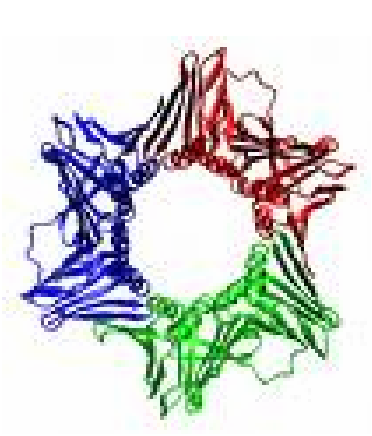

EMGEN Newsletter

Vol. 3, Issue 3, June 15 th, 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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ErbB Antagonists Patenting: Playing Chess with Cancer

The article entitled "ErbB Antagonists patenting: "Playing Chess with Cancer" focuses on critical role of ErbBs signaling as targets for cancer therapy. The corresponding author of this article Dr. Sami Aifa is a researcher unit of bioinformatics and signalling, centre of biotechnology of Sfax, Tunisia. This article has been published in the journal, Recent Patent on Biotechnology, 2008 November. 2(3):181-187.

Dr. Sami Aifa

Cancer is one of the main reasons of death in the world. Many of strategies were adopted to treat cancer but widely used in clinical practice are chemotherapy and radiotherapyagents. These treatments have infrequently cured the disease but improved the survival of patients. These obstacles in the long battle of humankind against cancer had prompted many molecular studies to focus on oncogenes as targets for therapy. The first oncogene to be purified and distinguished was the epidermal growth factor receptor (EGFR). This oncogene was later on revealed to be the cellular homologue ofthe avian erythroblastosis viral oncogene v-erbB. The recognition and isolation of EGFR led to the discovery ofits protein family called ErbB (avian erythroblastosisoncogene B) consist of 4 members: EGFR/ErbB1/HER1,ErbB2/Neu/HER2, ErbB3/HER3 and ErbB4/HER4. EGFR recognises at least ten ligands among which EGF and TGF while HER2 has no known ligand, HER3 binds heregulins but has a non-active tyrosine kinase domain and HER4 adopts the neuregulins as ligands (recently reviewed in). The existence of multiple ligands and receptors imparts theEGFR signaling network with an expanded repertoire of cellular responses, as the four receptors can potentially form distinct homo- and heterodimers that are activated by different ligands. In the non-existence of a specific ligand for HER2, this protein functions as the preferred heterodimeric partner of the other members of the EGFR family.

ErbBs signalling is always associated with the development of the majority of solid cancers via both the MAPK pathway leading to cell cycle progression and the PI3K pathway causing cell survival. Consequently, many ErbB antagonists have been developed and patented for cancer treatment purposes. These antagonists belong to two drug classes: monoclonal antibodies (mAbs) and small molecules competing with ATP and inhibiting the tyrosine kinase domain (TKIs). Three patented mAbs are currently approved in clinical cancer treatment: Trastuzumab (Herceptin) directed against HER2 and used to treat breast cancer, Cetuximab and Panitumumab which are anti-EGFR antibodies approved for colorectal cancer treatment. Trastuzumab® or Herceptin® is a monoclonal antibody specific to HER2 extracellular domain patented by *Genentech* as a recombinant version of the murine HER2 antibody. The history of Trastuzumab started with the cloning of HER2 cDNA . Hudziak *et al* succeeded the development of an anti-HER2 monoclonal antibody with an antiproliferative effects *in vitro* which acts by sensitizing human breast tumour cells to tumour necrosis factor. This antibody named Trastuzumab was patented for the first time in 1997 as a tool for detecting tumour cells expressing HER2 and in 1998 as an inhibitor of tumours expressing HER2. Trastuzumab or Herceptin was approved by the FDA in 1998 to treat breast cancer. The value of monotherapy in metastatic breast cancer did not exceed 15%. Many hypotheses were proposed to explain this low rate of response to Trastuzumab. Trastuzumab is targeting HER2 and the paracrine or endocrine activation of other erbBs allows tumour to escape the inhibitory effects of the therapy (Fig. **1**). In addition , activation of the intracellular signaling independently of ErbBs could maintain tumor progression and compensate HER2 blocking (Fig. **1**).

