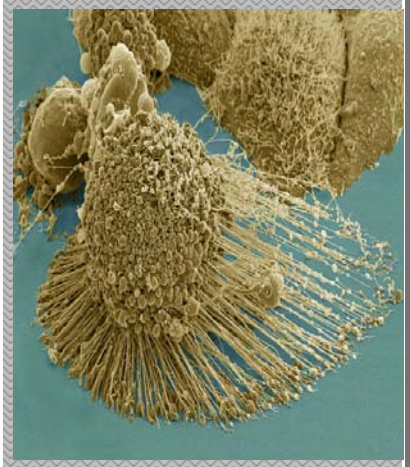

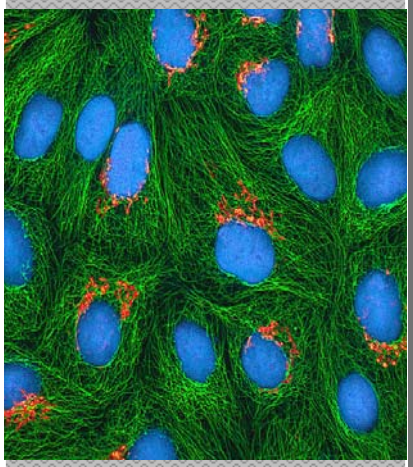

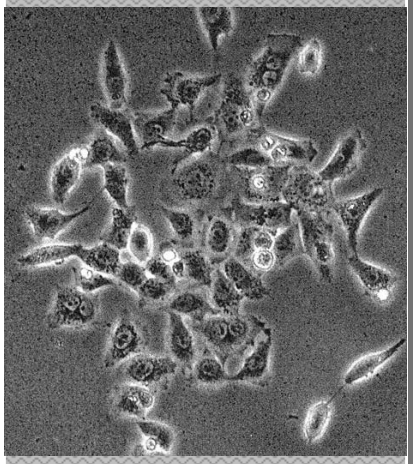

EMGEN Newsletter

Vol. 5 Issue 6

IN THIS ISSUE:

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

Address:
Biotechnology building, #69, Pasteur Ave., Pasteur Institute of Iran
Tehran, Iran, 13164
Tel: +98-21-66954324
Fax: +98-21-66465132
E-mail: emhgbn@gmail.com, emgen@pasteur.ac.ir
Websites: www.emgen.net
www.emhgbn.net

Prepared by: Fazeleh Hosseinpour
Page design: Fazeleh Hosseinpour
Assisted by: Mohammad Kargar
Editor: Dr. Soroush Sardari

INTRODUCTION TO CELL CULTURE

A single cell is very vital for human life. The genetic material of a cell in the human body contains the mystery to inborn diseases, such as Tay Sachs, cystic fibrosis, Alzheimer's disease, and other multifarious diseases like heart disease. Tissue culture was initially introduced in the early 1900's in order to study the attitude of cells as a response to regular and induced tentative stress. The scholars utilized fragments of tissues to survey the attitude of single cells. Therefore, the name of 'cell culture' was altered.

Cell cultures and DNA are composed of blood or small fragments of tissue (biopsies). We can immortalize Lymphocytes (white blood cells) by Epstein-Barr virus and replicate them in culture medium. Fibroblasts (cells from a skin biopsy) are developed for the establishment of the cell line, so that their growth in cell culture is exposed to limitation. The personnel of the Coriell Cell Repositories are able to make cultures out of blood and skin. The cells are kept in Institute. Each researcher who is interested in studying disease processes can receive these cells.

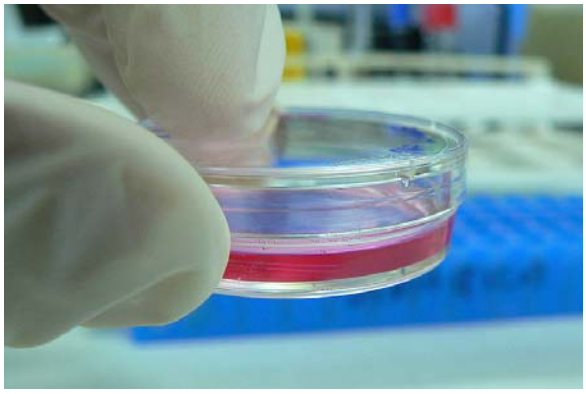

Figure 1: Cell Culture

Cell culture is in fact a complex process. The cells are grown under controlled conditions. The growth of explants which derivate straightly from the living organism (e.g. biopsy material) is recognized as primary cell culture. In fact, a variety of cell populations exist in the culture. Perhaps some cells survive without replication. Such cells are not so distinctive in the increasing population of those which can proliferate *in vitro*. Cells from explants sometimes my transform to cell lines by passage. These cells may continue to multiply for several cell generations. The primary cells are frequently mixed with immortal (cancer) cells to fabricate a hybridoma line. Many of the explanted cells can only survive for one or a few passages before death.

