IDHAYA COLLEGE FOR WOMEN-KUMBAKONAM

DEPARTMENT OF MICROBIOLOGY

COURSE	**:**	**II M.SC MICROBIOLOGY**
SEMESTER	**:**	**IV**
SUBJECT	**:**	**MICROBIAL BIOTECHNOLOGY**
SUBJECT CODE	**:**	**P16MBE5A**
UNIT	**:**	**V-ANIMAL BIOTECHNOLOGY AND IPR**
INCHARGE FACULTY	**:**	**Mrs. A. LAKSHMI**

TRANSGENIC ANIMALS

INTRODUCTION

- Transgenic animals are animals (most commonly mice) that have had a foreign gene deliberately inserted into their genome.
- Created by the microinjection of DNA into the pronuclei of a fertilised egg which is subsequently implanted into the oviduct of a pseudopregnant surrogate mother.

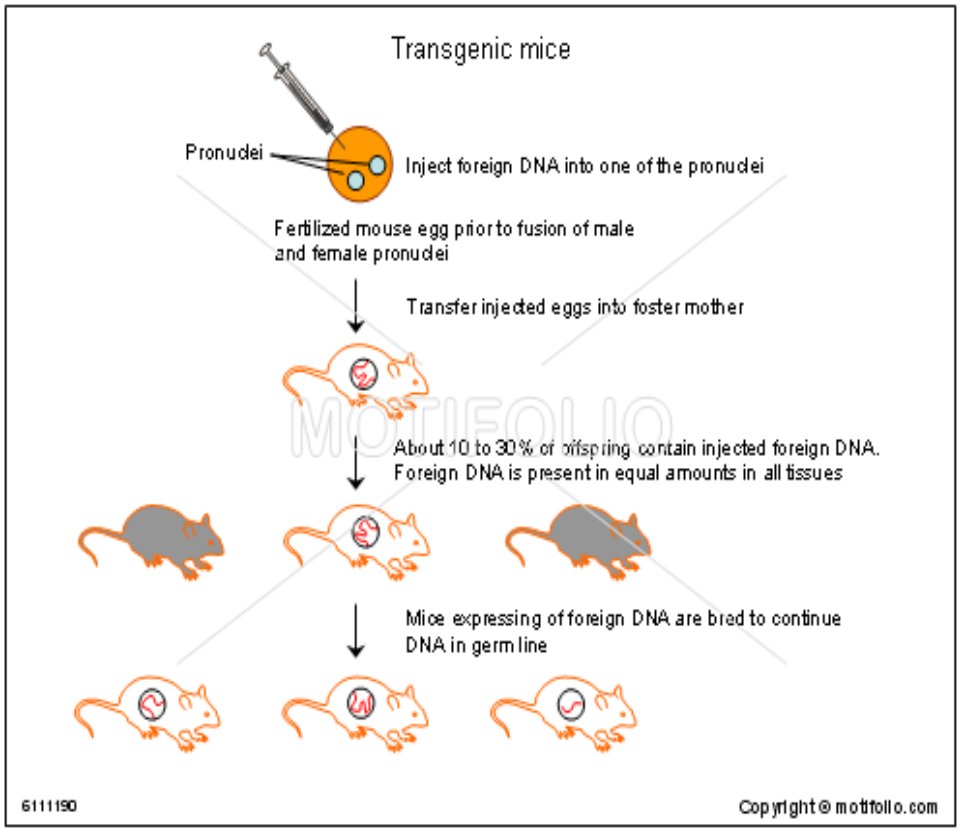
- Examples: sheep, goats, pigs, cows, rabbits, rats, mice, fish, insects, parasites and even humans.
- In 1974 Rudolf Jaenisch created a transgenic mouse.
- Transgenic Animals in Agriculture improve human health, enhance nutrition, protect the environment, increase animal welfare, and decrease livestock disease.

METHODS OF CREATION OF TRANSGENIC ANIMALS

(MICE, CATTLE & SHEEP)