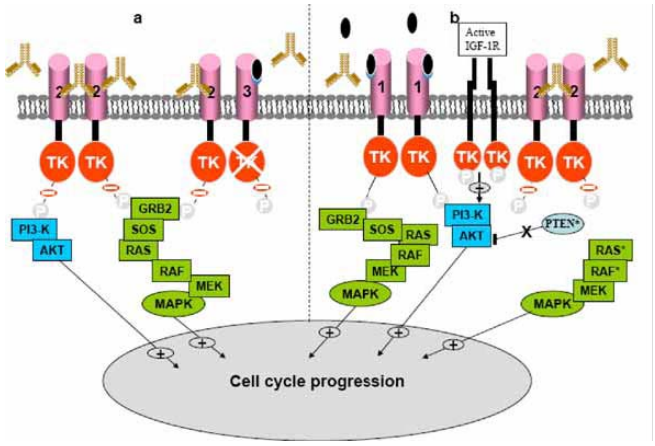

Figure 1: Mechanisms of action and resistance to Trastuzumab

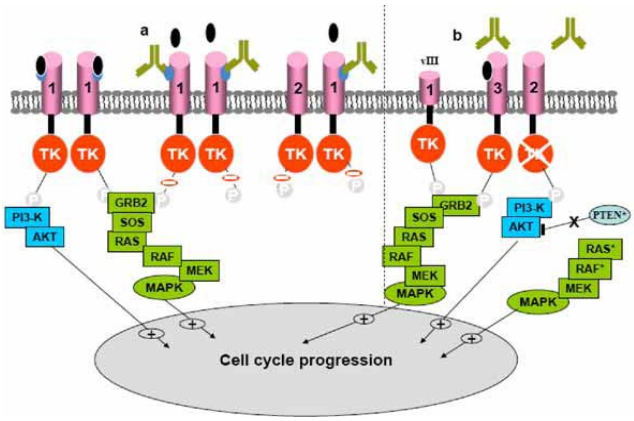

Figure 2: Mechanisms of action and resistance to anti-EGFR mAbs

Unfortunately, these mAbs are facing cancer resistance mediated by paracrine activation of other ErbB members or compensatory ErbB signalling factors. Separately, three TKIs have been approved to treat cancer: Gefitinib (Iressa®), Erlotinib (Tarceva®) inhibiting specifically EGFR and approved to treat non small cell lung cancer and Lapatinib (Tykerb®) which has the dual specificity EGFR/HER2 and recently approved to treat metastatic breast cancer.

Cetuximab and Panitumumab are approved in colorectal cancer treatment but they have potential applications in many other solid cancers. Cetuximab has also been approved by FDA for use in head and neck cancer over expressing EGFR in 2006. In clinical studies both antibodies have alike objective response rates as monotherapy in mCRC (~10%) and comparative side effects. Because Panitumumab is a humanized mAb, the risk for immunogenic reactions is expected to be lower. However, both antibodies are facing resistance from tumours as a result of mutations of EGFR or related signalling intracellular factors (Fig. **2**). EGFRvIII is obtained by an in frame deletion removing 801bp from the extracellular domain encoding mRNA; this deletion renders the receptor constitutively active (Fig. **2**) and independent from ligand binding and as a consequence Cetuximab and Panitumumab become unable to bind. Several mutations of intermediary signalling factors such as KRAS, RAF and PI3 kinase could influence the sensitivity to EGFR targeting agents. KRAS mutations were reported as a predictor of resistance to Cetuximab therapy and are associated with a bad prognosis.

Gefitinib (ZD1839, Iressa®) is an anilinoquinazoline with the chemical name 4-quinazolinamine, N-(3-chloro-4- fluorophenyl) -7-methoxy-6- [3-4-morpholin) propoxy]. Erlotinib (Tarceva®) is a quinazolinamine with the chemical name N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)- 4-quinazolinamine. Lapatinib (GW572016, Tykerb®) is a small molecule and a member of the 4- anilinoquinazoline class of kinase inhibitors with chemical name *N*-(3-chloro-4-{[(3-fluorophenyl) methyl] oxy}phenyl)-6-[5-({[2-(methylsulfonyl) ethyl] amino}methyl)-2- furanyl]-4-quinazolinamine bis(4-methylbenzenesulfonate). Gefitinib and Erlotinib are most selective to EGFR meanwhile Lapatinib is targeting both EGFR and HER2. The FDA approved Gefitinib for the treatment of patients with NSCLC previously treated with chemotherapy. In treated patients with non-small cell lung cancer, the administration of Gefitinib and Erlotinib are associated with objective tumour response rates of 8–19%. The responders systematically harboured specific mutations within the tyrosine kinase domain (example: L858R, G719S, delE746-A750) and were significantly sensitive to TKI than wild type EGFR expressing patients. However, the responders treated by TKIs develop very often subsequently secondary mutations that abolish their sensitivity to TKIs.

Many clinical trials are online to validate combinatory therapies by the use of mAb and TKIs together or with the classical chemotherapy or radiotherapy agents. Since cancer is a dynamic disease we will face new mechanisms of escape from the new therapeutic agents. The battle against cancer should continue and looks like playing chess with a very skilled player. Until now we succeeded to make the game lasting longer but cancer is winning by killing each year, millions of people worldwide. Let’s hope that the future will bring us a genuine “magic bullet” and a much needed victory.