History of Cell Culture

1907- Frog embryo nerve fiber outgrowth by Harrison.

1912- Explants of chick embryo tissues by Carrel, Burrows.

1943- Development of mouse lymphocyte cell line by Earle, et al.

1948- First use of antibiotics in tissue culture by Keilova.

1949- Growth of virus in cell culture by Enders, et al.

1952- Polio virus grown in monkey kidney cells by Kew, et al.

1952- Development of HeLa cell line by Gey, et al.

1955- Development of defined cell culture media by Eagle.

1958- Recognition of importance of mycoplasma by Coriell.

1961- Demonstration of the finite lifespan of normal human cells by Hayflick and Moorhead.

1964- Discovery of pluripotency of embryonic stem cells by Kleinsmith and Pierce.

1970- Development of laminar flow cabinets for cell culture, Kruse et al.

1976- Totipotency of embryonic stem cells described by Illmensee and Mintz.

1977- Cross-contamination of many cell lines with HeLa cells confirmed, Nelson-Rees &Glandermeyer.

1983- Regulation of cell cycle and cycling reported by many.

1983- Development of reconstituted cell cultures by Bell and others.

1989- Transformation, malignancy, oncogenes reviewed by Weinberg.

1990- Application of cell culture to production of biotherapeutic agents.

1998- Production of cartilage by tissue engineered cell culture by Aigner et al.

2000- Mapping of the human genome.

2007- Use of viral vectors to reprogram adult cells to embryonic state (induced pluripotent stem cells) by Yu et al.

2008 and beyond- Era of induced pluripotent stem cells – promises and challenges.

Primary Culture

Primary culture describes a culture process in which the cells are isolated from the tissue and reproduced under the suitable circumstances until they occupy the entire accessible substrate (i.e., reach confluence). Then, the cells must undergo another culture by moving them to a new vessel with fresh growth medium to provide more space for continued growth.

Cell Line

The primary culture is converted to a cell line or subclone after the first subculture. Cell lines which are taken from primary cultures do not live a long time. When they are put into passage, cells with high growth potential become dominant. Thus, the population bears a kind of genotypic and phenotypic homogeny.

Cell strain

If we choose a subpopulation of a cell line from the culture through cloning or another technique this cell line turns into a cell strain. A cell strain regularly obtains extra genetic modifications following to the beginning of the parent line.

Finite vs. Continuous Cell Line Normal cells are generally divided only a few times before missing their capability to reproduce. This occurrence is genetically established and is identified as senescence. These cell lines are finite. However, transformation makes cell lines immortal. This process may happen unexpectedly or can be chemically or virally induced. When there is transformation in a finite cell line we will witness a continuous cell line.

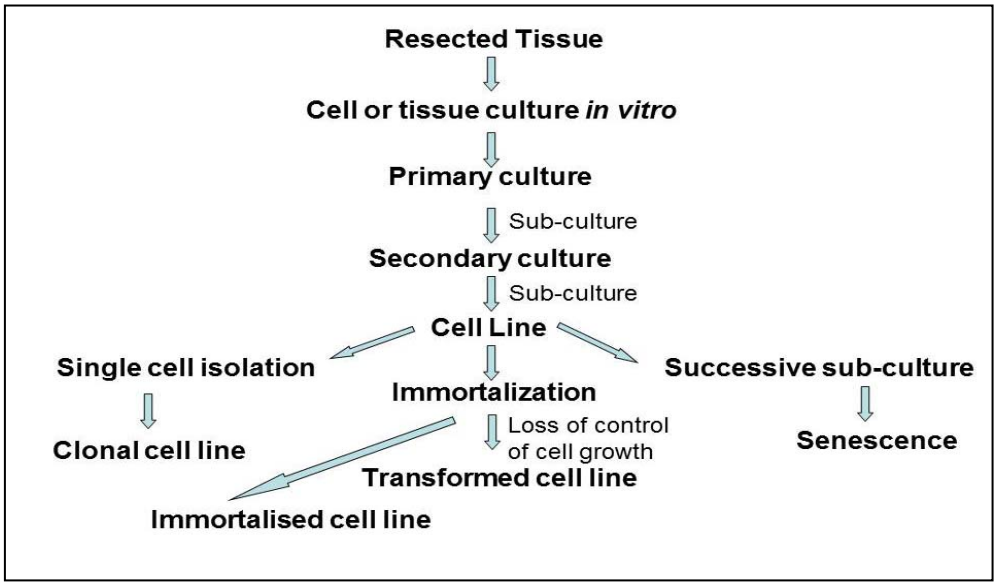

Figure 2: Isolation of cell lines for *in vitro* cell culture

Culture Conditions

Each cell has its own specific culture conditions. The artificial environment in which the cells are cultured perpetually composes of a proper vessel including a substrate or medium which provides the vital nutrients (amino acids, carbohydrates, vitamins, minerals), growth factors, hormones, and gases (O_2, CO_2), and controls the physicochemical environment (pH, osmotic pressure, temperature). Most cells are anchor age dependent, so that they should be fastened to a solid or semi-solid substrate for culturing (adherent or monolayer culture); while some other cells grow in the culture medium in a floating state (suspension culture).