- **DNA MICROINJECTION.**

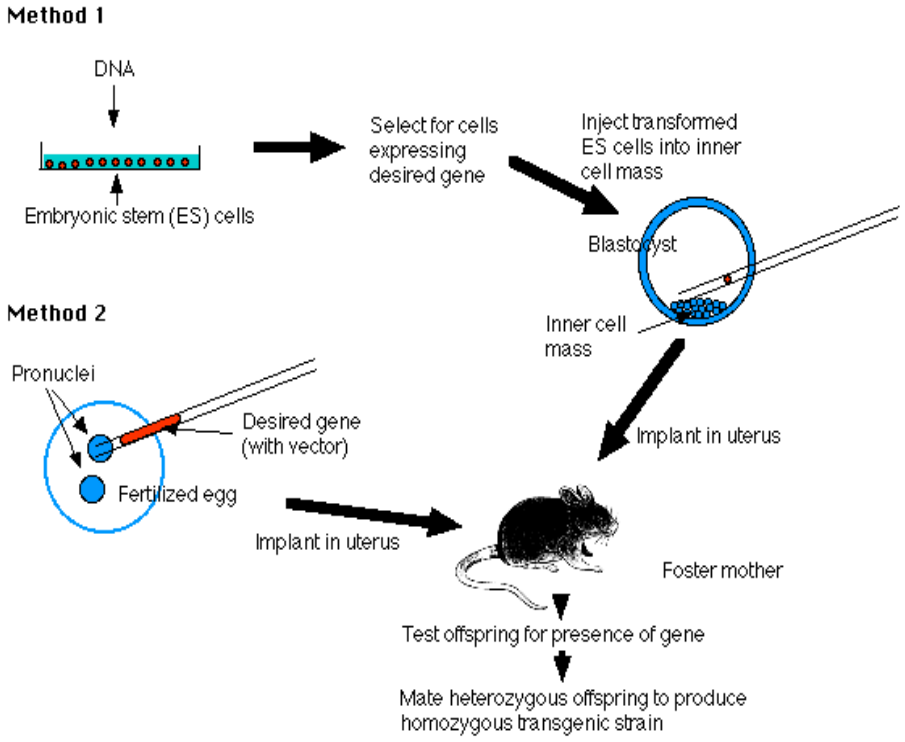
  - Microinjection is a direct method to introduce DNA into either cytoplasm or nucleus.
  - It is a microsurgical procedure conducted on a single cell, using a glass needle
  - There are two basic types of microinjection systems. The first is called a constant flow system and the second is called a pulsed flow system.
  - Constant flow of a sample is delivered from a micropipette.
  - This system typically requires a regulated pressure source, a capillary holder, and either a coarse or a fine micromanipulator.
  - A pulsed flow system, however, allows for greater control and consistency over the amount of sample injected.
  - Pronuclear injection is a technique used to create transgenic organisms by injecting genetic material into the nucleus of a fertilized oocyte.
  - A major advantage of this method is its applicability to a wide variety of species.



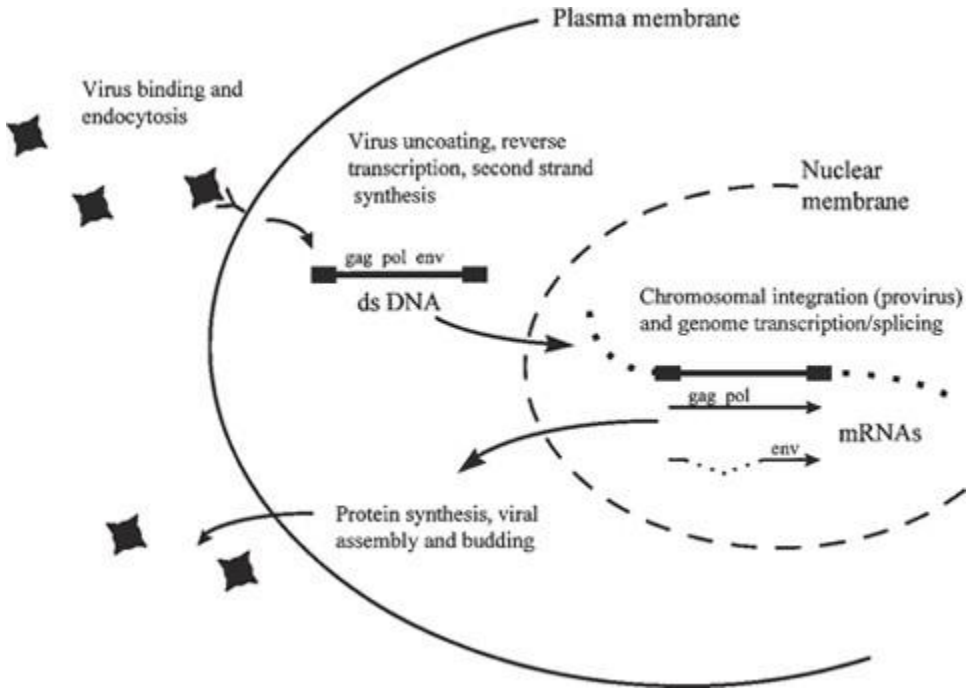
- **EMBRYONIC STEM CELL-MEDIATED GENE TRANSFER**.

  - This method involves prior insertion of the desired DNA sequence by homologous recombination into an in vitro culture of embryonic stem .
  - These cells are then incorporated into an embryo at the blastocyst stage of development. The result is a chimeric animal.
  - ES cells are from the very early mouse embryo and can differentiate into all types of cells when introduced to another embryo.

- DNA introduced into ES cells may integrate randomly, just like in pronuclear micro-injection.
- If the introduced DNA is similar in sequence to part of the mouse genome, it may undergo "homologous recombination" and integrate as a single copy at a specific site.
- ES cells will colonize a host embryo and often contribute to the germ line.
- This results in the production of some sperm carrying the extra DNA.
- When these transgenic sperms fertilize a normal egg, a transgenic mouse will be produced with the same foreign DNA in every cell.



