EMHGBN Newsletter

Vol. 2, Issue 5, April 10th, 2008

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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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Geroderma Osteodysplasticum Hereditaria and Wrinkly Skin Syndrome in 22 Patients from Oman

An article entitled "Geroderma osteodysplasticum hereditaria and wrinkly skin syndrome in 22 patients from Oman" aims to determine some points about diagnosis of wrinkly skin syndrome (WSS, OMIM 278250) and geroderma osteodysplasticum hereditaria (GO, OMIM 231070). The study was done by Rajab A. Kornak U, Budde BS, Hoffmann K, Jaeken J, Nürnberg P, Mundlos S. Corresponding author of this paper, Dr. Anna Rajab, is working in Genetic Unit, DGHA, Ministry of Health, Muscat, Sultanate of Oman and the paper was published in American Journal of Medical Genetics 2008;146(8):965-76.

Dr. Anna Rajab

Excessive skin wrinkling and cutis laxa are seen in many genetic conditions and overlapping features can make a clinical diagnosis difficulties. Here we report on 22 Omani patients from 11 consanguineous families with the diagnosis of wrinkly skin syndrome (WSS, OMI 278250), cutis laxa with growth and developmental delay (CLGDD, OMIM 219200), or geroderma osteodysplasticum hereditaria (GO, OMIM 231070). Most patients were followed up for a number of years to observe the evolution of the phenotype.

All 22 patients presented in this report had excessive skin wrinkling at birth, lax, translucent skin with a visible venous pattern, poorly developed and hypotonic skeletal musculature, mild ligamentous skin laxity, delayed bone age, thin long bones and osteopenia. All 22 patients were underweight for height in infancy and childhood. Osteoporosis and spinal mal alignments were observed in all adult patients. Irrespective of numerous common features there were also differences.

The WSS phenotype evolves during early childhood. Most dramatic features were observed in the first 2-3 years of life and includes a generalized and excessive skin wrinkling, excessive skin folds, poorly growing sparse hair, hypodontia, caries and broken dental crowns, herniae, diverticulae, poor nutritional status, infantile emphysema, malposition of the feet, delayed bone age, osteopenia, hip dislocations and persistence of anterior fontanel beyond 3 years of age. The facial gestalt is characterized by a broad nasal bridge, hypertelorism, and downslanting palpebral fissures. Among our patients there were two adult patients with autosomal recessive WSS which never reported previously. The resolving phenotype makes recognition of WSS in adults a challenging task. We were unable to differentiate between WSS and cutis laxa with growth and developmental delay (CLGDD, OMIM 219200) suggesting that both can be considered as one entity.

Distinct hallmarks of GO were skin wrinkling limited to the dorsum of hands and feet and to the abdomen, normal fontanelles, maxillary hypoplasia, bowed long bones, and osteopenia with frequent fractures. Our GO cases display a wide interfamiliar heterogeneity. Adult GO patients may be under-diagnosed presenting with early onset osteoporosis, tendency to fractures and vertebral collapse. In contrast to the attenuation of the skin phenotype with age in WSS, adult patients with GO appeared prematurely aged and suffered from bone fractures.

A serum sialotransferrin type 2 pattern was found in all four WSS patients tested. Apolipoprotein CIII (a marker for O-glycosylation) was normal suggesting that WSS is frequently associated with a N-protein glycosylation defect, probably at the level of processing (CDG-II). All four investigated GO patients showed normal sialotransferrin patterns. The known loci for cutis laxa and WSS on 2q31, 5q23-q31, 7q11, 11q13, and 14q32 were excluded. We suggest that WSS and GO are distinct entities with overlapping features.

Track Detection on the Cells Exposed to High LET Heavy-Ions by CR-39 Plastic and Terminal Deoxynucleotidyl Transferase (TDT)

An article entitled "Track detection on the cells exposed to high LET heavy-ions by CR-39 plastic and Terminal deoxynucleotidyl transferase (TdT)"aims to indicated the possible usefulness of both the CR-39 plastics and DNA labeling with TdT method for evaluating the biological effect of heavy-ions in comparison with low LET ionizing radiation.The study was done by Dr. P. Mehnati, A. Keshtkar, A. Mesbahi, H. Sasaki. Corresponding author of this paper, Dr. Parinaz Mehnati is working in Department of Medical Physics, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran and the paper was published in Iranian Radiation Research, 2006; 4 (3): 137-141

Dr. Parinaz Mehnati

The Cosmic radiation is considered to be a mixture of high-energy photons and radiation particles, such as iron ions. High-energy radiation poses a threat to astronauts, especially on long missions beyond the protection of Earth's magnetosphere. The greatest danger comes from two types of radiation: galactic cosmic rays (GCRs) and solar particle events (SPEs).