Cryopreservation

If a remaining of cells is obtainable from sub culturing, they must be treated with the correct defensive agent (e.g., DMSO or glycerol) and maintained at temperatures below -130°C (cryopreservation) until they are required.

Morphology of Cells in Culture

Cells in culture can be divided into three fundamental groups considering their figure and emergence (i.e., morphology).

Fibroblastic (or fibroblast-like) cells are bipolar or multipolar, have elongated shapes, and grow attached to a substrate.

Epithelial-like cells are polygonal in shape with more regular dimensions, and grow attached to a substrate in discrete patches.

Lymphoblast-like cells are spherical in shape and usually grown in suspension without attaching to a surface.

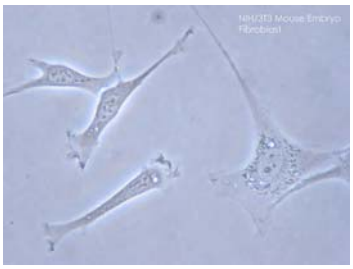

Figure 3: Fibroblastic Cells

Applications of Cell Culture

Cell culture is one of the main instruments exercised in cellular and molecular biology, offering outstanding model systems for surveying the normal physiology and biochemistry of cells (e.g., metabolic studies, aging), the effects of drugs and toxic compounds on the cells, and mutagenesis and carcinogenesis. It is furthermore employed in drug screening and development large scale production of biological compounds (e.g., vaccines, therapeutic proteins). The steadiness and reproducibility of outcomes that can be acquired from using a batch of clonal cells is the chief benefit of using cell culture for any of these applications.

Cell Culture Basics

This section is in regard to the basics of cell culture, together with the assortment of the suitable cell line for your tests, media requirements for cell culture, adherent versus suspension culture, and morphologies of continuous cell lines. It is noteworthy that the following information is only considered as an introduction to the basics of cell culture, and it is proposed as a preliminary point. One can use in print text and books, in addition to the manuals and product information sheets provided with the products to get more comprehensive information.

Selecting the Appropriate Cell Line

Think about the subsequent principles for choosing the appropriate cell line for your tests:

Species: Non-human and non-primate cell lines typically have less biosafety constraints, but eventually your tests will order whether to employ species specific cultures or not.

Functional characteristics: What is the reason of your tests? For example, liver- and kidney-derived cell lines may be more suitable for toxicity testing.

Finite or continuous: While choosing from finite cell lines may provide you more alternatives to state the accurate function, continuous cell lines are frequently easier to clone and keep.

Normal or transformed: Transformed cell lines typically have an bigger growth rate and higher plating effectiveness, are continuous, and need less serum in media, except they have experienced a permanent change

Growth conditions and characteristics: What are the necessities regarding growth rate, saturation density, cloning efficiency, and the ability to grow in suspension? for instance, to express a recombinant protein in high yields, one would like to choose a cell line with a quick growth rate and a capacity to grow in suspension.

Other criteria: If you are using a finite cell line, are there enough stocks accessible? Is the cell line well-distinguished, or you are obliged to carry out the validation yourself? If one is using an irregular cell line, does he have an equivalent normal cell line that you can use as a control? Is the cell line steady? If not, how simple it is to clone it and produce adequate frozen stocks for your tests?

Acquiring Cell Lines

One might set up own culture from primary cells, or may decide to buy established cell cultures from commercial or non-profit contractors (i.e., cell banks). Trustworthy suppliers offer premium cell lines that are cautiously examined for their reliability and to make sure that the culture is free from contaminants. We do not suggest borrowing cultures from other laboratories because they bear a high risk of contamination. Regardless of their source, confirm that all new cell lines are tested for mycoplasma contamination before you start to use them.

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1. Maqsood, M.I., Maryam M. M., Bahrami A. R. and Ghasroldasht M. M. (2013). Immortality of Cell Lines: Challenges and Advantages of Establishment. *Cell Biology International Cell Biol Int*, 37(10): 1038-045.
2. Meenakshi. A, (2013). Cell Culture Media: A Review. *Materials and Methods MATER METHODS* 3 (3): 175-180
3. https://en.wikipedia.org/wiki/File:Cell_Culture_in_a_tiny_Petri_dish.jpg
4. https://en.wikipedia.org/wiki/File:NIH_3T3.jpg