Performed Research in Applied Biotechnology and Genomics on the grant of COMSTECH

On the base of WHO Regional Office for Eastern Meditation report, the Regional Office in partnership with the Standing Committee for Science and Technology of the Organization of Islamic Countries (COMSTECH) founded a individual grant for Research in Applied Biotechnology and Genomics (RAB&GH) in 2004. The overall intend of the grant was to endorse research, give confidence networking, engender novel knowledge and arouse the application of biotechnology and genomic driven interventions in health care.

The precedence areas for research were selected on the basis of recommendations made at Muscat (Executive Course on Genomics and Public Health Policy), and contained;

1. Diagnosis of infectious and communicable diseases
2. Development and production of pharmaceuticals, recombinant proteins and products
3. Vaccine development
4. Bioinformatics and proteomics
5. Social, cultural, legal and cultural issues with gene data bases
6. Issues of patenting in genomics and biotechnology

There was an overpowering response to the 1st call for research in 2005 from the countries of the Region and 17 research projects in applied biotechnology and genomics are continuing (Table 1).

For the 2nd call for EMRO-COMSTECH Grant 2006-2007 there was a strict condition of collaboration between at least two PIs from two different institutes, preferably from different Eastern Mediterranean countries. As a result of this call 18 collaborative projects are ongoing (Table 2).

No	Country	Title of the project
1	Egypt	Production of human recombinant anti-tetanus Fab using high throughout of phage display and *Pichia pastoris*
2	Egypt	Bioinformatics in tissue engineering science and technology
3	Egypt	The role of selected gene mutations in the pathogenesis of congenital heart disease in Egypt
4	Islamic Republic of Iran	Preparation of diagnostic kit using *L. infantum* C-terminal extension of type I cysteine proteinase for early detection of human visceral leishmaniasis
5	Islamic Republic of Iran	Improving human recombinant calcitonin expression level in transgenic potato tuber by using patatin class i promotor
6	Islamic Republic of Iran	Molecular diagnosis of vancomycin resistant genes in *Enterococci* and *Staphylococcus aureus* strains isolated in municipal and hospital wastewater in Iran
7	Islamic Republic of Iran	Determination of toxicity of Iranian *Helicobacter pylori* strains: from gene to protein to function; application to diagnostics and patient screening
8	Islamic Republic of Iran	Production of pharmaceutical proteins in semi-desert plants
9	Islamic Republic of Iran	Proteomics Analysis of Immunologic Infertility: detection of immunodominant sperm surface antigens in Iranian infertile patients
10	Jordon	Invasive *Streptococcus pneumoniae* serotypes: genotypic and phenotypic characteristics in Norht Jordan
11	Morocco	Preparation of diagnostic kit using *L. infantum* C-terminal extension of type I cysteine proteinase for early detection of human visceral leishmaniasis
12	Oman	Social, cultural, legal and ethical issues related to gene in a developing country
13	Pakistan	Application of the biotransformation techniques to produce value added compounds using plant cell cultures
14	Pakistan	Studies on the IL-8 levels and mutations in E2 and NS5A genes of hepatitis C virus in resistance to antiviral therapy
15	Syrian Arab Republic	Diagnosis and genotyping HCV RNA in Syria by applying molecular biology techniques
16	Tunisia	Green Fluorescent Recombination Antibody: novel in vitro tools for detecting the rabies virus antigen
17	Tunisia	Integrated biomedical, bioinformatic, genomic and molecular biology approaches for the development of novel tools for the diagnosis of leishmaniases in humans.