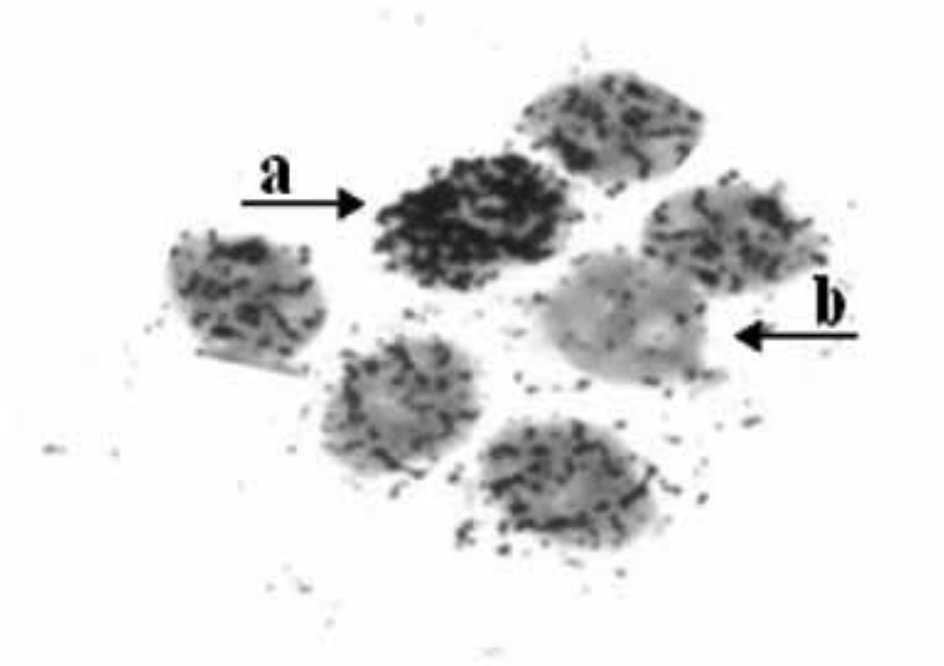
These contain charged particles (mainly protons) that are trapped by Earth's magnetic field so that spacecraft in low Earth orbit, such as the Space Shuttle and International Space Station, are relatively well-protected.

But the danger of radiation exposure is very real, for example, in the case of a manned mission to Mars Heavy ions are known to contribute significantly to the estimated total radiation exposure during manned space missions. Fatal effect of ionizing radiation on cells depends on Linear Energy Transfer (LET) level. The distribution of ionizing radiation is sparse and homogeneous for low LET radiations such as X or γ, but it is dense and concentrated for high LET radiation such as heavy-ions radiation.

Material and Methods: Chinese hamster ovary cells (CHO-K1) were exposed to 4 Gy Fe-ion 2000 keV/ m. The CR-39 is a special and sensitive plastic used to verify exact position of heavy-ions traversal. Terminal deoxynucleotidyl transferase (TDT) is an enzyme labelled with [3H] dATP for detection of cellular DNA damage by autoradiography assay.

Results: The track of heavy ions traversals presented by pit size was almost similar for all different doses of radiation. No pits to show the track of traversal were found in 20% of the cell nuclei of the irradiation. Apparently these fractions of cells wave not hit by heavy ions.

An example of [3H] dATP incorporation into a CHO cells.

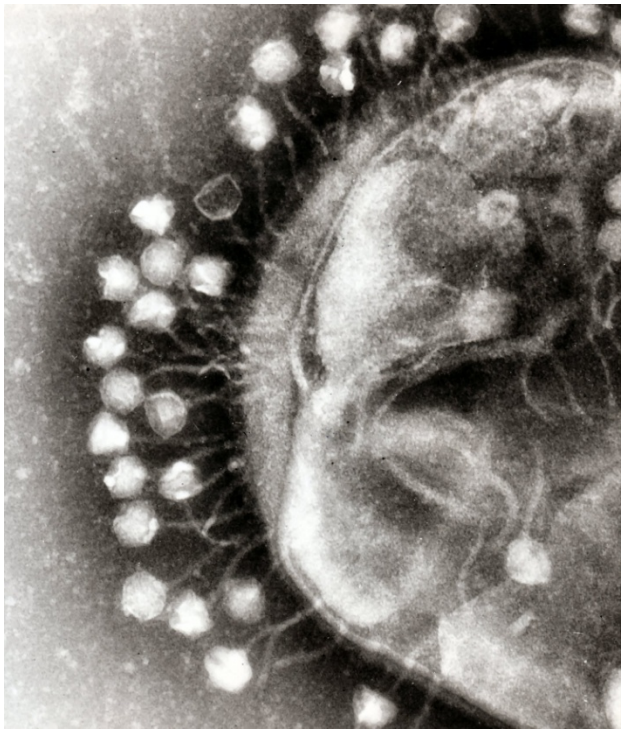


(a) Typical densely labelled nuclei. (b) Non-hit cell with negative labelled nuclei.

Phage Display in Biotechnology and Drug Discovery

Introduction

Phage display technology provides a remarkably versatile instrument for exploring the interactions between proteins, peptides, and small molecule ligands. As such it has become extensively adapted for use in epitope mapping, identification of protein–peptide and protein–protein interactions, protein–small molecule interactions, humanization of antibodies, recognition of tissue-targeting peptides, and many other functions. However, it must be kept in mind that phage display is a combinatorial biology approach, not a combinatorial chemistry approach. The enormous strength of phage display over combinatorial methods that are severely chemical is that the isolation of a single interacting protein or peptide attached to a phage particle is enough to permit the complete characterization of the isolate: the interacting virus can be grown up in bulk and the sequence of the displayed protein or peptide inferred from the DNA sequence carried within the viral particle.



Phage display is a powerful technology for choosing and engineering polypeptides with new functions. If DNA fragments encoding polypeptides are fused to definite bacteriophage coat protein genes, the fusion genes can be encapsulated within phage particles that also show the encoded polypeptides on their surfaces. This sets up a physical linkage between phenotype and genotype. Highly various libraries can be constructed by fusing degenerate DNA to a coat protein gene, and library members with desired binding specificities can be isolated by binding to an immobilized receptor *in vitro*. The sequences of selected polypeptides can be determined from the sequence of the encapsulated, encoding DNA.

Phage display was first developed with the *Escherichia coli* specific bacteriophage M13, and the success of M13 phage display has encouraged the development of plentiful alternative display systems. Polypeptides have been presented on the surfaces of bacteria and yeast and also other display systems including: eukaryotic virus, mammalian cell, ribosome, mRNA and covalent DNA display. Although these alternative systems have proven advantageous in particular applications, M13 phage display remains the dominant technology.

Developments in phage-display technology

Library construction

The success of any collection experiment finally depends on the diversity and superiority of the primary library. Over the years, methods have been refined to the point where enormously large libraries can now be rapidly and reliably created. Sidhu *et al.* (2000) have explained optimized methods that make possible the construction of libraries with diversities greater than 1012, almost 100-fold greater than previously thought practical.

Vectors and display formats

The M13 phage particle consists of a single-stranded DNA core surrounded by a coat composed of five diverse proteins. The length of the filament is covered by several thousand copies of the main coat protein, protein- 8 (P8). Each end of the particle is capped by five copies each of two minor coat proteins: protein-3 (P3) and protein-6 (P6) at one end, and protein-7 (P7) and protein- 9 (P9) at the other end [8]. In early examples of phage display, polypeptides were fused to the amino-terminus of either P3 or P8 in the viral genome. These systems were harshly limited because large polypeptides (>10 residues for P8 display) compromised coat protein function and so could not be efficiently displayed.

The progress of phagemid display structures solved this problem because, in such systems, polypeptides were fused to an extra coat protein gene encoded by a phagemid vector. Subsequent infection with a helper phage produced particles with phagemid DNA encapsulated in a coat composed mainly of wild-type coat proteins from the helper phage but also containing some fusion coat proteins from the phagemid. Also an interactive animation about phage display technology is available with this address:

http://www.dyax.com/discovery/phagedisplay.html

Applications for phage-displayed peptide libraries

Phage-displayed peptide libraries can be used to isolate peptides that attach with high specificity and similarity to practically any target protein. These binding peptides can be used as reagents to understand molecular recognition, as minimized mimics for receptors, or as lead molecules in drug design. Some applications exist for phage displayed peptide libraries such as mimics of intracellular protein–protein interactions, Intracellular protein-binding domains and Enzyme inhibitors but here for the purpose of brevity we only discuss about enzyme inhibitor.

Enzyme inhibitors

Enzymes typically hold many deep clefts — including active sites and allosteric regulatory sites— that are well suited for the binding of small ligands. Dennis *et al.* (2000) isolated a peptide that non-competitively slowdowns the activity of the serine protease factor VIIa (FVIIa) with delicate specificity and high potency.

Extensive mutational and structural analyses showed that the peptide binds at a beforehand unknown 'exosite' distinct from the active site, and in fact inhibits activity by an allosteric mechanism. These results are of substantial therapeutic relevance; FVIIa is a key regulator of the blood coagulation pathway and, in the past, it has been really difficult to selectively inhibit individual proteases of the coagulation cascade.

Phage-displayed peptide libraries seem to be perfect sources of peptidic enzyme inhibitors. Inhibitory peptides should confirm useful as drug discovery reagents, or perhaps even as drugs themselves. Furthermore, the phage-display process discovers the entire exposed surface of a target enzyme and, finally, it can sometimes recognize new sites for inhibitor design.

Applications for phage-displayed proteins

The ability to display large proteins on M13 phage has led to numerous applications. Some of these applications are: Antibody phage, Phage-displayed cDNA libraries, mapping protein functional epitopes and engineering binding affinity and specificity. Here we will give a brief overview on antibody phage:

Antibody phage

Over the past decade, phage-displayed antibody fragments have been the subject of intensive research. As a result, antibody phage libraries have become useful tools for drug discovery and several phage-derived antibodies are in higher clinical trials. Although most libraries have been constructed by cloning the natural immune repertoire into phage-display vectors, an important advance has been the development of high-quality libraries with completely synthetic complementarity-determining area.

Knappik *et al* (2000). have constructed a library in which a limited number of human frameworks are used and diversity is established by means of synthetic cassettes. Such a system is very amenable to the generation of therapeutic antibodies because preferred frameworks can be used and similarity maturation is helped by the use of distinct mutagenic cassettes.

The construction of large, high-quality libraries should also be aided by common improvements in library construction methodologies and by the introduction of improved *in vivo* recombination systems. Although it is possible to get definite antibodies directly from immature phage-displayed repertoires, another main application for phage-display technology has been the humanization and affinity maturation of usual murine antibodies. Such antibodies have been proven effective in an amount of therapeutic functions. For example, a humanized antibody to vascular endothelial growth factor (VEGF) is in clinical trials as a cancer treatment, and Chen *et al* (1999). have used phage display to produce an affinity matured variant that is ~100-fold improved in both affinity and potency.

Some other Phage display application

Applications of phage display that have surfaced recently reflect the potential that phage display technology represents. An example of integration of phage display with advanced biotechniques is the use of real-time polymerase chain reaction (PCR) to make easy identification of cell- and tissue-specific peptides. Quantitative PCR permits to measure numbers of library clones bound to cells of interest, which was demonstrated for selections on live cells and on formalin-fixed, paraffin embedded tissue parts. Real-time PCR was also adopted to monitor the changes in phage binding to cardiac vascular epitopes upon aging. A method with potential for clinical diagnostics is phage display-mediated immuno-PCR (PD-IPCR), which is a modification of immuno-PCR (IPCR), performed with a recombinant phage particle instead of a monoclonal antibody.