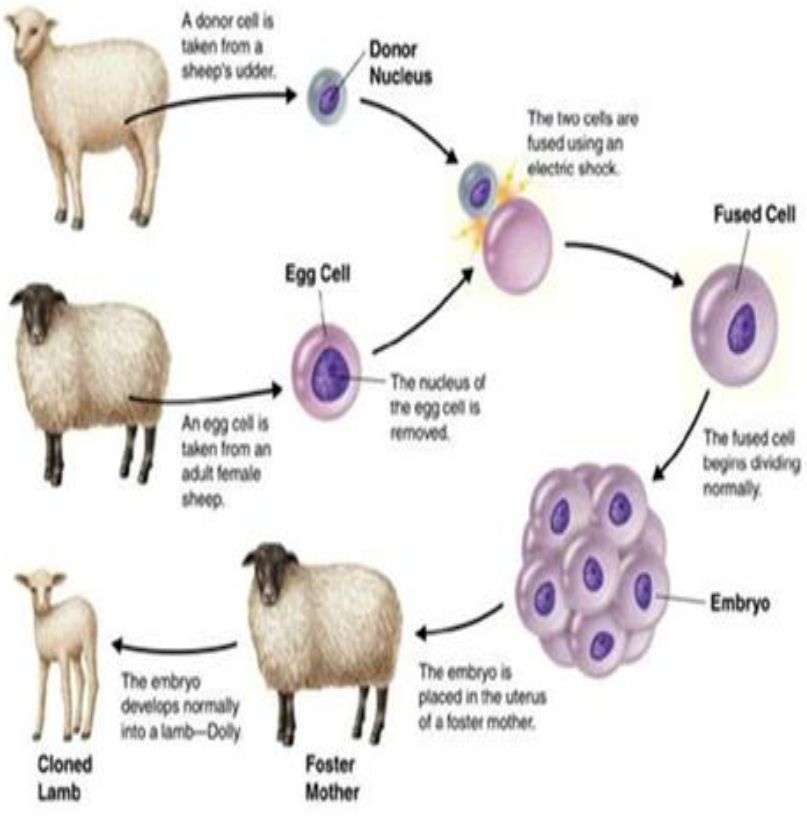
- **RETROVIRUS-MEDIATED GENE TRANSFER**.
  - Retroviruses are commonly used as vectors to transfer genetic material into the cell.
  - It takes advantage of their ability to infect host cells in this way.
  - Offspring derived from this method are chimeric, i.e., not all cells carry the retrovirus.
  - Transmission of the transgene is possible only if the retrovirus integrates into some of the germ cells.
  - Transgenic mice produced by retroviral transduction of male germ line stem cells.
  - Male germ line stem cells have ability to self-renew and genetic modification of these cells.



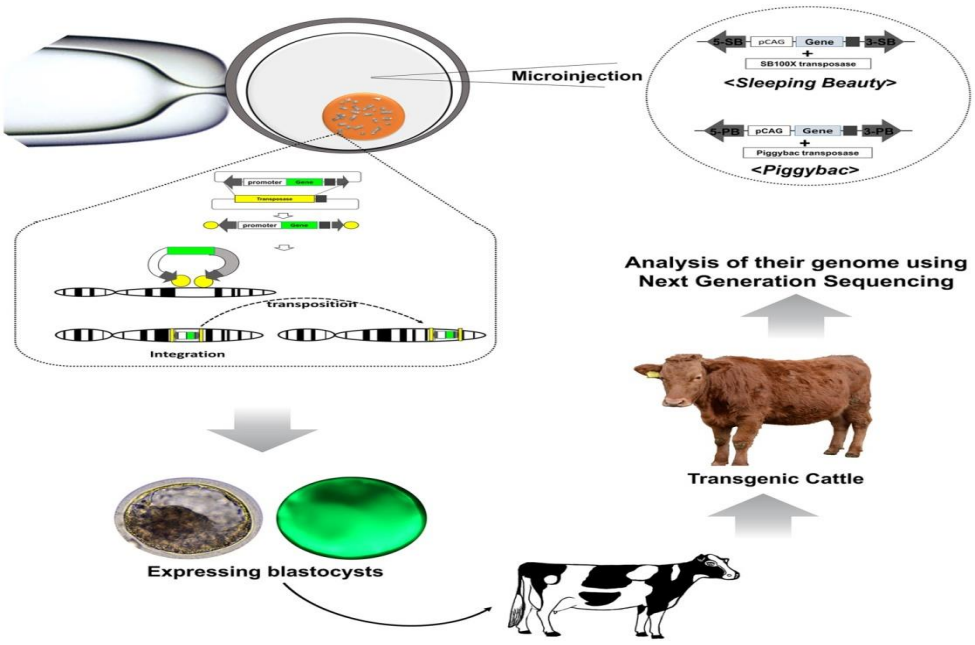
- **NUCLEAR TRANSFER METHOD:**
  - In this method, the transgenic goats were produced by nuclear transfer of fetal somatic cells.
  - Donor karyoplasts were obtained from a primary fetal somatic cell line derived from a 40-day transgenic female fetus produced by artificial insemination of a nontransgenic adult female with semen from a transgenic male.
  - Live offspring were produced with two nuclear transfer procedures.
  - Oocytes at the arrested metaphase II stage were enucleated, electrofused with donor somatic cells, and simultaneously activated.
  - In the second procedure, activated in vivo oocytes were enucleated at the telophase II stage, electrofused with donor somatic cells, and simultaneously activated a second time to induce genome reactivation.
  - There was generation of three healthy identical female offspring.
  - Genotypic analyses confirmed that all cloned offspring were derived from the donor cell line.
  - Analysis of the milk of one of the transgenic cloned animals showed high-level production of human antithrombin III.
  - The nuclear transfer application may be more useful and beneficial for agricultural is the ability to efficiently produce a large number of identical offspring derived from a particular mating.