3D CELL CULTURE TECHNIQUES: BIOLOGICAL SCAFFOLDS

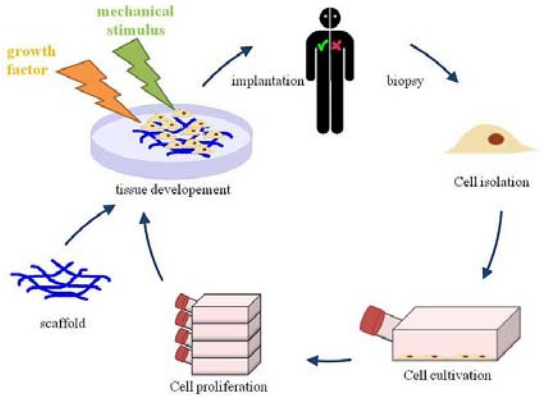


Figure 1: Cell Culture Process

Over the last decade, an essential spotlight of drug discovery attempts has been the integration of *in vitro* testing models that improved mimic *in vivo* conditions found within the target patient. An early stage saw a deviation from biochemical assays by means of purified drug target, in agreement of a cell-based procedure that utilized over-expression of drug target in ordinary host cell lines, such as CHO and HEK-293. The search for better physiological significance led to the use of primary cells, rather human if supply was sufficient, and the dependence on endogenous expression of drug target should detection technology be perceptive enough. Most of these cell types, being naturally adherent, permitted plain culturing workflows that seeded cells in a coated micro-plate well, incubating the micro-plate to encourage the cells to put together in a two dimensional (2D) monolayer before executing the prescribed assay. While offering preliminary developments over bio-chemical and immortalized cell lines, a great deal of proof now supports the fact that culturing cells in this 2D mode is frequently difficult and is a comparatively poor model for *in vivo* conditions and behaviors. Using a 2D model, abrasion rates of drug candidates for cancer were roughly 95%, stemming from *in vitro* drug effi-ciency values that did not convert to the clinic, as well as unexpected toxicity concerns. In 2011 alone, out of almost 900 anti-cancer therapies in clinical trials or under Federal Drug Administration review, only twelve attained authorization; resulting in the loss of hundreds of millions of dollars that were used up on pre-clinical and clinical trials. The basis for these deficits can be drawn to using conventional 2D conditions, where ex-tracellular matrix (ECM) components, cell-to-cell and cell-to-matrix interactions, imperative for differentia-tion, proliferation and cellular functions *in vivo*, are lost.

Similar investigation also shows that conventional 2D cell culture techniques may not precisely copy the 3D *in vivo* atmosphere in which cancer cells live, as the 2D atmosphere does not let for areas of hypoxia, heterogeneous cell populations (including stromal cells), changeable cell proliferation zones (quiescent vs. replicating), ECM influences, soluble signal gradients, and differential nutrient and metabolic waste transport. Consequently, the unnatural 2D atmosphere may give erroneous data concerning the foreseen reaction of cancer cells to chemotherapeutics.

Further research reveals that individual drug targets may not be expressed, or the level of cell signaling may not be equal to that seen *in v*ivo, thus influencing experimental outcomes. Undeniably, an examination showed that in melanoma cells, 106 genes were up-regulated and 73 genes down-regulated using tumor-like models compared to baseline expression of 2D monolayer cell cultures of the same cells. What is attention-grabbing is the reality that the genes found to be up-regulated in the 3D model were also found to be up-regulated in tumors.

Most of the same concerns with using 2D cell culture to make exact tumor models broaden to liver toxicity research as well. While the gold standard for xenobiotic toxicity testing engages *in vivo* animal studies, growing animal wellbeing concerns, as well as the poor coordination of animal study outcomes to disease phenotypes examined in heterogeneous human populations, make integration of a practical, analytical *in vitro* testing technique a main concern. While immortalized liver-derived cell lines make procedures easier and reduce the requirement for whole animal testing, the expression profile of genes concerned in phase I and phase II metabolism do not associate well to that perceived in liver tissue. Primary hepatocyte cultures offer levels of functionality much closer to that seen *in vivo*, but these cells are challenging when used *in vitro*. Under traditional 2D culture conditions, the cells de-differentiate, quickly reduce expression of cytochrome P450 enzymes, and finally miss feasibility.

