there are many therapeutic monoclonal antibodies in the market and the basic concepts are not considerably changed in last decades.

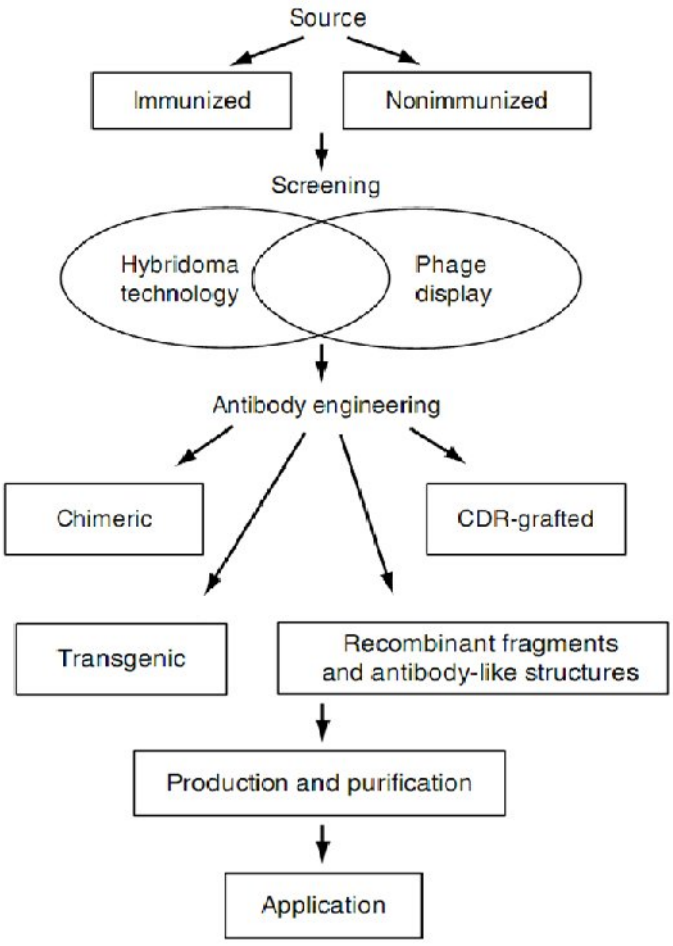


Figure2: Exploitation of hybridoma and phage-display technologies for production of recombinant antibodies.

These current technologies will come to their ends in close future?

Now there are some limitations with current technologies as the most therapeutic monoclonal antibodies have problems such as low half life, penetration to solid tumors and finally cost of production. Now it seems that the future technologies which focus on producing small antibodies which can resolve such problems or perhaps by producing larger and multifunctional antibodies linked to toxin molecules or nanoparticles that will create some amazing full properties.

Which diseases are more targeted by monoclonal antibodies?

Totally 22 MAbs are at present approved by the US FDA for clinical use; almost all of them are for treatment of cancer and autoimmune disease. Many more MAbs are in clinical trials (1373 entries for ongoing or completed clinical trials). Every day more new targets are discovered and so many companies are working on related antibodies as the latest and largest meeting on Molecular Targets and Cancer Therapeutics, October 22–26, 2007, San Francisco, indicated that the percentage of presentations due to MAbs has increased drastically compared to previous years. Rituxan (for treatment of non-Hodgkin's lymphoma) was one of the cash cow revenues of Genentech Company in 1997 that could encourage its authorities to develop more their research on therapeutic monoclonal antibody. Now Rituximab (1997), Herceptin (1998), Remicade (1998), Synagis (1998), Humira (2002), and Avastin (2004); are the first six blockbusters and have made total revenues of more than $12 billion in 2006.

What are current views for monoclonal antibody improvement?

Antigen targeting isn't conclusive to one company and on average 1-3 different antibodies are designed for the same antigen in different companies. There is an exception about IGF-IR that its role in angiogenesis is clear and is targeted by 10 different monoclonal antibody. Second and third generation of MABs is based on previous antibodies but with more high affinity and specificity. For example Motavizumab targets RSV with much more affinity and specificity in comparison to Synagis. There are some strategies to improve the existing antibodies such as an boost (to a certain extent) in their binding to Fc receptors for enhancement of ADCC and half-life, selection of appropriate frameworks to increase stability and yield, decrease of immunogenicity by using in silico and in vitro methods, and conjugation to small molecules and various fusion proteins to enhance cytotoxicity. As a result most of the new antibody therapeutics or improvements in existing ones which could be clinically used are expected to be developed at large companies. So this trend may continue until saturation in improvement and finding novel targets come to end and another significant turning point occurs in antibody development.

Prosperous antibodies in current and future market

In the future, some key MABs will play an important role in Great Avenue with broad spectrum in different diseases like AVASTIN which inhibits angiogenesis and is predicted to be on record sale by 2012. Also it is anticipated that rival between companies on the same target but different antibodies Decline Avenue like HUMIRA that is expected to compete with REMICADE.

Is there a new paradigm change in generating a new remarkable expansion of novel, unknown, types of therapeutics?