- Therefore, nuclear transfer using a embryonic cell lines derived from that mating maybe more attractive.

- **TRANSGENIC SHEEP**
  - In sheep, pronuclear microinjection of several hundred copies of the foreign gene into embryos is the only published method used to regularly produce transgenics and it will be the standard by which future methods for incorporation of the transgene are judged.



- **TRANSGENIC CATTLE**
  - Transgenic cows are genetically modified (GM) cows.
  - They have an extra gene or genes inserted into their DNA.
  - The extra gene may come from the same species or from a different species.
  - First, the gene for the desired product is identified and sequenced.
  - Then a gene construct containing this desired gene is created using DNA cloning, restriction enzyme digests and ligation.
  - The gene construct is then introduced into female bovine (cow) cells by transfection.
  - Transgenic bovine cells are selected and fused with bovine oocytes that have had all of their chromosomes removed.
  - Once fused with the oocyte, the transgenic cell's chromosomes are reprogrammed to direct development into an embryo, which can be implanted into a recipient cow.
  - After a 9-month gestation period, a female calf is born. She will only express the transgene in her milk during lactation after her first calf is born.
  - This is because expression of the transgene is controlled by a promoter specific to lactating mammary cells.



HUMAN GENE THERAPY – IN VIVO AND EX VIVO GENE THERAPY

Introduction

Gene therapy is the use of genes to treat disease. It represents a quantum leap in our approach to the treatment of human disease and will have a significant effect on medicine over the next ten years. William French Anderson, Michael Biase, and Ken Culver performed the first successful gene therapy on a human in 1990.

Concept of Gene Therapy

- The term gene therapy originally referred to proposed treatments of genetic disorders that would involve replacing a defective gene with its normal counterpart

- Current usage of the term now extends to include all treatments in which there is an introduction of genetic material into body cells to treat a variety of diseases.

Gene therapy utilizes two theoretically possible approaches:

1) **Somatic gene therapy** entails the transfer of a gene or genes into body cells other than germ (egg or sperm) cells with effect only on the patient.
    - The new genetic material cannot be passed on to offspring.
    - Examples of Somatic gene therapy have already proven to be clinically effective.
    - The first successful treatments of adenosine deaminase deficiency took place in 1990 in 1991 with two patients aged 4 and 11. Both are thriving with continuing treatment.
    - The first successful treatment of familial hypercholesterolemia, a genetic condition, which affects the livers regulation of cholestrols in the blood, took place in 1992 of a 29-year-old woman.
    - Her improvement was stable for the 18 months of the study and liver biopsy demonstrated activity of the inserted gene and no discernible abnormalities.
    - Five patients have been treated as of 1994.
    - Current research involving Somatic gene therapy is focusing on a number of areas.
    - Clinical trials are being performed on a treatment for cystic fibrosis, a chronic genetic disorder.
2) **Germline gene therapy** would involve the genetic modification of germ cells.

- Therapy would change the genetic make up of the egg or sperm of an individual and would be carried on to future generations.
- This would offer the possibility of removing an inherited disorder from a family line forever.
- This could be achieved by other methods, such as, at present, diagnosis when there is a known risk before embryo implantation during IVF.
- Germ line therapy is a remote prospect and general opinion is strongly negative; such therapy is currently illegal in most of Europe.
- Somatic and Germ line gene therapy raise different issues.
- Somatic gene therapy offers the prospect of effective treatment and cure for previously fatal disorders.
- Until now it has only been used experimentally for a small range of genetic disorders; even in these cases treatment is complex, difficult and success uncertain.

TYPES OF GENE THERAPY

Virtually all cells in the human body contain genes, making them potential targets for gene therapy. However, these cells can be divided into two major categories: somatic cells (most cells of the body) or cells of the germline (eggs or sperm). In theory it is possible to transform either somatic cells or germ cells.

- Gene therapy using germ line cells results in permanent changes that are passed down to subsequent generations.
- If done early in embryologic development, such as during preimplantation diagnosis and in vitro fertilization, the gene transfer could also occur in all cells of the developing embryo.
- The appeal of germ line gene therapy is its potential for offering a permanent therapeutic effect for all who inherit the target gene.

- Successful germ line therapies introduce the possibility of eliminating some diseases from a particular family, and ultimately from the population, forever.
- However, this also raises controversy. Some people view this type of therapy as unnatural, and liken it to "playing God."
- Others have concerns about the technical aspects.
- They worry that the genetic change propagated by germ line gene therapy may actually be deleterious and harmful, with the potential for unforeseen negative effects on future generations.
- Somatic cells are nonreproductive.
- Somatic cell therapy is viewed as a more conservative, safer approach because it affects only the targeted cells in the patient, and is not passed on to future generations.
- In other words, the therapeutic effect ends with the individual who receives the therapy.
- Transporting the gene to the target cells or tissue is also problematic.
- somatic cell gene therapy is appropriate and acceptable for many disorders, including cystic fibrosis, muscular dystrophy, cancer, and certain infectious diseases.
- Clinicians can even perform this therapy in utero, potentially correcting or treating a life-threatening disorder that may significantly impair a baby's health or development if not treated before birth.