Table 1: List of research proposals funded under EMRO-COMSTECH Grant 2004-2005

No	Country	Title of the project
1	Islamic Republic of Iran	Collaborative Research: Genome Analysis of *Plasmodium Falciparum* for Antimalarial Drug Monitoring in Baluchistan Iran
2	Islamic Republic of Iran	Collaborative Research: Genome Analysis of *Plasmodium Falciparum* for Antimalarial Drug Monitoring in Baluchistan Iran
3	Pakistan	Studies on the Genetic & Molecular Basis of hearing and Vision Impairment
4	Syrian Arab Republic	Genetic basis of Hearing Impairment in Syrian Population
5	Iran	Genetic Basis of Vision Impairment (Glaucoma) in Iran
6	Morocco	Collaborative Research on: The Assessment of Epidermal Growth Factor Receptor (EGFR) Abnormalities as a Prognostic Marker in Cervical Cancer
7	Morocco	Collaborative Research on: The Assessment of Epidermal Growth Factor Receptor (EGFR) Abnormalities as a Prognostic Marker in Cervical Cancer
8	Lebanon	Collaborative Research on the Anti-inflammatory and Anti-cancer Effects of Gallotannin in Human Colon Cancer Cells: Anti-cancer Effects of Gallotannin
9	Lebanon	Collaborative Research on the Anti-inflammatory and Anti-cancer Effects of Gallotannin in Human Colon Cancer Cells: Anti-cancer Effects of Gallotannin
10	Islamic Republic of Iran	Collaborating Research: Developing a Molecular Kit for Monitoring Insecticide Resistance in Four Major Malaria Vectors of Eastern Mediterranean Region (EMR)
11	Pakistan	Collaborating Research: Developing a Molecular Kit for Monitoring Insecticide Resistance in Four Major Malaria Vectors of Eastern Mediterranean Regions (EMR)
12	Morocco	Collaborative Research on Tuberculosis in Morocco: Evaluation of the Performance of Antigenic Epitopic Peptides for the Development of a New Test Allowing the Differential Diagnosis Between the Active Tuberculosis and the Latent Tuberculosis Infection
13	Morocco	Collaborative research on tuberculosis in Morocco : Diagnosis of the active tuberculosis when fast *Mycobacterium tuberculosis* identification is negative
14	Pakistan	Collaborative Research on Structural and Mechanistic Studies of Merozoite Surface Protein-1 (MSP-1) for Preparation of Recombinant MSP-1 Malaria Vaccine-Experimental Aspects
15	Pakistan	Collaborative Research on Structural and Mechanistic Studies of Merozoite Surface Protein-1 (MSP-1) for Preparation of Recombinant MSP-1 Malaria Vaccine-Computational Studies
16	Islamic Republic of Iran	Collaborative Research on Structural and Mechanistic Studies of Merozoite Surface Protein-1 (MSP-1) for Preparation of Recombinant MSP-1 Malaria Vaccine-Study on C-terminus 19 kDa Fragment of MSP1
17	Egypt	Use of cDNA microarray for discovery of prognostic Markers for Squamous Cell Carcinoma of the Bladder
18	Egypt	Use of Immunohistochemistry to validate cDNA Microarray Results for prognostic markers of Squamous Cell Carcinoma of the Bladder

Table 2: List of research proposals funded under EMRO-COMSTECH Grant 2006-2007

Reference:

http://www.emro.who.int/rpc/Biotechnology_Genomics-research.htm

Drug discovery

Drug discovery is the procedure by which drugs are discovered and/or designed in medicine, biotechnology and pharmacology.

Drug discovery process has been appraised to take 10 years averagely and cost more than 800 million dollars. This long and costly process contains four main stages:

- Lead identification
- Lead optimization (involving medicinal and combinatorial chemistry)
- Lead development (including pharmacology, toxicology, pharmacokinetics ADME [absorption, distribution, metabolism, and excretion], and drug delivery)
- Clinical trials.

Lead identification is the first step in a lengthy drug discovery procedure and the base of successful medicinal plant discovery (Balunas *et al.*, 2005).

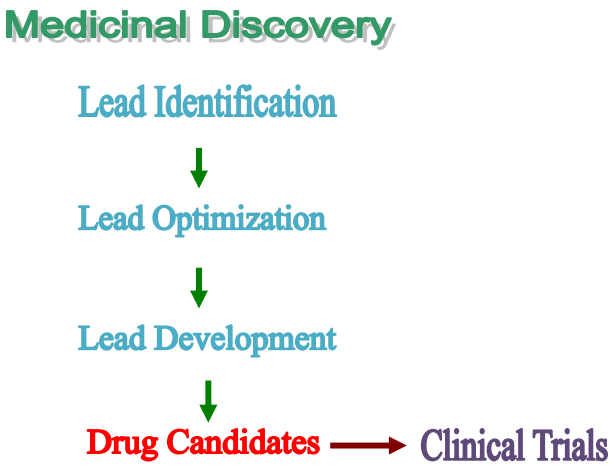

Figure 1: Drug Discovery process

Most drugs have been discovered either by finding the active component from traditional medicines or by serendipitous discovery some time ago. A novel method has been to appreciate how disease and infection are controlled at the molecular and physiological level and to target specific entities rooted in this facts.

The procedure of drug discovery includes the identification of candidates, synthesis, characterization, screening, and tests for therapeutic efficacy. When a compound has exposed its value in these tests, it will begin the procedure of drug development prior to clinical trials.

Target as a common definition is applied in the pharmaceutical research related to industry.

"New" target and "established" target is different and their difference is typically made by pharmaceutical companies engaged in discovery and development of small molecule therapeutics.

"Established targets" reports directly to the amount of background information available on a target, especially functional information. The more such data is available, the less investment is essential to develop a therapeutic directed against the target. The process of collecting such functional data is named "target validation" in pharmaceutical industry idiom. But, "new targets" are named to all those targets that are not "established targets" but which have been or are the theme of drug discovery campaigns. These normally involved newly discovered proteins function has now become clear as a data of essential scientific research.

Another common definition in drug discovery is high-throughput screening (HTS) that defined as the process of discovering a novel drug against a special target for a particular disease wherein large libraries of chemicals are investigated for their capacity to modify the target.

Also HTS present how find a molecule which will interfere with only the special target, but not other, related targets. Other screening process is cross-screening present whether the "hits" against the special target will interfere with other related targets.

The importance of cross-screening is related to this key point that more unrelated targets a compound hits, the more probable that off-target toxicity will happen with that compound once it reaches the clinic.