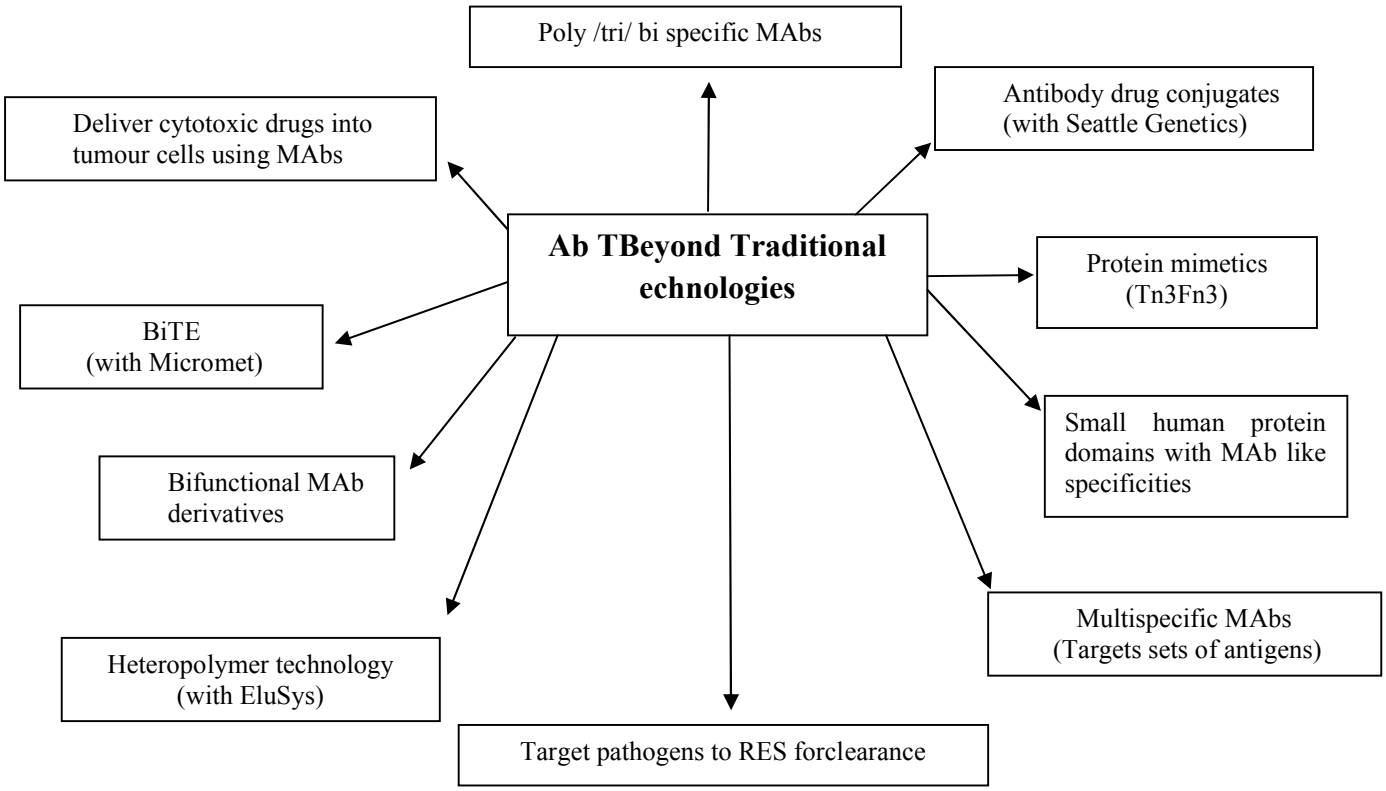
It seems that currently there is not any paradigm change in antibody development and more focus is put on two areas comprising improvement of present antibodies and design of new antibodies for novel targets with current methodologies. But one of the areas that could be considered as a significant change in course of antibody production is to go beyond the traditional structures of antibodies that of course are subject of discussion in meetings and conferences. Currently, the most monoclonal antibodies in market except (ReoPro, Lucentis, Cimzia which are Fabs), are full size antibodies even majority of those in clinical trials with most IgG format of about 150 KDs-size.

Many large companies are investigating to develop more different types of antibodies with various functionality and technology. For example Medimmune is one of those companies that has extensive strategies in antibody pipeline.

Current, emerging and novel technologies within Medimmune Company

- Naked MAbs
- MAbs with altered effector function
- MAbs with altered half-lives
- MAb conjugates or fusion proteins
- Bifunctional MAb derivatives (BiTE , dAb etc)
- Polyspecific MAbs (target 2 or more Ags); oligoclonal Abs
- Ab mimetics
- Peptides/polypeptides

The other technologies as "Beyond Traditional Ab Technologies" are illustrated in the following diagram



What are the features of the dAbs which make them attractive as candidate therapeutics?