I. Ex vivo gene therapy:

- This involves the transfer of genes in cultured cells (e.g., bone marrow cells) which are then reintroduced into the patient.

- The ex vivo gene therapy can be applied to only selected tissues (e.g., bone marrow) whose cells can be cultured in the laboratory.

- The technique of ex vivo gene therapy involves the following steps

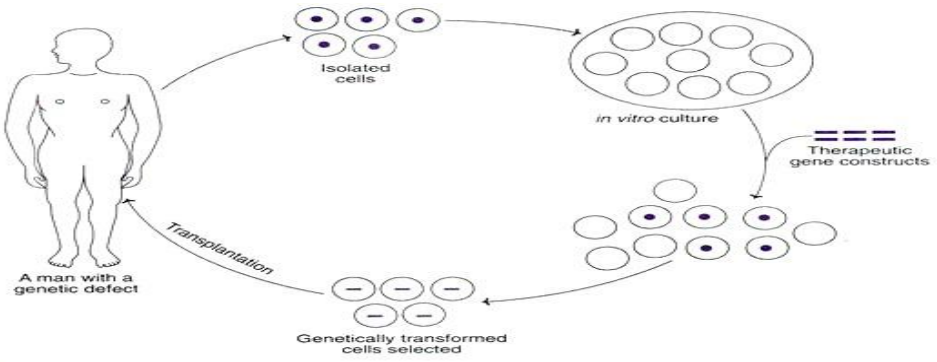


Fig. 13.2 : The procedure for ex vivo gene therapy.

Isolate cells with genetic defect from a patient.

- Grow the cells in culture.
- Introduce the therapeutic gene to correct gene defect.
- Select the genetically corrected cells (stable trans-formants) and grow.
- Transplant the modified cells to the patient.

II. In vivo gene therapy:

- The direct delivery of genes into the cells of a particular tissue is referred to as in vivo gene therapy.

- The direct delivery of the therapeutic gene (DNA) into the target cells of a particular tissue of a patient constitutes in vivo gene therapy .

- Many tissues are the potential candidates for this approach.

- These include liver, muscle, skin, spleen, lung, brain and blood cells. Gene delivery can be carried out by viral or non- viral vector systems.

- The success of in vivo gene therapy mostly depends on the following parameters

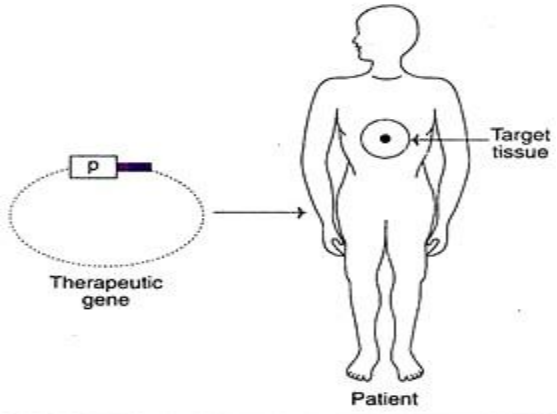


Fig. 13.6 : Diagrammatic representation of in vivo gene therapy. (p-Promoter gene specific for therapeutic gene)

  - The efficiency of the uptake of the remedial (therapeutic) gene by the target cells.

  - Intracellular degradation of the gene and its uptake by nucleus.

  - The expression capability of the gene.

  - In vivo gene therapy with special reference to gene delivery systems (viral, non-viral) with suitable examples is described.

MOLECULAR DIAGNOSTICS FOR GENETIC DISEASES.

INTRODUCTION

Molecular diagnostics is a collection of techniques used to analyse biological markers in the genome and proteome,The individual's genetic

code and how their cells express their genes as proteins, by applying molecular biology to medical testing. The technique is used to diagnose and monitor disease, detect risk, and decide which therapies will work best for individual patients.

Development from research tools

- The industrialisation of molecular biology assay tools has made it practical to use them in clinics.
- Miniaturisation into a single handheld device can bring medical diagnostics into the clinic and into the office or home.
- The clinical laboratory requires high standards of reliability; diagnostics may require accreditation or fall under medical device regulations
- As of 2011, some US clinical laboratories nevertheless used assays sold for "research use only".
- Automation and sample barcoding maximise throughput and reduce the possibility of error or contamination during manual handling and results reporting.
- Single devices to do the assay from beginning to end are now available.

Assays

- Molecular diagnostics uses in vitro biological assays such as PCR-ELISA or Fluorescence in situ hybridization.
- The assay detects a molecule, often in low concentrations, that is a marker of disease or risk in a sample taken from a patient.