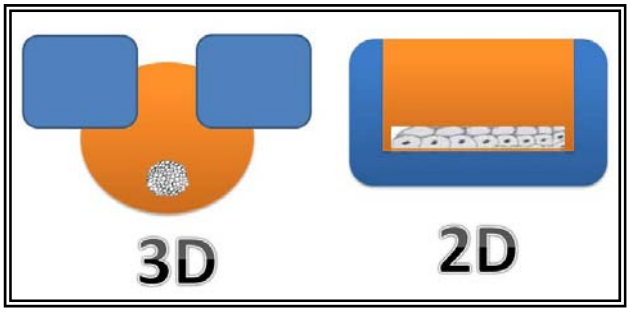


Figure 2: Difference Between 3D and 2D Cell Culture

The affluence of studies emphasizing the limitations of 2D cell culture, both as *in vivo* tumor and liver models, emphasizes the need for new cell models in research methods. This requisition can be met throughout the embracing of 3D cell models, as 3D cultured cells demonstrate characteristics that are closer to complex *in vivo* conditions. Benefits of incorporating 3D cultured cells, compared to 2D culture models, for assessment of drug candidates can consist of: (1) oxygen and nutrient gradients, (2) augmented cell-to-cell and cell-to-ECM interactions, (3) uncoordinated exposure of cells within a 3D structure to the test molecule, (4) different cell multiplication zones, and (5) the effect of site specific stromal cells in the tumor microenvironment[5]. Studies demonstrate that tumor cells of specific cell lines, when assessed in a 3D format, are less responsive to anti-cancer agents than when the same cells are cultured in 2D formats. Nevertheless, other investigation illustrates that diverse cell lines, using a different 3D technology, demonstrate the conflicting effect. These results draw attention to how the use of 3D cell culture in cancer research may offer key viewpoints into drug activity *in vivo* that may be ignored if limited to 2D cell culture models merely. Additionally, the mechanisms entailed to create these distinctions can be clarified, such as signaling pathway variations, or a change in the reliance on the target in a 3D system compared to cells cultured using 2D techniques.

While cells are developed in basement membrane-like gels, there is a common incorporation of the signaling pathways16. A549 3D spheroids reveal continually high levels of IL-6 and IL-8 secretion when compared with their monolayer counterparts. Increased extracellular matrix deposition for improved biomarker expression was stated using 3D culture systems. The differentiation of mesenchymal stromal cells to chondrocytes using hyaluronic acid (HA) 3D model was also examined. It was noticed that the cell receptors could interact with HA better and influence cell differentiation. Diverse factors, including biologically functional microenvironment, material chemistry, cellular interactions, and mechanical property improved chondrogenesis.

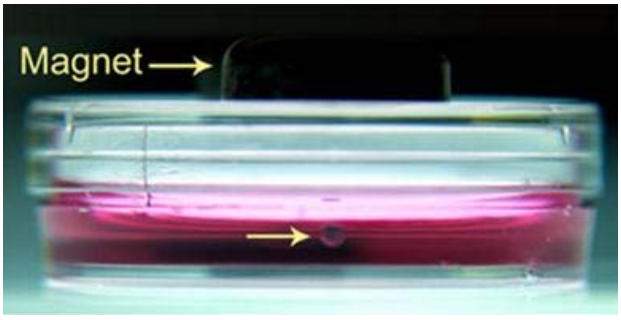


Figure 3: 3D Cell Culture Grown with Magnetic Levitation

Similar findings to those seen with 3D tumor models are also observed when intercalating 3D cell cultures in hepatotoxicity studies. Wu et al. found that 3D cultured rat hepatocytes uphold a more distinguished state as compared to a monolayer culture. Swift declines in CYP1A2 and -1A1 expression using conventional 2D monolayer culture of mouse hepatocytes, compared to constantly high levels using a 3D model were also identified over a five day incubation period. Lengthy evaluations were conducted by Kratschmar et al., with the assessment of rat hepatocytes kept for 25 days using either a 2D sandwich culture or 3D co-culture process. High expression of Nrf2-, as well as glucocorticoid-dependent genes, were observed using the 3D culture method, while 2D hepatocytes revealed quick decrement, followed by constant low expression of both gene sets.

3D Cell Culture Models

Various methods currently exist to culture cells into 3D structures. These can be classified into two major groups; scaffold and non-scaffold based, and comprise the following individual technologies:

Scaffold Based

- Polymeric Hard Scaffolds
- Biologic Scaffolds
- Micropatterned Surface Microplates

Non-Scaffold Based

- Hanging Drop Microplates
- Spheroid Microplates containing Ultra-Low Attachment (ULA) coating
- Microfluidic 3D Cell Culture

Biological Scaffolds

Scaffolds may also be made from constituents of a more natural or biological root, such as proteins usually seen in the *in vivo* ECM. These generally include, but are not restricted to, fibronectin, collagen, laminin, and gelatin. Biological scaffolds not only present a matrix to which the cells can join and restructure into 3D structures, but more prominently, they give the accurate microenvironment of soluble growth factors, hormones, and other molecules that cells interact with in an *in vivo* environment, which can modify gene and protein expression. Existing procedures necessitate cells to either be combined with scaffold proteins in a liquid status (hydrogel) earlier than plating in a microplate well or adjoined to previously shaped scaffolds, or to have the protein combination overlaid onto cells previously collected into 3D spheroids. Cells can then reorganize the

adjacent environment to discharge signaling molecules, permit migration, or accommodate other cellular functions. The final result is the formation of a suitable homeostatic state.

Since these hydrogels are obtained from natural origins, they promote many cellular functions, directing to improved practicality, and reproduction of various cell types. They can also be beneficial to employ over polymeric scaffolds, as the last lack innate factors that encourage proper cell performance and take action mostly to authorize cell function.