It is notable that regardless of the rise of combinatorial chemistry as an integral stage of lead discovery procedure, the natural products still act a main task as opening matters for drug discovery. Report findings in 2007 related publication, covering years 1981-2006 details showed that the 974 small molecule new chemical entities, 63% were natural derived or semisynthetic derivatives of natural products.

Lead Identification and Lead Optimization

Early drug discovery includes several stages from target identification to preclinical development. The Hit-to-Lead phase is usually the follow of high-throughput screening (HTS). It contains the below steps:

1. **Hit confirmation**

- Re-testing
- Dose response curve generation
- Orthogonal testing
- Secondary screening
- chemical amenability
- Intellectual Property evaluation
- Biophysical testing
- Hit ranking and clustering

2. **Hit explosion**

- having compound elements which display a high affinity towards the target (below 1 µM)
- explaining chemical tractability
- be gratis of Intellectual properties
- not be nosy with the P450 and P-glycoproteins

- not interact and bind to human serum albumin
- solubility in water(above 100 µM)
- stability
- having a well drug likeness
- displaying cell membrane permeability
- demonstrating biological activity in a cellular assay significantly
- not show signs of cytotoxicity
- not be metabolized quickly
- demonstrate discriminatorily against other related targets

3. Lead generation phase

The main aim of this drug discovery stage is to synthesize lead compounds, novel analogs with better potency, decreased off-target activities, and physiochemical/metabolic properties investigative of reasonable in vivo pharmacokinetics. This optimization is able throughout experiential modification of the hit structure and by using structure-based design if structural data about the target is accessible.

4. Lead optimization phase

It is common several compounds that find in early stages of drug discovery process show some degree of activity, and if these compounds share common chemical features, one or more pharmacophores can then be expanded. At this time, medicinal chemists will challenge to imply structure-activity relationships (SAR) to get better certain features of the lead compound:

- Enhance activity against the chosen target
- Decrease activity against unrelated targets
- Get better the "drug-like" or ADME properties of the molecule.

When a lead compound series has been confirmed with enough target potency and selectivity and approving drug-like properties, as best candidate compounds will be offered for drug development stage.

Lead Development

Drug development or preclinical development is described as finally stage that it allows a new chemical lead compound to take necessary steps for testing in human clinical trials. New chemical entities (**NCEs**) as lead compounds with promising activity against a particular biological target are assessed to know their safety, toxicity, pharmacokinetics and metabolism additional chemical makeup, stability, solubility in humans through drug development process.

The procedure by which the chemical compound will be optimized so that from being prepared at the bench on a milligram level by a synthetic chemist, it can be artificial on the kilogram and then on the ton level. It will be more tested for its suitability to be made into capsules, tablets, aeresol, intramuscular injectable, subcuteneous injectable, or intravenous formulations. All these procedures are identified in preclinical development as **CMC**: Chemistry, Manufacturing and Control.

The essential goals of pre-clinical development performed before clinical trials (testing in humans) are to verify a product's crucial safety profile. Several types of preclinical research are included pharmacodynamics (PD), pharmacokinetics (PK), ADME, and toxicity testing through animal testing.
These findings approximate a safe starting dose of the drug for clinical trials in humans.
In general, both *in vitro* and *in vivo* tests will be done. Drug's toxicity tests are performed to show which organs are targeted by that drug, in addition to if there are any long-standing carcinogenic properties or toxic effects on mammalian reproduction.
The data gathered from these findings is critical so that safe human testing can begin.

Clinical trial

Clinical trials are performed to allocate safety and efficacy data to be composed for novel drugs or devices. Clinical trial processes are approval by Health Authority/Ethics Committee in several countries.

Regularly a clinical trial is supervised by an outsourced colleague such as a contract research organization (CRO).

Throughout the clinical trial, the researchers: recruit patients with the programmed characteristics, administer the treatment(s), and gathered information on the patients' health for a described time period. These information involved dimensions similar to vital signs, whole of study drug in the blood, and whether the patient's health gets improved or not. The investigators send the information to the trial support who then analyzes the pooled information using statistical tests.

A clinical trial may be proposed in below pattern:

- Evaluating the safety and effectiveness of a novel medication on an explicit class of patient.
- Evaluating the safety and effectiveness of a several dose of a medicine than is commonly used.
- Evaluating the safety and effectiveness of an previously marketed medicine for a novel indication, i.e. a disease for which the drug is not specially approved
- Evaluating whether the novel medicine is further efficient for the patient's condition than the previously used.
- Evaluating the efficiency in patients with a exact disease of two or further already approved or ordinary interventions for that disease.

Clinical trials commonly are classified in two ways:

1. **by the way the researchers behave:**

- In an observational study, the researchers view the subjects and determine their results. The researchers do not vigorously control the test. This is as well named a natural experiment.
- In an interventional study, the researchers provide the research subjects a exacting medication or other interference.

2. **by the clinical trial purpose:**

- Prevention trials
- Screening trials

- Diagnostic trials
- Treatment trials
- Quality of life trials
- Compassionate use trials

Clinical trials including novel drugs are normally organized into four phases. Each phase of the drug approval procedure is cared for as a divide clinical trial. The drug-development process will generally progress during all four phases. If the drug effectively obsoletes during Phases I, II, and III, it will typically be approved by the national regulatory authority for employ in the universal population. Phase IV are 'post-approval' studies.

Phase 0

Phase 0 is a topical description for investigative, first-in-human trials performed in agreement with the United States Food and Drug Administration's (FDA) 2006 Guidance on Exploratory Investigational New Drug (IND) Studies.

Phase I

Phase I trials are the first phase of testing in human themes. Usually, a little (20-50) set of healthy unpaid assistants will be chosen. This phase involves trials designed to evaluate the safety (pharmacovigilance), tolerability, pharmacokinetics, and pharmacodynamics of a drug. There are several types of Phase I trials:

- SAD
- MAD
- Food effect

Phase II

Formerly the early safety of the study drug has been verified in Phase I trials, Phase II trials are done on superior sets (20-300) and are planed to evaluate how well the drug vocations, plus to keep on Phase I safety evaluations in a better set of helpers and patients. When the development process for a new drug fails, this typically take places

through Phase II trials when the drug is discovered not to vocation as designed, or to have toxic effects.
Phase II studies are occasionally separated into Phase IIA and Phase IIB. Some trials join Phase I and Phase II, and investigate both efficacy and toxicity.

Phase III

Phase III studies are randomized proscribed multicenter trials on great patient sets and are intended at being the ultimate evaluation of how effectual the drug is, in contrast with present 'gold standard' treatment.

Nearly all drugs experiencing Phase III clinical trials can be marketed under FDA norms with correct recommendations and laws, but in case of any unfavorable results being reported everywhere, the drugs require to be remembered instantly from the market. Even as most pharmaceutical companies cease from this perform, it is not abnormal to see many drugs experiencing Phase III clinical trials in the market.

Phase IV

Phase IV trial is as well identified as **Post Marketing Surveillance Trial**. Phase IV trials include the safety surveillance (pharmacovigilance) and continuing technical support of a drug after it obtains consent to be sold.

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http://en.wikipedia.org/wiki/Clinical_trial
Balunas, J., M., Kinghorn, D. A., Drug discovery from medicinal plants: Life Sciences (2005).Vol.78:431–441.

Using of Computer Simulations to Discover Molecular Keys to Combat HIV

According to research accepted, by the *Journal of Chemical Information and Modeling*, investigators have recognized specific molecules that could block the means by which HIV increases by carrying away its capability to bind with other proteins.

At this research group (Barron were Manthos Papadopoulos of the National Hellenic Research Foundation, Athens; Serdar Durdagi of the National Hellenic Research Foundation and the Freie Universitat, Berlin; Claudiu Supuran of the University of Florence, Italy; T. Amanda Strom, Nadjmeh Doostdar and Mananjali Kumar of Rice; and Thomas Mavromoustakos of the National Hellenic Research Foundation and the University of Athens), by using computer simulations, over 100 carbon fullerene, or C_{60} were tested, derivatives at first developed at Rice for other principles to observe if they could be applied to control a strain of the virus, HIV-1 PR, by fixing themselves to its binding pocket.

Actually, throughout their "in-silico," or computer-based, calculations, researchers set up two fine fits among the fullerene derivatives assessed and are now doing effort to boost their binding properties to get that great molecule, one that sticks "like Velcro" to the virus and can be all right-tuned for a range of strains (ScienceDaily (May 25, 2009)).

HIV Vaccine produced by Engineered Plants

According to investigation performed in Örebro University of Sweden, ScienceDaily reported investigator team has been successful in modifying the genes in plants so they can role as a vaccine against HIV. Throughout gene modification the plants have obtained the capability to generate a protein that is part of the virus, and the research has done a giant step forward in that mice that have been supplied the plants have reacted and structured antibodies against the protein. The main goal of this research is the producing of drugs with the help of plants to combat diseases.

To obtain plants to generate the p24 protein (be present in every HIV viruses and appears approximately the similar in the various virus lines), the gene that underlies the procedure must be a part of their own genetic structure, but while it’s unfeasible to transfer the gene

directly from the virus to the plant, the investigators had to get a detour. This was done by first placing the gene into a bacterium that could then transmit it to the plants. The effort be successful; the plants generated p24 and also exceeded on this capability to their offspring.

At the further step, mice were fed with the p24 plants, and these trials as well confirmed to be successful. The mice's immune defense reacted just as the investigators had expected, producing antibodies against the protein, this functioned as a vaccine (Science Daily (May 18, 2009).

Virus Tamed To Devastate Cancer Cells

In accordance with Science Daily news, an investigation was performed in Oxford University by Cawood *et al*. that this researcher team has been presented a virus so that it attacks and destroys cancer cells but does not harm healthy cells. They strong-minded how to generate replication-competent viruses with input toxicities eradicated, given that a new stage for development of improved cancer treatments and improved vaccines for a wide variety of viral diseases.

This current research was aimed principally to investigate and display the potential of this novel mechanism to regulate virus activity. Though the current tumor-killing virus is useful in mice, transfer of the knowledge into the clinical setting will necessitate re-engineering of the virus to defeat virus pathologies seen in humans, and it will be at least two years earlier than this can be assessed in the clinics (Science Daily (May 25, 2009)).

Computer Simulation imprisons Immune Response to Influenza Type A

In accordance with research accepted, by the Journal of Virology, investigators have fruitfully tested for the first time a computer simulation of major portions of the body's immune reaction with influenza type A. This novel "global" flu model is built out of preexisting, slighter-range models that imprison in mathematical equations millions of simulated interactions between virtual immune cells and viruses.
A group of immunologists, mathematical modelers, statisticians and software developers generated the novel model more than three years inside the Center for Biodefense Immune Modeling at the University of Rochester Medical Center.

The project was directed by Hulin Wu, Ph.D., principal researcher of the project, manager of the Center for Biodefense Immune Modeling (CBIM) and division chief of the Department of Biostatistics and Computational Biology, and by Martin S. Zand, M.D., Ph.D., co-manager of the CBIM. The research was supported by the National Institute of Allergy and Infectious Diseases (NIAID).

The novel model predicts how quickly the T and B cells respond to influenza type A virus infection. For the reasons of the simulation, the model set aside the function of the innate immune system, but the investigators arrangement to add that aspect to future simulations. Conditional on the pathogen at hand and a given patient's past contact, either T cell or B cell responses may take part in a superior function in clearing the virus. One cell type may direct the immune counterattack in someone with a first-instance infection, and one more in a patient who has been infected before or vaccinated (Science Daily (May 20, 2009).

Influenza Virus Resource presents findings achieved from the NIAID Influenza Genome Sequencing Project as well as from GenBank, combined with tools for flu sequence analysis and explanation. Furthermore, it makes available links to other resources that include flu sequences, publications and general data about flu viruses.

All submitted influenza sequences are available in GenBank as soon as they are processed. The 2009 H1N1 influenza virus sequences are listed in **GenBank sequences from 2009 H1N1 influenza outbreak (NCBI)** and are accessible for BLAST searching, additionally they are accessible in the **NCBI Influenza Virus Sequence Database**, and can be rescued with sequences from other influenza viruses for additional analyses using tools included to the database.

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Introduction of EMRO Regional Health Centre

World Health Organization
Regional Office for the Eastern Mediterranean

Centre for Environmental Health Activities (CEHA)

What is CEHA?

The WHO Centre for Environmental Health Activities (CEHA) is a particular centre for environmental health established in 1985 in Amman, Jordan, by the WHO Regional Office for the Eastern Mediterranean. CEHA's mission is to promote environmental health through strengthening national capabilities and programmes for environmental health in countries of the Eastern Mediterranean Region.

Where do CEHA operate?

CEHA's activities and services are available to the countries of the WHO Eastern Mediterranean Region: Afghanistan; Bahrain; Djibouti; Egypt; Islamic Republic of Iran; Iraq; Jordan; Kuwait; Lebanon; Libyan Arab Jamahiriya; Morocco; Oman; Pakistan; Palestine; Qatar; Saudi Arabia; Somalia; Sudan; Syrian Arab Republic; Tunisia; United Arab Emirates; Yemen.

Why environmental health?

Environmental degradation is an important factor causal to the burden of disease. Premature death and illness caused by environmental factors account for one-fifth of the global burden of disease. In the Eastern Mediterranean Region, this proportion ranges from 19% to 25%.

The resulting human, economic and social costs are considerable, threatening the foundation for sustainable development. The annual cost of damage to health and quality of life due to environmental degradation is estimated to be 1.8% to 3.4% of gross domestic product in some countries of the Region.

CEHA working priorities

CEHA is directed by a Technical Advisory Committee consisting of international experts, WHO staff and representatives of Member States and donor agencies. The Committee convenes on a biennial basis to determine CEHA's working priorities based on review of global, regional and national environmental health strategies, recommendations of regional and national meetings, and yield of technical support and assessment missions. Current working priorities areas follow.

- Water, sanitation and hygiene
- Healthy environments for children
- Air quality (indoor and outdoor)
- Hazardous, chemical and health care waste
- Environmental health in emergencies and conflicts
- Food and chemical safety

CEHA partners

Actions to protect populations from environmental hazards often lie within the domain of other divisions; however, the health division has a responsibility to report and act on all health risks. Addressing such risks needs partnership relating health, environment and other divisions. CEHA works closely with countries and other related United Nations agencies, together with local and international colleagues, to ensure a coherent approach to policies, programmes and action. Since its organization, CEHA has reached out to national, regional and international institutions and other specialized and funding agencies to look for collaboration in activities of mutual interest. Over the past 20 years, these attempts have resulted in a number of profitable partnerships to encourage efficient environmental health interventions.

Reference: http://www.emro.who.int/ceha/aboutceha.htm

Announcement

IOMC 2010 is the 3rd International Online Medical Conference which will take place on March 6 & 7, 2010. Building upon the success of previous IOMC conferences, IOMC 2010 aims to provide a forum for discussing and presenting research findings, studies, and experiences in the field of medicine, to create an opportunity for medical researchers, activists, scientists, students, and specialists to meet each other online and share their research papers, and to provide a chance to find new research colleagues and partners for future research works.

IOMC 2010 is chaired by Dr. Jaspreet S. Brar and managed by Mostafa Nejati and Forouzan Bayat Nejad. Besides, an International Advisory Board, comprising of International experts and Medical Professors guide the development of the conference program and agenda. A Conference Scientific Committee supplements the activities of the Advisory Board, and decides on identification of moderators and speakers, evaluates conference papers, and finalizes the agenda for the conferences.
Authors are invited to submit papers related to one of the conference themes.

All conference accepted papers will be published in Conference Proceedings E-Book and/or indexed Journals.

IOMC will take place completely online. This is what makes IOMC quite different from ever-introduced and held conferences. IOMC has already held two successful conferences in 2008 and 2009.

The online nature of IOMC saves the conference participants from paying extra costs of travel, accommodation, and visa. Instead, conference participants can simply register to the conference and log in to conference website in order to attend different conference presentations and workshops online, and use the conference portal to easily interact with presenters and other participants.

Announcement

Conference Themes

The conference welcomes papers in the field of medicine. Themes may include (but not limited to):

- Allergology **- Anaesthesia** **- Anatomy** **- Cancer** **- Cardiology** **- Cell Biology** **- Chemotherapy** **- Clinical Bacteriology** **- Clinical Biochemistry** **- Clinical Pharmacology** **- Clinical Virology** **- Dermatology** **- Emergency Medicine** **- Endocrinology** **- Epidemiology** **- Family Medicine** **- Gastroenterology** **- Gene Therapy** **- Genetics** **- Geriatrics** **- Hematology** **- Histology** **- HIV/Aids** **- Hygiene & Tropical Medicine** **- Immunology** **- Infectious Diseases**	**- Intensive Care Medicine** **- Mental Health** **- Microbiology** **- Nephrology** **- Neurology** **- Nutrition** **- Obstetrics and Gynecology** **- Oncology** **- Ophthalmology** **- Otolaryngology** **- Orthopedics** **- Parasitology** **- Pediatrics** **- Palliative care** **- Pathology** **- Physiology** **- Preventive Medicine** **- Public Health** **- Pulmonary Diseases** **- Radiology** **- Radiotherapy** **- Sexual & Reproductive Health** **- Surgery** **- Toxicology** **- Urology**

Reference: http://www.iomcworld.com/2010

Cover picture

Title: Proliferating Cell Nuclear Antigen
Description: Proliferating Cell Nuclear Antigen commonly known as PCNA, is a protein that acts as a processivity factor for DNA polymerase delta in eukaryotic cells. It achieves this processivity by encircling the DNA, thus creating a topological link to the genome. It is an example of a DNA clamp. The protein encoded by this gene is found in the nucleus and is a cofactor of DNA polymerase delta. The encoded protein acts as a homotrimer and helps increase the processivity of leading strand synthesis during DNA replication. In response to DNA damage, this protein is ubiquitinated and is involved in the RAD6-dependent DNA repair pathway. Two transcript variants encoding the same protein have been found for this gene. Pseudogenes of this gene have been described on chromosome 4 and on the X chromosome.
Source: en.wikipedia.org/wiki/PCNA

Title: Innate immune system
Description: The innate immune system comprises the cells and mechanisms that defend the host from infection by other organisms, in a non-specific manner. This denotes that the cells of the innate system recognize and respond to pathogens in a generic way, but unlike the adaptive immune system, it does not grant long-lasting or protective immunity to the host. Innate immune systems provide immediate defence against infection, and are found in all classes of plant and animal life.
Source: en.wikipedia.org/wiki/Innate_ immune_ system

Title: Prescription drugs
Description: Prescription drugs are commonly administered by veterinarians, dentists, optometrists, and medical practitioners. It is commonly needed that an MD, DO, PA, OD, DPM, DVM, DDS, or DMD write the prescription; basic-level registered nurses, medical assistants, clinical nurse specialists, nurse anesthetists, and nurse midwives, emergency medical technicians, psychologists, and social workers as instance, do not have the influence to stipulate drugs.
Source: en.wikipedia.org/wiki/drug development