- Preservation of the sample before analysis is critical. Manual handling should be minimised.
- The fragile RNA molecule poses certain challenges.
- As part of the cellular process of expressing genes as proteins, it offers a measure of gene expression but it is vulnerable to hydrolysis and breakdown by ever-present RNAse enzymes.
- Samples can be snap-frozen in liquid nitrogen or incubated in preservation agents.
- Because molecular diagnostics methods can detect sensitive markers, these tests are less intrusive than a traditional biopsy.
- For example, because cell-free nucleic acids exist in human plasma, a simple blood sample can be enough to sample genetic information from tumours, transplants or an unborn fetus.
- Based on nucleic acids detection use polymerase chain reaction (PCR) to vastly increase the number of nucleic acid molecules, thereby amplifying the target sequence(s) in the patient sample.
- PCR is a method that a template DNA is amplified using synthetic primers, a DNA polymerase, and dNTPs.
- The mixture is cycled between at least 2 temperatures: a high temperature for denaturing double-stranded
- DNA into single-stranded molecules and a low temperature for the primer to hybridize to the template and for the polymerase to extend the primer.

- Each temperature cycle theoretically doubles the quantity of target sequence.
- Detection of sequence variations using PCR typically involves the design and use oligonucleotide reagents that amplify the variant of interest more efficiently than wildtype sequence.
- PCR is currently the most widely used method for detection of DNA sequences.
- The detection of the marker might use real time PCR, direct sequencing, ,
- microarray chips—prefabricated chips that test many markers at once, or MALDI-TO
- The same principle applies to the proteome and the genome.
- High-throughput protein arrays can use complementary DNA or antibodies to bind and hence can detect many different proteins in parallel.

BIOSAFETY AND BIOETHICS.

INTRODUCTION

Biosafety is the prevention of large-scale loss of biological integrity, focusing both on ecology and human health. These prevention mechanisms include conduction of regular reviews of the biosafety in laboratory settings, as well as strict guidelines to follow. Biosafety is used to protect from harmful incidents.

- The international Cartagena Protocol on Biosafety deals primarily with the agricultural definition but many advocacy groups seek to expand it to include post-genetic threats
- Biosafety in agriculture, chemistry, medicine, exobiology and beyond will likely require the application of the precautionary principle.
- When biological warfare or new, currently hypothetical, threats (i.e., robots, new artificial bacteria) are considered, biosafety precautions are generally not sufficient.
- Biosafety level refers to the stringency of biocontainment precautions deemed necessary by the Centers for Disease Control and Prevention (CDC) for laboratory work with infectious materials.

Biosafety is related to several fields:

- In ecology (referring to imported life forms from beyond ecoregion borders),
- In agriculture (reducing the risk of alien viral or transgenic genes, genetic engineering or prions such as BSE/"MadCow", reducing the risk of food bacterial contamination)
- In medicine (referring to organs or tissues from biological origin, or genetic therapy products, virus; levels of lab containment protocols measured as 1, 2, 3, 4 in rising order of danger),
- In chemistry (i.e., nitrates in water, PCB levels affecting fertility)
- In exobiology (i.e., NASA's policy for containing alien microbes that may exist on space samples. See planetary protection and interplanetary contamination), and
- In synthetic biology (referring to the risks associated with this type of lab practice)

- Chemical hazards typically found in laboratory settings include carcinogens, toxins, irritants, corrosives, and sensitizers.
- Biological hazards include viruses, bacteria, fungi, prions, and biologically-derived toxins, which may be present in body fluids and tissue, cell culture specimens, and laboratory animals.
- Routes of exposure for chemical and biological hazards include inhalation, ingestion, skin contact, and eye contact
- A complete understanding of experimental risks associated with synthetic biology is helping to enforce the knowledge and effectiveness of biosafety.
- With the potential future creation of man-made unicellular organisms, some are beginning to consider the effect that these organisms will have on biomass already present.
- Scientists estimate that within the next few decades, organism design will be sophisticated enough to accomplish tasks such as creating biofuels and lowering the levels of harmful substances in the atmosphere.
- Scientist that favor the development of synthetic biology claim that the use of biosafety mechanisms such as suicide genes and nutrient dependencies will ensure the organisms cannot survive outside of the lab

RISK GROUPS OF BIOSAFETY

- Risk Group 1: (no or low individual and community risk) A microorganism that is unlikely to cause human or animal disease.[12]

- Risk Group 2 : (moderate individual risk, low community risk) A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.[10]
- Risk Group 3 : (high individual risk, low community risk) A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.[10]
- Risk Group 4 : (high individual and community risk) A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available

BIOETHICS

INTRODUCTION

Bioethics is the study of the ethical issues emerging from advances in biology and medicine. It is also moral discernment as it relates to medical policy and practice. Bioethics are concerned with the ethical questions that arise in the relationships among life sciences, biotechnology, medicine and medical ethics, politics, law, theology and philosophy. It includes the study of values relating to primary care and other branches of medicine ("the ethics of the ordinary").

principles

The field of bioethics has addressed a broad swathe of human inquiry; ranging from debates over the boundaries of life

(e.g. abortion, euthanasia), surrogacy, the allocation of scarce health care resources (e.g. organ donation, health care rationing), to the right to refuse medical care for religious or cultural reasons.

Bioethicists often disagree among themselves over the precise limits of their discipline, debating whether the field should concern itself with the ethical evaluation of all questions involving biology and medicine, or only a subset of these questions.

Some bioethicists would narrow ethical evaluation only to the morality of medical treatments or technological innovations, and the timing of medical treatment of humans.

Others would broaden the scope of ethical evaluation to include the morality of all actions that might help or harm organisms capable of feeling fear.