Hydrogels also present the admonition of using multi-layer formats to figure tissue-like structures. Individual cell types are inserted into detached hydrogel suspensions and layered on top of each other. Cells then put in order within the hydrogel to shape the layers observed within *in vivo* tissues. Porous supports can also be integrated to incite various air-liquid interfaces in an *in vitro* state. Examples include bilayers reminding you of the dermis and epidermis of human skin and human corneal limbal crypts.

References:

1. Zhang, W., Zhuang, A., Gu, P., Zhou, H., & Fan, X. (2016). A Review of the Three-Dimensional Cell Culture Technique: Approaches, Advantages and Applications. *CSCR Current Stem Cell Research & Therapy*, *11*(4), 370-380.
2. Ravi, M., Paramesh, V., Kaviya, S., Anuradha, E., & Solomon, F. P. (2014). 3D Cell Culture Systems: Advantages and Applications. *J. Cell. Physiol Journal of Cellular Physiology*, *230*(1), 16-26.
3. https://en.wikipedia.org/wiki/File:Tissue_engineering_english.jpg
4. https://en.wikipedia.org/wiki File:3D_Cell_Culturing_by_Magnetic_Levitation_Introduction_Picture.jpg

FIRST DISEASE-SPECIFIC STEM CELL LINE BY SCNT

Some researchers directed by the NYSCF Research Institute's Dr. Dieter Egli state the initial ever patient-specific, diploid (i.e. with two sets of chromosomes, the normal number in human cells) embryonic stem cell line made from an adult with type 1 diabetes by somatic cell nuclear transfer (SCNT). Additionally, the researchers could induce these stem cells into developing into beta cells, the insulin-producing cells missed in type 1 diabetes. The study was published in *Nature.*

This ground-breaking research points to a massive pace forward in the search to develop healthy stem cells from a patient that could be utilized to substitute diseased or dead cells of that same patient, e.g. with type 1 diabetes. This development toward probable regenerative cell substitution therapies is important not only for diabetes but also for many other diseases and conditions, as well as Parkinson's, macular degeneration, multiple sclerosis, and damaged bones, among others.

Although there remain other research obstacles to conquer before this study can attain the clinic, NYSCF researchers and coworkers are once again the pionner in breaking barriers to treatments and cures for the main disease of our era.

References:

https://nyscf.org/news/nyscf-press-releases/item/1643-first-disease-specific-stem-cell-line-by-scnt

SCIENTISTS GENERATE A NEW TYPE OF HUMAN STEM CELL THAT HAS HALF A GENOME

Researchers have achieved in producing a novel kind of embryonic stem cell which contains a sole copy of the human genome, instead of the two copies usually seen in ordinary stem cells. These are the primary human cells that are recognized to be capable of cell division with only one copy of the parent cell's genome. Because the stem cells were a genetic equivalent to the egg cell contributor, they could likewise be employed to develop cell-based treatments for illnesses such as blindness, diabetes, or other conditions in which genetically indistinguishable cells provide a therapeutic benefit. Since their genetic content is equal to germ cells, they may also be valuable for reproductive goals.

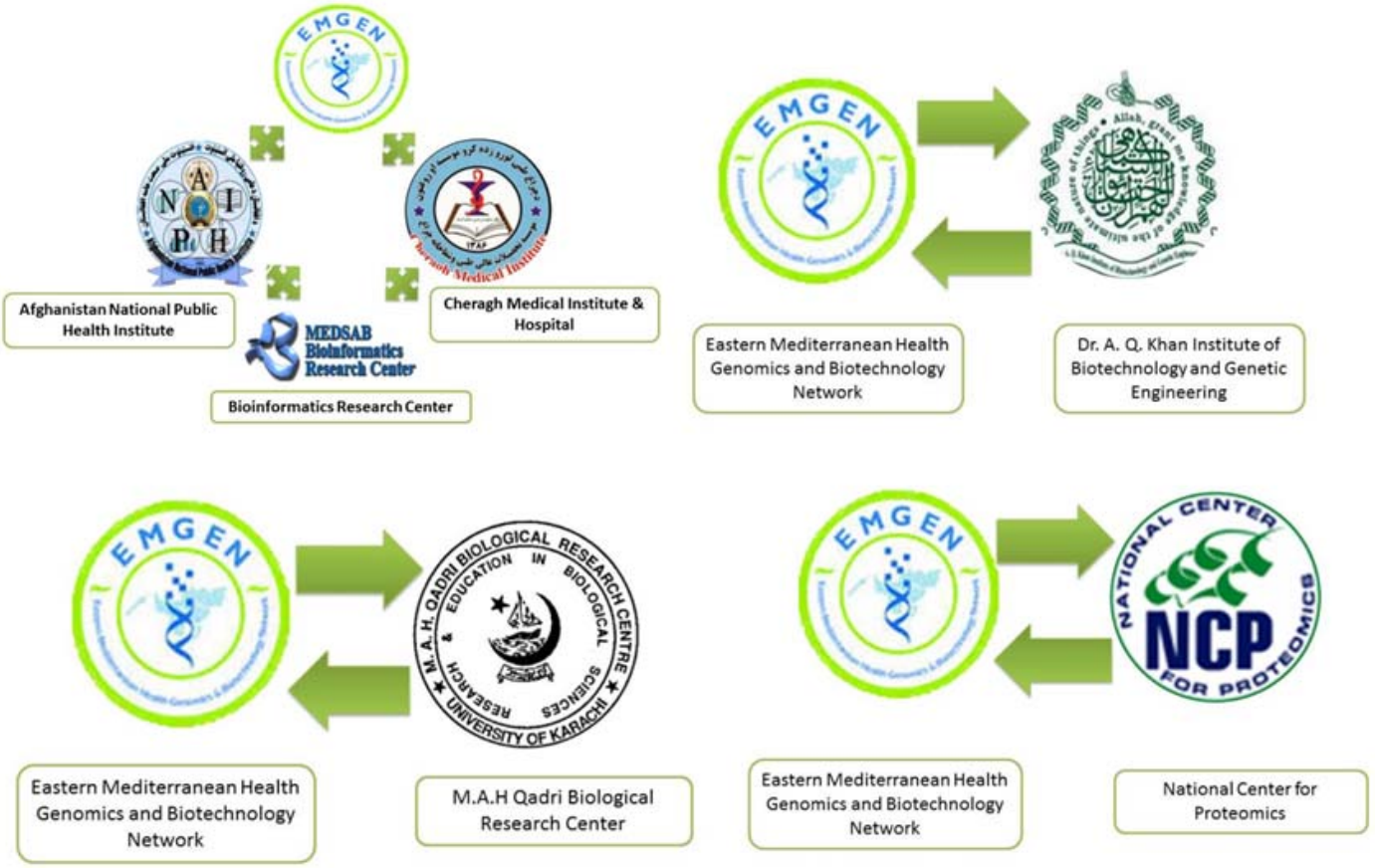
References:

https://www.sciencedaily.com/releases/2016/03/160316140421.htm

EMGEN REPORT

Eastern Mediterranean Health Genomics and Biotechnology Network (EMGEN) was created in 2004 for representatives of selected centers of excellence in (health related) molecular biology, biotechnology & genomics in the eastern mediterranean region by recommendation of WHO/EMRO efforts.

A variety of projects have been accomplished since EMGEN was found which include exchange of researchers for scientific projects, collaboration between Iranian and regional scholars, introduction of papers, books, journals and useful all-inclusive databases, containing research centers, 1200 companies and also more than 7000 active scientists in the field of genomics and health biotechnology. In this regard in 2015, EMGEN signed a five year memorandum of understanding (MoU) between Dr. A. Q. Khan Institute of Biotechnology and Genetic Engineering (KIBGE), M.A.H Qadri Biological Research Center and National Center for Proteomics (NCP) of Pakistan, separately, to joint scientific activities. both sides briefed each other about the programs of their respective organizations and thoroughly discussed various areas of collaboration.

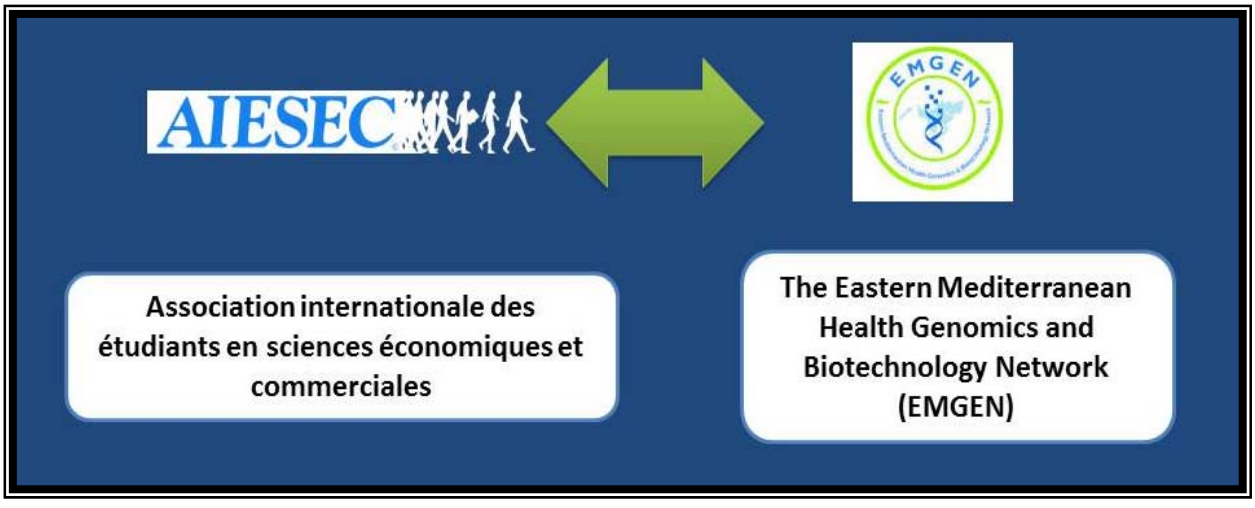


Report

EMGEN and AIESEC (Association Internationale des Étudiants en Sciences ÉconomiquesetCommerciales) amend and extend their agreement to continue activities like exchange scientists for 5 more years.

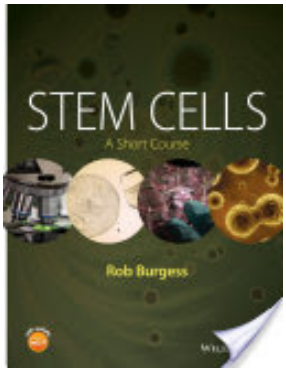
Also a Memorandum of Understanding (MOU) was signed to foster cooperation between Eastern Mediterranean Health Genomics and Biotechnology Network (EMGEN), Bioinformatics Research Center of Sabzevar, Afghanistan National Public Health Institute (ANPHI), and Cheragh Medical Institute & Hospital (CMI), through mutual cooperation in the areas of education, research and industrial/ production collaboration.

The MoU's focus points are collaborative projects, researcher exchange, and to hold common scientific events such as conferences, seminars, workshops, mutual cooperation, also helping to develop industrial parts of countries.



Book Alert

STEM CELLS: A SHORT COURSE



Author: Rob Burgess

Publisher: John Wiley & Sons, 2016

ISBN: 1118439198, 9781118439197

BIOREACTORS: DESIGN, OPERATION AND NOVEL APPLCATIONS

Author: Carl-Fredrik Mandenius

Editor: Carl-Fredrik Mandenius

Publisher: John Wiley & Sons, 2016

ISBN: 3527337687, 9783527337682

MAMMALIAN CELL CULTURES FOR BIOLOGICS MAFATURING

Editors: Weichang Zhou, Anne Kantardjieff

Publisher: Springer, 2014

ISBN: 3642540503, 9783642540509

Announcements

https://www.gtcbio.com/conferences/cell-culture-cell-line-development-overview?alias=cell-culture-cell-line-development

http://www.ngsasia-congress.com/

http://www.chi-peptalk.com/

Announcements

conferenceseries.com

International Conference on

Molecular Biology

October 10-11, 2016 Dubai, UAE

CPD

Accredited cpd Event

http://molecularbiology.conferenceseries.com/

Pasteur-Mérieux Course: **Advanced Course on Antibiotics**

Institut Pasteur

Nom du cours	Advanced Course on Antibiotics (AdCAb)
Langue	English
Participants	40
Durée	October 10-21, 2016
Informations/Inscriptions	http://www.fondation-merieux.org/advanced-course-on-antibiotics-adcab
Dead line for inscriptions	June 26, 2016
Contacts	valentina.picot@fondation-merieux.org cindy.grasso@fondation-merieux.org

Hela or hela cell, is a cell kind in an immortal cell line employed in academic studies. It is considered as the oldest and most regularly used human cell line. The cell line was introduced in 1951 from samples gathered during a biopsy on Henrietta Lacks, a deprived 31-year-old African-American patient undergoing a cervical tumor. The designation HeLa, stemmed from the first two letters of her first and surnames, was used to retain her identity unidentified. Henrietta Lacks, who deceased later in 1951, was not widely recognized as the source of the cells for another two decades.

Reference: Ewen. C. (2013). Deal Done over HeLa Cell Line. *Nature* 500(7461): 132-33.

HELA CELL

Multiphoton fluorescence image of cultured Hela cells with a fluorescent protein targeted to the Golgi apparatus (orange), microtubules (green) and counterstained for DNA (cyan).

Reference: https://en.wikipedia.org/wiki/File:HeLa-IV.jpg

APOPTOTIC HELA CELL

Scanning electron micrograph of an apoptotic HeLa cell. Zeiss Merlin HR-SEM.

Reference: https://en.wikipedia.org/wiki/File:HeLa-I.jpg

HUMAN EMBRYONIC KIDNEY 293 CELLS

Originally derived from human embryonic kidney cells grown in tissue culture, HEK 293 cells are very easy to grow and transfect very readily and have been widely used in cell biology research for many years. They are also used by the biotechnology industry to produce therapeutic proteins and viruses for gene therapy.

Examples of applications include: A study of the effects of a drug on sodium channels, testing of an inducible RNA interference system, testing of an isoform-selective protein kinase C agonist, investigation of the interaction between two proteins, analysis of a nuclear export signal in a protein

Reference: https://en.wikipedia.org/wiki/File:HEK_293_cells_grown_in_tissue_culture_medium.jpg