In PD-IPCR, the phage-displayed scFv and the encoding phage DNA combine the detection and the template units. The sensitivity of this analyse is a 1,000-fold over that achieved with conventional enzyme- linked immunosorbent assays (ELISAs). Another latest illustration of the development resulting from co-evolving technologies is the combination of phage display with laser capture microdissection (LCM) used to isolate cells of exact origin from sectors of complex heterogeneous tissues such as biopsies or autopsies. Recovery of phage binding to cells of interest was successfully assisted by LCM in mice after *in vivo* library administration, as well as after *ex vivo* application of phage to freshly collected oral squamous cell carcinomas.

Also, fluorochrome labeling of phage in display libraries has been introduced as a technique for studying binding specificities, as well as phage display applications in flow cytometry and fluorescence microscopy. Furthermore, phage display has been used to functionally target specific cell sections of non-protein nature. For example, a peptide library was selected for peptides that bind to liposomes in pH-dependent manner, some of which were able to cause leakage of liposome contents.

Lipopolysaccharides were also recently discovered as targets of peptides displayed by phage libraries. Diverse computational implements and algorithms have been created to facilitate prediction of protein interaction sites based on phage display binding data. Combination phage-displayed random peptide library selection with such computational predictions have, for example, allowed mapping a neutralizing antibody epitope on the spike protein of severe acute respiratory syndrome (SARS) coronavirus, as well as to define cellular coronavirus receptor and thus approaches to expansion of SARS inhibitors. Provided that phage has long been used as an antibacterial agent in the pre-antibiotic era, and current FDA approval of bacteriophage preparation as a food additive on ready-to-eat meat and poultry products, vehicles based on phage may finally be proven particularly helpful for treatment of infectious diseases.

Display of a bacteria- or fungus targeting moiety on phage surface can further advance the delivery of cytotoxic payload to pathogens. Application of phage-displayed random peptide libraries for identification of motifs facilitating transport across the gastrointestinal mucosal barrier, as well as transdermal transport through intact skin may also accelerate translation of phage based technologies in imaging and therapy. A possibly of using phage-displayed peptides and antibodies in high throughput microarray formats has also been explored. Altogether, phage display technology has been and will likely remain instrumental in identification, validation, and prioritization of ligands to molecular targets expressed on the cell surface, as well as of peptide drug leads directed to these targets.

Future directions

The future of display technologies will largely depend on improvement of screening approaches, vectors for library construction, and optimization of display scaffolds. The results from various display library screenings indicate that in many cases the selected peptide motifs target receptors via mimicking biological ligands of these receptors. Analysis of peptide motifs targeting an individual receptor provides a basis for rational drug design of targeted peptidomimetics, which is currently being undertaken based on the ligand-directed map of IL-11/IL-11Rα interaction mapped with *in vivo* phage display as a follow up of the human vascular mapping effort.

Integration of present technologies with nanotechnology is rising as a field in which targeted nanoparticles will be pursued as multifunctional entities with diverse biomedical purposes.

Combination of display technologies with high-throughput screening approaches is likely to significantly progress the rate with which information is generated, similarly to the way it had been realized for the genome project. Finally, development of *in silico* bioinformatics and systems biology equipments for controlling three-dimensional information-intensive data that come out of display selections is also happening. Combination of this effort will become a major driving force for the continued application of display technologies for the needs of clinical proteomics and drug discovery**.**

[Refs: 1) Phage Display in Biotechnology and Drug Discovery, Edited by Sachdev S. Sidhu Published in 2005 by CRC Press, International Standard Book Number-10: 0-8247-5466-2 (Hardcover)

2) Renata Pasqualini, Wadih Arap, Display technologies: Application for the discovery of drug and gene delivery agents, Advanced Drug Delivery Reviews (2006) 1622–1654

3) Sachdev S Sidhu, Phage display in pharmaceutical biotechnology, Current Opinion in Biotechnology (2000) 11:610–616**]**

RNA-based Therapies

RNA-based therapeutics hold the promise of enormously expanding the number of 'druggable' targets by conquering the major limitation of existing drugs, which are able to target only a limited number of proteins involved in disease pathways. Over the past 20 years, scientific and technical advancements have significantly improved the field of RNA-based therapeutics. Several classes of molecules and approaches have been researched as RNA therapeutics, including antisense RNA, ribozymes, RNA decoys, aptamers, small interfering RNA (siRNA) and microRNA (miRNA) (table 1). However, potential applications of RNA medicines in the treatment of human diseases remain in their infancy (table 2). Multiple challenges, such as optimization of selectivity, stability, delivery and long term safety, have to be regarded in order for RNA drugs to turn into a successful therapeutic category. However, this area represents a key value creation opportunity in the industry, as confirmed by the increasing number of high-profile partnerships and merger and acquisition deals between pioneering biotechnology companies and traditional huge pharmaceutical companies (fig.1).

Drugs on the market

No ribozymes or RNA decoys were ever successfully developed as drugs. The only approved antisense RNA drug up to now is fomivirsen for the treatment of cytomegalovirus retinitis in patients with AIDS. The only marketed aptamer is pegaptanib for wet age-related macular degeneration (AMD). Neither drugs are commercially successful, as fomivirsen is prescribed only on a limited basis, while sales of pegaptanib eroded due to competition from ranibizumab, which contributed to the decision by OSI Pharmaceuticals to divest its ophthalmology assets.

Antisense RNA

Major advances in RNA chemistry led to the design of second-generation antisense technology that is expected to conquer many of the limitations of the original approach. With more than 1,500 patents covering biology, chemistry and production of antisense drugs, Isis Pharmaceuticals is a leading company in this field. Isis' antisense drug candidates are targeting multiple conditions, including cardiovascular disease, diabetes, ulcerative colitis and asthma. The company also has a number of partnered programs in cancer, multiple sclerosis, ocular diseases, HIV and amyotrophic lateral sclerosis.

Lead agent ISIS 301012, which is now in Phase II trials, could appear as one of the most potent low-density lipoprotein cholesterol lowering medicines. If approved, it is posed to produce the first substantial sales of any RNA-based therapeutic. Isis is pursuing an accelerated regulatory approval for ISIS 301012 in patients with homozygous familial hypercholesterolemia, and has been granted orphan drug status in this indication.

Characteristics	Old generation antisense	Ribozyme	New generation antisense	RNA interference
Structure of molecule	ssRNA or ssDNA	RNA molecule with enzymatic activity	ssRNA or ssDNA	dsRNA
Catalytic mode of action	No	Yes	No	Yes
Activity related on RNA structure	Yes	Yes	Yes	No
Specificity at therapeutic doses	Low	Moderate	High	High
Stability	Low	High	High	High
Potency	Low	Low	High	High
Methods for delivery	Limited	Limited	Multiple	Multiple

Table1: comparison of gene-silencing drug strategies

Company	Program	Indication	Status
Antisense			
Isis	ISIS301012 ISIS113715	High cholesterol Diabetes	Phase II Phase II
OncoGenex, Isis	OGX-011	Cancer	Phase II
Eli Lilly, Isis	LY2181308	Cancer	Phase I
Aptamer			
Archemix	ARC1779	Acute coronary syndrome, percutaneous coronary intervention	Phase I
Small-interfering RNA			
Opko Health	Bevasiranib (C and 5)	Wet AMD	Phase III
Alnylam	ALN-RSV01	RSV infection	Phase II

Table2: Some RNA-based therapies in development.
AMD, age-related macular degeneration; RSV, respiratory syncytial virus.

RNA interference

RNA interference (RNAi) quickly emerged as a novel therapeutic approach to treat human disease soon after its Nobel-prize winning discovery in 1998. The first siRNA, bevasiranib, has newly entered a pivotal Phase III trial for the treatment of wet AMD. The study will evaluate whether bevasiranib administered every 8 or 12 weeks is safe and has the same efficacy in preventing vision loss as ranibizumab administered every 4 weeks. Data are likely to be available in mid‑2009. In a Phase II trial, bevasiranib was shown to be safe and well tolerated and showed advantages against several end points, including near vision and lesion size. Allergan's AGN211745 (formerly Sirna‑027), also in development for wet AMD, has reached Phase II; in an earlier trial, it was reported to make better or stabilize visual acuity in a subset of patients.

The leader in the siRNA field is Alnylam Pharmaceuticals, and its most advanced drug candidate, ALN-RSV01, is in a Phase II clinical trial for the treatment of respiratory syncytial virus (RSV) infections. The trial will include adult subjects experimentally infected with RSV.
A Phase II trial in naturally infected patients is planned for 2008. This year, Alnylam also expects to file an investigational novel drug application for either ALN-PCS01 for the treatment of hypercholesterolemia, or ALN-VSP01 for the treatment of liver cancers and potentially other solid tumors. This application would be particularly important as it would be the first time a systemically delivered siRNA will came into clinical development. Tackling the systemic delivery difficulty remains one of the most critical challenges on the road of bringing RNAi medicines to the market. Success or failure in this arena could mean the difference between becoming at best a one-off drug technology, or the next big wave of biotechnology therapeutics.

miRNA

A recently formed joint venture between Isis and Alnylam — Regulus Therapeutics — invests on intellectual property created by both companies around miRNA. miRNAs are thought to control the expression of roughly 30% of all human genes.
Consequently, in comparison with antisense and RNAi, which target single genes, targeting miRNAs has the possibility of addressing whole disease pathways. Regulus' lead program targets miR-122, an endogenous host gene needed for viral infection by hepatitis C virus. Additional therapeutic areas that Regulus plans to explore comprise cancer, other viral diseases, metabolic disorders and inflammatory diseases.

To date most of the large pharmaceutical companies cannot compete with biotechnology companies, such as Amgen, Genentech or Biogen Idec, with regards to discovery and development of traditional biologics. Given the blockbuster potential of RNA-based therapeutics, some of the most strategically and economically significant deals between biotechnology and pharmaceutical companies in the past 2 years were signed around RNAi, antisense and aptamers (fig. 1).

Silence Therapeutics joined with Alnylam has come into nonexclusive licensing agreements with Novartis and Roche — deals potentially worth US$700 million and $1 billion, respectively. AstraZeneca ($400 million) to develop RNAi drugs for respiratory diseases. Isis licensed its preclinical antisense programs in diabetes, obesity and metabolic disorders to Bristol–Myers Squibb ($192 million) and Ortho-McNeil/Johnson and Johnson ($460 million). Archemix, a pioneer aptamer company, has partnered with Elan ($360 million), Merck Serono, Pfizer and Takeda. Also, Merck paid a 100% premium to acquire Sirna for $1.1 billion. These contracts generated great value for pioneering biotechnology companies and their investors, and provided further confirmation of the potential of RNA-based drugs to become a vital next generation class of medicines.

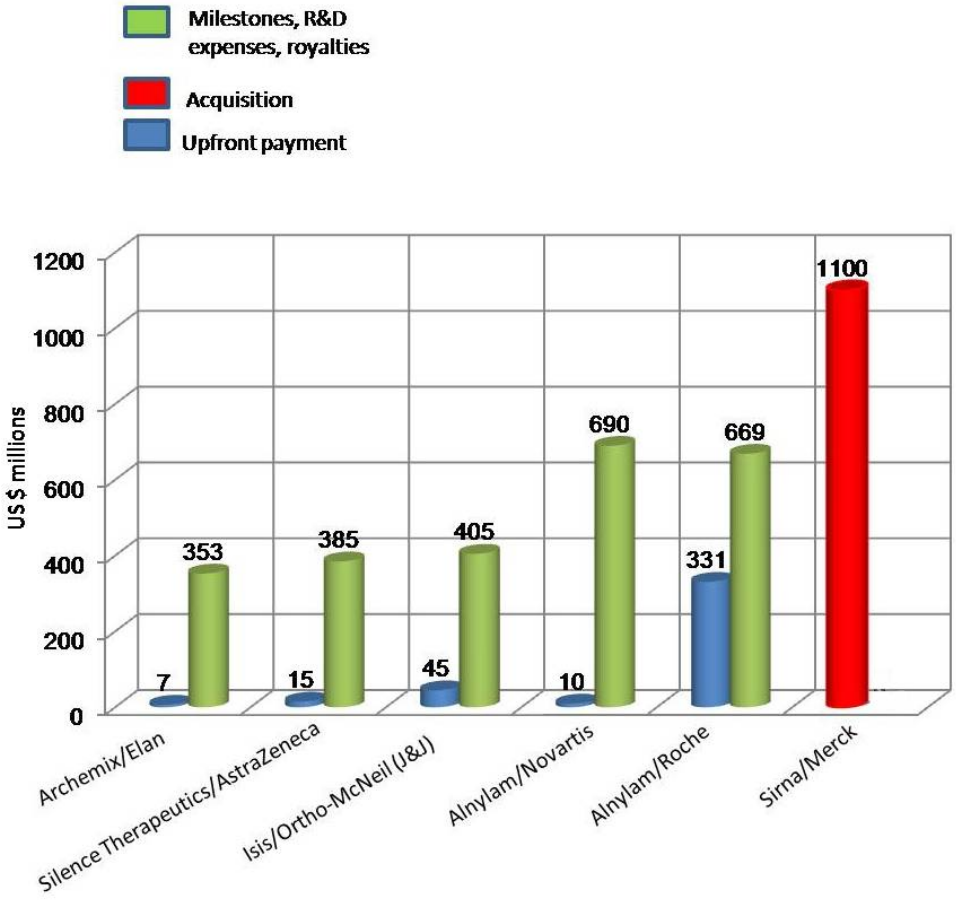


Figure 1: Selected RNA therapeutics biotechnology and pharmaceutical company deals

[Ref: Irena Melnikova, RNA-based therapies, nature reviews drug discovery, volume 6 November (2007) 863-864**]**

Promoting Biotechnology Innovation in Developing Countries

Here in this article we mention some important factor essential for promoting biotechnology innovation, with particular emphasis on some developing countries. These countries are: Egypt, Brazil, South Korea, Cuba, India, China and South Africa.

Characteristics that define a successful biotech sector

Focus on local health needs

Although having limited resources the countries studied have found ways to use biotechnology to meet local health requirements. For instance, Egypt, in the face of a severe insulin shortage, has emphasized the development of affordable recombinant insulin to decrease its reliance on expensive imports. It now has a 2-year supply of insulin in storage. Cuba responded to a meningitis epidemic caused by meningococci serotype B by effectively developing the world's first and only meningitis B vaccine.

Indian biotechnology companies now produce hepatitis B vaccine at a much lower cost than developed countries. They sell the vaccine within India and to the United Nations Children Foundation (New York). This concentrate on local health requests counters the generally held belief that health research in developing countries is oriented toward the problems of developed countries that have wealthier markets rather than toward local health problems.

Success is expressed in many ways

There is no one-size-fits-all solution. Actually there are lots of different ways of succeeding in health biotechnology. We see success in the development of leading-edge innovation, such as the example of the meningitis B vaccine in Cuba, but most countries have found success in licensing pre-existing technology, as was the case for recombinant insulin progress in Egypt. In Egypt, an ability to locally produce recombinant insulin permits the country to address diabetes locally and meet health needs of their people. With rising geopolitical uncertainties in some parts of the world, self-sufficiency in providing health products has become essential to many countries. Because health biotechnology is fairly risky, there is no guarantee that these countries will be able to maintain their successes and obtain both health and economic profits in the long run. Continued success will depend on many features, including how well the innovation systems develop and function.

What is obvious is that countries with strong scientific foundations are well positioned to succeed, but economic profits will likely be linked to how well they can engage and maintain private sector growth and commercialize scientific discoveries as products.

Build on educational and health systems

Good basic education and health systems as building blocks for health biotechnology expansion are crucial. All the countries in this study have relatively good schools, at least for a division of their citizens. Good education has enabled their specialists to understand the potential of biotechnology and grasp new opportunities offered by the technology at the same time that their policy makers, business people and the general public have identified the significance of biotechnology and have supported its development.

A well-functioning health system is also critical for health biotechnology improvement. Through their connections with the health system, researchers create innovative ideas for solutions to problems and use the health systems for testing, clinical trials and the commercialization of the final products.

How to promote health biotechnology in developing countries?

Political will

Political incentive for promoting health biotechnology innovation in developing countries is important. The governments of nearly all of the seven countries began to pay attention to biotechnology in the 1980s (that is, quite early in the development of the field) and have sustained to support its development. For example, we can mention Egypt's National policy for Genetic Engineering and Biotechnology, which outlined short and long-term objectives with specific disease targets and technologies to make better the health of its citizens.

Governments in this study have also found solutions to the ongoing challenge of brain drain. In China, for example, since the late 1990s the authorities have made intensive efforts to encourage expatriate experts to return. Incentives include the supply of funding for the establishment of laboratories in China and plan to enable returning scientists to establish firms. In fact, political will and a strong government role have been indispensable for all countries with strengths in biotechnology.

Individual leadership

A common theme on health biotechnology development is that a few persons have played key leadership roles and have been involved in setting health biotechnology development in motion for their countries. These individuals have not been limited to government positions; they have come from the universities, public research system or the business sector.

These individuals are people with vision who recognize the potential of the technology early on in its development. They show creativity and determination to conquer the challenges that inexorably arise in promoting a new technology development of this sort. They work vigorously and relentlessly to set up conditions and align the essential factors to encourage health biotechnology innovation.

Define niche areas

Some of the countries have recognized areas that leverage some specific technological strength or other sources they possess. South Korea has emphasized microarrays/biochips and bioinformatics to exploit its competitive benefit and local know-how in information and communication technologies. India also has been able to invest on its large pool of well-trained English-speaking science and technical specialists, as well as its relatively cheaper expenses in R&D. The Egyptian Agricultural Genetic Engineering Research Institute's previous successes in agricultural biotechnology are providing the country with a platform for probable developing a plant-made hepatitis B vaccine.

Some of the other countries, such as South Africa and Brazil are using their native knowledge and biodiversity to develop innovative products. Defining niche areas and relying on some kind of competitive advantage in these areas are lessons that are commonly applicable to all developing countries. Because of their restricted resources for technological development, it is vital that developing nations prioritize specific areas and depend on their existing strengths for health biotechnology development.

Close linkages

Close linkages and active knowledge flows are necessary for innovation to happen. By encouraging co-operations and resource sharing among different institutions in its innovation system, Cuba has been able to thrive in health biotechnology, in spite of its very limited financial resources.

Lack of connections, especially between universities and industry, has slowed innovation attempts in Brazil and Egypt. Those countries have succeeded more for the reason that strong individuals who played pioneering roles in their health biotechnology development. Although participation of 'champion' individuals can never be downplayed, in the long run a systemic approach is expected to be more sustainable.

Several of the countries here have embarked on an active policy of encouraging closer collaborations. Promoting clusters in health biotechnology has turned into a standard policy, and most of the countries have initiated cluster development of some kind. Examples comprise India's Genome Valley, Cuba's West Havana Scientific Pole and Egypt's Mubarak City for Scientific Research and Technology Applications.

Enterprise creation

It is found that private firms were necessary for integrating various sources of knowledge in health biotechnology and turning them into products and services. A deficiency of financing mechanisms and resources for fostering start up creation and sustainability is a frequent problem. In health biotechnology, the Chinese have changed some existing research institutions into companies that produce medicine. Also former employees of public research institutes and Chinese experts who have returned from abroad have set up small companies that are becoming a new force in the health biotechnology sector.

Government policies have consequently played diverse roles in promoting private sector development in this field. The venture capital sectors in the countries studied here so far made inadequate investments in health biotechnology development. In most cases, the venture capital sectors are roughly nonexistent or immature. Some governments have placed a stress on encouraging venture capital development. In India, venture capital for biotechnology is emerging from various resources, including state governments, insurance companies and banking institutions. This, in turn, is helping to encourage overseas investors. Developing countries that have not yet pursued on health biotechnology should consider the role of the private sector and recognize promising ways to encourage its development.

Intellectual property

Patent legislation has played an important role for private sector progress in health biotechnology. All of the countries in this study initiated their health biotechnology development under moderate patenting environments, which offered them opportunities for reverse engineering of pre-existing technologies and brand products and the creation of low-priced generic products.

With agreement to the World Trade Organization's (Geneva) Agreement on Trade-Related features of Intellectual Property Rights (TRIPS), countries that have not built creative capacity in the health biotechnology field may find it more difficult to achieve success. Encouraging commercialization and a well developed private sector is an important way to tackle this challenge.

The end result: seize the opportunity

The lessons explained above are vital for fostering the development of a successful health biotechnology sector in the seven countries studied. They present a strong message that developing countries can successfully build capacity in health biotechnology to both raise the accessibility of health products for their residents and provide opportunities for their economic development.

[Ref: Halla Thorsteinsdóttir, Uyen Quach, Abdallah S Daar & Peter A Singer, Conclusions: promoting biotechnology innovation in developing countries, Nature Biotechnology 22, DC48 - DC52 Volum22 December 2004**]**

Interview with Dr. Elfadil Abass

Dr. Elfadil Abass is a Ph.D student in microbiology in Ahfad University for Women, Omdurman, Sudan.

What is your idea about medical biotechnology and its application?

Well I think biotechnology is a technology which is used in vaccine production, drug, treatments and genetic engineering.

What is your field of research?

My research is about leishmaniasis in animals and concern diagnostic techniques. We need to develop new techniques for early detection of visceral leishmaniasis. My research is a comparative study between serological techniques and molecular tools.

Are you aware of any biotechnology centre in your country or any governmental or private company?

I do not think we have any biotechnology company in our country. But some universities exist in our country which are active in biotechnology research.

How do you predict your job market in the future after your graduation, I mean what opportunities exist upon your graduation?

I think it is possible to join universities and there you have both chance of being a lecturer or master and also you can get involved in research projects.

What is your idea about commercialization of researches in the field of bioscience?

I think it is an important aspect of science. In future we need to commercialize and we will start commercialization of our researches so we want to distribute our leishmania research locally in Sudan and in the future we hope to export our leishmania research to other countries. But I am not aware of exact mechanisms and features involved in research commercialization and of course it is interesting for me to become more familiar with this topic.

What about the quality of knowledge you gain in your university? Are you satisfied about educational infrastructure and all the equipments in your university?

I believe the theoretical aspects are very good but face shortage in our laboratories. We do not have enough equipments.

Why do you face with the shortage of facilities?

Because of funding problems, also Sudan is involved in internal war, and consequently this war has got its own negative impacts. We have to seek national funding agencies. We receive very little grants so we can not support all equipments, just reagents.

What about your university's policy, about giving scholarship to their students to go abroad?

No we dont have such opportunities, again because of funding problem, so we should continue our education in our own country.

Do you have communication with other EMRO countries?

Yes, we have collaboration with EMRO countries; sometimes we have financial supports from these countries. Also it is possible to attend some workshops in EMRO countries for example recently I attend a workshop on RT-PCR in Pasteur institute of Iran.

At the end of interview do you want to mention anything special?

We hope to have collaboration with other peoples mainly in Iran. It is my second visit to Pasteur institute of Iran and I hope to come here again.

Announcement

The First Ever International Pharmaceutical and Biotechnology Exhibition Comes to Dubai

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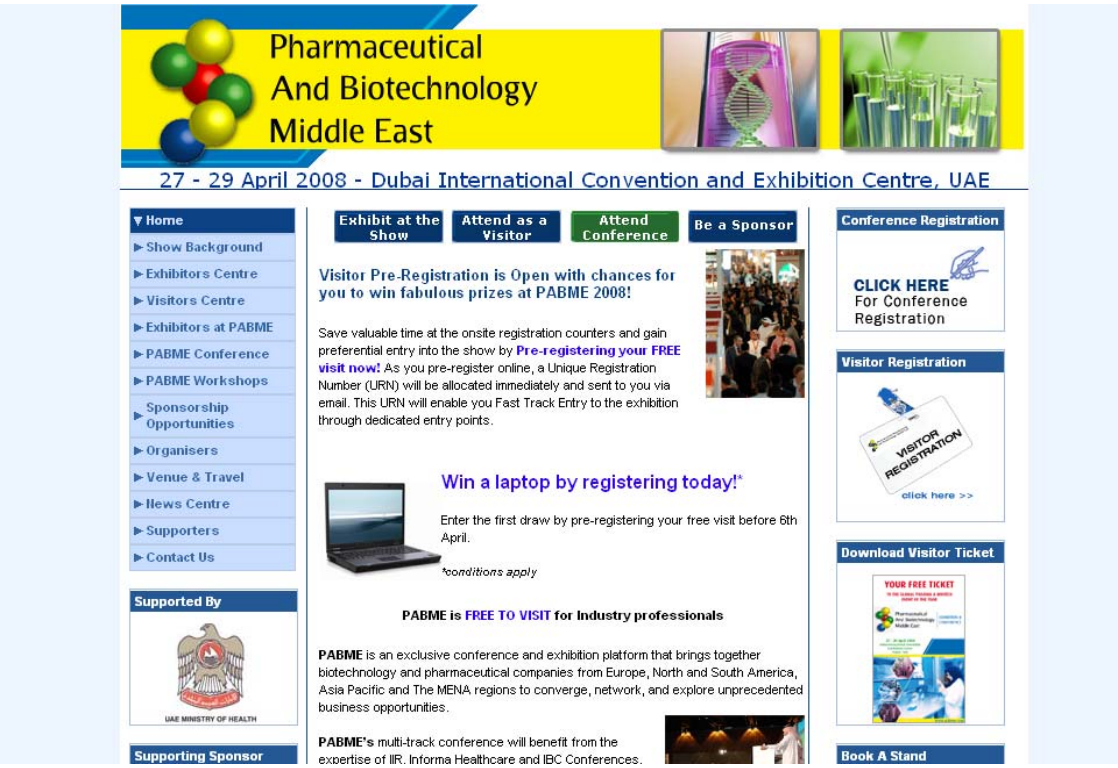

Cover Pictures Description (up to down)

The first three pictures

Title: Early Examples of Gene Silencing in Transgenic Plants.

Description: Example petunia plants in which genes for pigmentation are silenced by RNAi. The first plant is wild-type; the second plants contain transgenes that induce suppression of both transgene and endogenous gene expression, giving rise to the unpigmented white areas of the flower.
Authors: Marjori A. Matzke, Antonius J. M. Matzke; credit Jan Kooter for the first and second images, and Natalie Doetsch and Rich Jorgensen for the third image.

Source: http://en.wikipedia.org/wiki/Rnai

Title: The dicer protein from *Giardia intestinalis*, which catalyzes the cleavage of dsRNA to siRNAs. The RNase domains are colored green, the PAZ domain yellow, the platform domain red, and the connector helix blue.

Description: One molecule of the Dicer-homolog protein from *Giardia intestinalis*, colored by domain (PAZ domain yellow, platform domain red, connector helix blue, RNase and bridge domains green). Dicer is an RNase that cleaves long double-stranded RNA molecules into short interfering RNAs (siRNAs) as a first step in the RNA interference response, and also initiates the formation of the RNA-induced silencing complex (RISC).

Source: http://en.wikipedia.org/wiki/Rnai