Medicine

One of the first areas addressed by modern bioethicists was that of human experimentation.

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was initially established in 1974 to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects.

The fundamental principles announced in the Belmont Report (1979) namely, respect for persons, beneficence and justice have influenced the thinking of bioethicists across a wide range of issues.

Others have added non-maleficence, human dignity, and the sanctity of life to this list of cardinal values.

Education

Bioethics is taught in courses at the undergraduate and graduate level in different academic disciplines or programs, such as Philosophy, Medicine, Law, Social Sciences.

It has become a requirement for professional accreditation in many health professional programs (Medicine, Nursing, Rehabilitation), to have obligatory training in ethics (e.g., professional ethics, medical ethics, clinical ethics, nursing ethics).

Interest in the field and professional opportunities have led to the development of dedicated programs with concentrations in Bioethics

INTELLECTUAL PROPERTY RIGHTS

INTRODUCTION

Intellectual property is a category of property that includes intangible creations of the human intellect. There are many types of intellectual property, and some countries recognize more than others. The most well-known types are copyrights, patents, trademarks, and trade secrets.

PATENTS

A **patent** is a right granted to an inventor by the federal government that permits the inventor to exclude others from making, selling or using the invention for a period of time. The **patent** system is designed to encourage inventions that are unique and useful to society.

There are three types of patents:

1) **Utility patents** may be granted to anyone who invents or discovers any new and useful process, machine, article of manufacture, or composition of matter, or any new and useful improvement thereof;
2) **Design patents** may be granted to anyone who invents a new, original, and ornamental design for an article of manufacture; and
3) **Plant patents** may be granted to anyone who invents or discovers and asexually reproduces any distinct and new variety of plant.

COPY RIGHT AND NEIGHBORING RIGHTS

Copyright is a form of protection provided to the authors of "original works of authorship" including literary, dramatic, musical, artistic, and certain other intellectual works, both published and unpublished.

The 1976 Copyright Act generally gives the owner of copyright the exclusive right to reproduce the copyrighted work, to prepare derivative works, to distribute copies or phonorecords of the copyrighted work, to perform the copyrighted work publicly, or to display the copyrighted work publicly.

The copyright protects the form of expression rather than the subject matter of the writing

.For example, a description of a machine could be copyrighted, but this would only prevent others from copying the description

It would not prevent others from writing a description of their own or from making and using the machine.

Copyrights are registered by the Copyright Office of the Library of Congress.

PATENTS FOR INVENTION, -

Provisional Patent Application:

- A provisional patent application (PPA) is a way of claiming that you are the first to invent your invention.
- It establishes a “priority date” and serves as a reservation that secures your rights for up to one year.
- Within that year, you can file a non-provisional patent application to maintain your priority date and proceed to seeking an issued patent.
- Patent examiners do not review a PPA and a PPA cannot be enforced to stop someone from copying your invention.
- PPAs are also not published so no one knows what you are likely to claim.
- When you’ve filed a PPA you can say your invention is “patent pending” and that serves as a warning that you are in the process of getting a patent that could be enforced in the future.
- PPAs are less formal and cost much less to file than non provisional patent applications.
- They are good for doing market research to determine whether or not you want to move forward with your invention idea.

Non-Provisional Patent

- When people say that something is “patented” they are referring to a non-provisional patent that has been issued with claims that can be enforced.

- A non-provisional patent application goes through an examination process and is published so the public can see it while it is still pending.

How Much Does a Patent Cost

- The cost for a PPA can be less than $100 if you write file it yourself and up to $2000+ if you have it written and filed by an attorney.
- For a simple invention, the cost for a non-provisional utility patent, from writing and filing through issuance, can run between between $5,000 to $15,000 if you work with a professional.
- Filed through an attorney a design patent costs between $1500 and $3000.
- The discussion above refers to patents in the USA.

Patent Guidelines

1. Confidentially confirm and research your idea by talking to family and friends. Look for competitive products and patents online. Consider Invention City's Brutally Honest Review.
2. File a provisional patent application, create a presentation and do a market research survey.
3. Develop and refine your concept with a working prototype.
4. Get advice from a reputable patent lawyer or agent.
5. File a non-provisional patent.

Learn About Invention Protection

- Confidentiality Agreement Review - Invention City Article. Learn about the most basic tool of invention protection. Examples provided.
- The Disclosure Dilemma - Invention City Article.
- Overview of Patent Law - Brief 1-page summary of patent law from Cornell Law School.
- United States Patent and Trademark Office - The USPTO web site is a must visit for every inventor.
- Patent It Yourself - David Pressman's classic belongs on every inventor's bookshelf. It provides an in-depth understanding of the patent process and will help you make intelligent decisions regardless of whether or not you actually do it yourself. The cost is $39.96. The value is easily twice that much.