The main problem with full antibodies is their week penetration to solid tumors and also absent in binding to surface molecules of antigen on desired target. So one of the interesting areas is concentrations on new scaffolds with higher stability and much smaller size. These small molecules could be human or non human and are categorized in two groups consisting those that are antibody derived and the latter which are not derived. If we want to say about scaffolds from derived antibody, the best example is domain antibodies (dABs) like current ALX-0081 which is a camelid dAb targeting the von Willebrand factor (vWF). These antibodies are also called nanobodies as their small size. Another dAB is ART621, a human protein that targets TNF α. The both drugs have passed the phase 1 trials and had good results.

The features of dABs:

Their small size which is about 10 folds less than full antibodies (10-15 KDs)
A good penetration in solid tumors
Excellent accessible to binding sites and cavities of desired antigen.
Treatment of viruses like HIV that are refractory to human immune response and their antigenic surface is covered in front of full IgGs.
Higher stability in blood circulation and can be engineered easier to be more stabilized.
As they are more stabilized, they are less aggregated.
Can be administered orally or pulmonary and or even pass blood brain barrier.
Tolerant to sever conditions like freeze drying and heat denaturation.

Research on novel scaffolds is going on. Some companies are investing on VH based platforms that offer a good solubility. One of the authors has suggested using engineered antibody constant domains (CH2 of IgG, IgA, and IgD, and CH3 of IgE and IgM) as scaffolds for construction of libraries. As being small size and having the small fraction of effector function. They are termed nanoantibodies. They are the smallest fractions that have antigen –binding and effector function together.

Which cell lines are now under research for producing monoclonal antibodies?

Although about 60% of therapeutic proteins such as monoclonal antibodies in market are produced by CHO cells, now more research for producing antibodies in other hosts like Ecoli and pichia pastors is under investigation. The great advantage of Ecoli is related to its high rate of expression although creating inclusion bodies and lake of glycosylation is considered as disadvantages. Truncated antibodies like scfv and Fab molecule which don't require glycosylation are suitable for expression in Ecoli. Pichia pastoris is a type of yeast that is recently more focused in monoclonal production. One of the most important drawbacks in pichia pastoris is attributed to hyperglycosilation that is now removed by glycoengineering of glycosylation pathways to humanized forms. The strong point of pichia pastoris is its high rate of expression along with simple and inexpensive culture media for cell density growth.

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Announcement

Please kindly note that this announcement is addressing Honorable Heads and Professors of Institutes and Universities

We are pleased to announce you that EMGEN in collaboration with TWAS is going to establish short term training periods during 2-3 months, related to health genomics and biotechnology fields for EMRO researchers. If you consider your institute to be able to **HOST** the researchers in this regard and have sufficient facilities in PhD/Post doc levels, please kindly inform and send us your CV and list of related facilities as soon as possible. It is notable that TWAS would cover the travel costs, including visa expenses, plus a contribution towards incidental local expenses, while the host centers should fund accommodation, food and laboratory expenses of accepted researchers.

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Cover Picture

Title: Stem cell specific and conventional cancer
Description: A few populations of cancer cells are called Cancer Stem Cells (CSC). We don't know exactly whether CSCs originate from cancer cells or backwards. Since these cells have the ability to get rise to all other cell types in other cancer cells so they are considered as tumorigenic possibly quite the opposite to other non-tumorigenic cancer cells. Such cells are proposed to persist in tumors as a distinct population and cause relapse and metastasis by giving rise to new tumors .The important point is that current chemotherapy treatment doesn't cover CSCs and proper targets on CSCs are not still found to be used for drug designing.
Source: http://en.wikipedia.org/wiki/Cancer_stem_cell

Title: Soluble receptors as therapeutic proteins
Description: Before designing of monoclonal antibodies by DNA technology and protein engineering, it is necessary to discover specific receptors over expressed in related pathogenic tissues. With knowing about the structure of antigenic receptors, making antibody becomes straightforward. Antibodies have neutralizing and/or apoptotic properties as coupling with their targets that may create side effects as linking with other receptors with similar structure. This phenomenon most happens when specificity and affinity is low. Another strategy for blocking preferred targets is to design and deliver the related receptors to body like Enberel that is a soluble receptor for blocking TNFα helpful in treatment of inflammatory diseases like rheumatoid arthritis. It is a fusion protein produced in dimmer form.
Source: http://en.wikipedia.org/wiki/Enbrel

Title: The RIKEN MDGRAPE-3 supercomputer for *Ab initio* protein modeling
Description: *Ab initio*- or *de novo*- protein modeling methods predict 3D protein structure based on physical properties. Many other procedures would be able to mimic protein folding or apply some methods with having a random probability distribution or pattern that can be analyzed statistically but not predicted precisely like (i.e., global optimization of a proper energy function). For doing such processes computational resources are needed that can only work on small proteins. To predict protein structure for larger proteins, improved algorithms and superior computational resources are required. While these computational barriers are enormous, but the potential advantages of structural genomics (by predicted or experimental methods) make *Ab initio* structure prediction an active research field
Source: http://en.wikipedia.org/wiki/MDGRAPE-3