DRAFTINGAND FILING A PATENT APPLICATION,

Specification [Description and Claims]

The following order of arrangement should be observed in framing the application:

(a) Application transmittal form

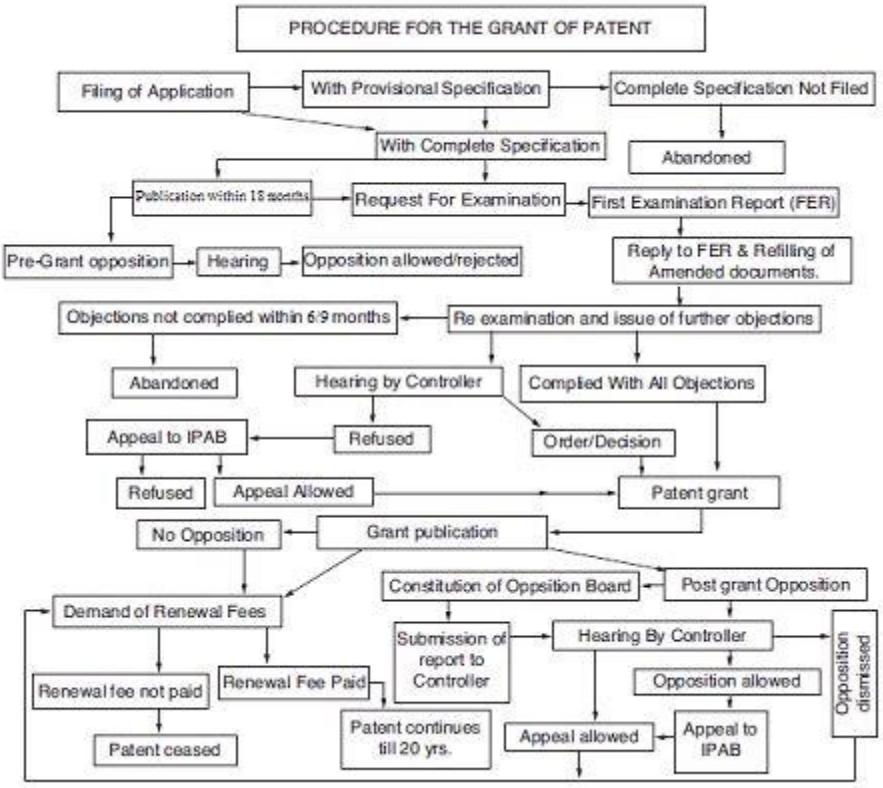
(b) Fee transmittal form

(c) Application Data Sheet

(d) Specification

(e) Drawings

(f) Executed Oath or declaration



The specification should have the following sections, in order:

(1) Title of the Invention

(2) Cross Reference to related applications (if any). (Related applications may be listed on an application data sheet, either instead of or together with being listed in the specification.)

(3) Statement of federally sponsored research or development (if any)

(4) The names of the parties to a joint research agreement if the claimed invention was made as a result of activities within the scope of a joint research agreement

(5) Reference to a ”Sequence Listing,” a table, or a computer program listing appendix submitted on a compact disc and an incorporation by reference of

the material on the compact disc. The total number of compact disc including duplicates and the files on each compact disc shall be specified.

(6) Background of the Invention

(7) Brief Summary of the Invention

(8) Brief description of the several views of the drawing (if any)

(9) Detailed Description of the Invention

(10) A claim or claims

(11) Abstract of the disclosure

(12) Sequence listing (if any)

EXPLOITATION OF PATENTED INVENTION.

- A patent grants exclusive rights to an inventor for a fixed period of time in exchange for the public disclosure of that invention.
- A patent is an exclusionary right which gives the owner the right to exclude others from making use of or infringing the patent in any way.
- However, that does not necessarily give the owner of the patented invention the right to patent exploitation.
- There are critics of patents, and this has resulted in the formation of groups who oppose patents in general, or specific types of patents.
- One criticism that is often heard is that a patent only gives a negative right to its owner, allowing him to prevent competitors from using or exploiting his inventions.
- A patent is looked upon as any other type of property, and so it may be disposed of like any other property right – it may be sold, licensed, mortgaged, assigned or transferred, given away, or simply abandoned.

- A patent may be sold by the inventor to another party, or it may be licensed for other people's use with a license agreement.
- In such an agreement the holder of the patent holds on to all rights of ownership and the licensee has the right to use or exploit the invention in return for paying a fee.
- Eligible patent protection is governed by the Patents Act of 1978, which governs Patent Law in South Africa.
- When a patent is granted, it provides the patentee with the exclusive right to stop all others from exploiting the invention for the life of the patent, which in South Africa is 20 years from the date of the first patent application being filed.
- All patent rights are territorial, which means that a South African patent is only valid in South Africa.
- If the inventor wishes to be protected outside South Africa, he or she must apply for patent rights in each of the countries where protection is required.

INDIAN PATENT LAWS.

- Procedure for Grant of a Patent in India
- After filing the application for the grant of patent, a request for examination is required to be made for examination of the application in the Indian Patent Office within 48 months from the date of priority of the application or from the date of filing of the application.
- After the first examination report is issued, the applicant is given an opportunity to meet the objections raised in the report.

- The applicant has to comply with the requirements within 6 months from the issuance of the first examination report which may be extended for further 3 months on the request of the applicant.
- If the requirements of the first examination report are not complied with within the prescribed period of 9 ;months, then the application is treated to have been abandoned by the applicant.
- After the removal of objections and compliance of requirements, the patent is granted and notified in the Patent Office Journal.
- The process of the grant of patent in India can also be understood from the following flow chart: