MODULE - 3
BIOTECHNOLOGY AND IPR

- **BASICS**

→ **Genetic Material** → Responsible for [transfer of character] from one generation to other. (attributes — weight, skin, voice)

→ **RNA** → [Single helical] [Adenine, Uracil, Cytosine, Guanine]

→ **Virus** → Border of living and non-living [dead outside living cell]

→ [Inside living system → active] → b/c it utilizes the host machinery. (multiplies only living cells)

→ Composed of a [protein Code], inside which genetic material is present. (either RNA or DNA)

→ No [Enzymes → bio catalysts]

→ Virus having RNA (RetroVirus) e.g. HIV, Corona virus

→ **DNA** → Double helical

operates on [Principle of complementarity] [Adenine (A), Thiamine (T), Cytosine (C), Guanine (G)] Nitrogenous Bases

makes [Base Pair] [A → T, C → G]

→ **Genome** → Organism's complete set of [genetic instructions.]

→ **Genome Sequencing** → [determining DNA sequence of genome.] → [arrangement of Base pairs]

e.g. Genome of cobra → [to make anti-venom]

" " wheat → [to determine strength and weakness of wheat crop.]

→ **Gene** → [That part of DNA which determines the character, by determining protein synthesis]

→ Role of Gene in Protein synthesis → [Carry info of arrangement of Amino Acid]

Gene → [Information of arrangement of amino acid] → DNA → [mRNA] → [tRNA] [mobilizes Amino Acid.]

[Ribosomal RNA] (Binds Amino Acid) → [makes Protein] → [is a polymer]

[Amino Acid] → [Any amino acid can come in any combination to form protein.]

→ **Grey Matter** → [Upper part of Brain] → determines Quality of Brain.

↳ Thick → G

↳ Thin → g

GG → extraordinary

Gg → average

gg → weak

→ **Chromosomes** → DNA wraps around protein to make thread like structure chromosomes

→ Each species → [fixed no.]

→ [46] → humans (~~Pair - 23~~)

→ **Cell** → [Somatic cell / Vegetative cell] (2x)

→ No role in reproduction

→ Complete set of chromosomes

→ humans → 46 chromosome

e.g. [Skin cell], [liver cell etc.]

[Gamete] (x)

→ Reproductive cells

→ Half of somatic cell

→ [humans → 23]

e.g. male → sperm

female → ovum

→ **Reproduction** → [Sexual]

Role of sperm is mandatory

[Asexual]

No role for sperm.

● [CLONING] Science of making "exact replica" of an organism.

→ [DOLLY - sheep] → Cloned by using [Somatic Cell Nuclear Transfer]

→ [Somatic Cell Nuclear Transfer] → [Somatic cell of a sheep] was taken.

→ An [ovum of sheep] also taken.

→ Nucleus of ovum was removed.

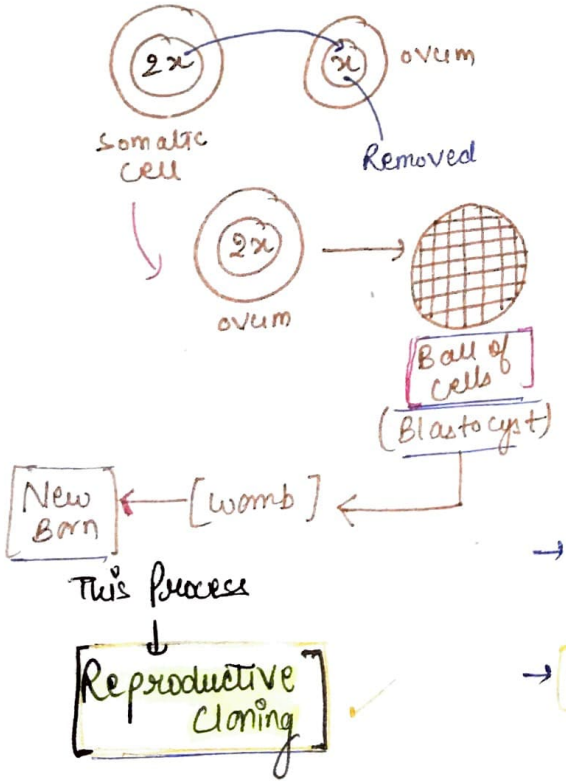
→ Nuclear cell of somatic cell was transferred to ovum.

→ ovum fertilised → giving rise to ~~4~~ 230-300 cells.

→ Blastocyst (Ball of cells)

→ Transferred to womb of surrogate mother to develop normally and naturally

→ Newborn [Exactly similar b/c all chromosome from one sheep]



This Process

↓

[Reproductive Cloning]

→ But at age of 5 Dolly developed every possible health problem

→ had to give euthanasia

→ [GARIMA 1, 2] → Cloned by National Dairy Research Institute, Karnal

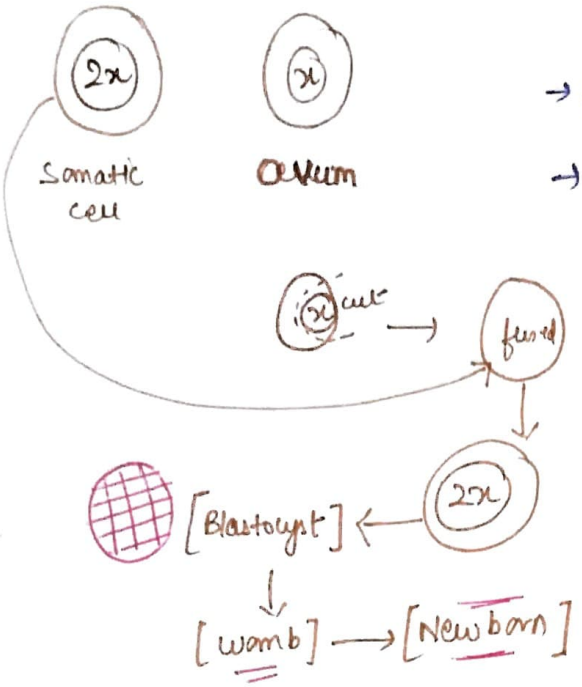
NDRA, Karnal

→ By using [Hand Guided Cloning method.]

→ [Hand Guided Cloning Method] → Somatic cell and ovum.

→ Nucleus of ovum is shifted in the periphery of cell.

→ That part having nucleus of ovum is cut
→ Entire somatic cell is merged (fused) into ovum.
→ forms Blastocyst → transferred into womb
↓
[New Born]



Pros of Cloning → Maintain good DNA in animal reproduction
→ Genetically modified animals
→ can clone endangered species
→ Can clone cattle for good dairy products

Cons of cloning → Insufficient
→ Clones die mysteriously
→ High costs
→ Morally wrong
→ Can lead to human cloning

- **HUMAN CLONING** → There is a complete Ban on human cloning.

Reasons of BAN
1. clone will die mysteriously
2. Against Bioethics (human body not for satisfying scientific fantasies)
3. what will be the relation of clone to cell donor?
4. Will he have legal Recourse?
5. People may do → organ trade
6. Terrorist organization → may raise armies.

- **GENETIC MODIFICATION** → Adding / Removing any pair of DNA
  → Transfer of gene within same species
  → Hemophilia → blood doesn't clot normally
  → can be cured by gene modification
  → Transfer gene of healthy person in gene of Hemophilic

- **TRANSGENICS** → Transgenic organism → developed by transferring a gene from one species to another.
  → plant / animal
  e.g. → liger (lion/tiger); spider Goat, BT cotton; BT Brinjal etc.

- **TRANSGENIC CROPS** → Purpose → make crop → Pest resistant, salt, drought resistant, water resistant, ↑ shelf life, ↑ nutrient, pharmaceutical substances.

→ **BT Cotton**

→ BT → Bacteria → Bacillus Thuringiensis (soil bacteria) → toxin (Crystal Protein) Kills pest

[→ ↳ sprayed over cotton crop → pest eats → toxin enters gut
→ becomes active due to alkaline condition → Pest dies.]

But in BT cotton → A gene → CRY1Ac transfer into cotton cell.

[Pest Resistant] → [cotton plant capable of producing toxin] [recombinant DNA tech]

[2002] → BT cotton was introduced by Monsanto - Mahyco Biotech ltd. (MNC) (Maharashtra Hybrid seeds Co.)

→ only ~~crop~~ Transgenic crop in India
→ productivity ↑; [2nd → 2nd largest producer of cotton.]
→ Total area under cultivation → 95% BT cotton,
→ BT cotton / GM crop India 5th largest (in terms of Area) (MH, GUJ, Telangana)

3 VARIETIES OF BT COTTON

BOLLGARD I
2002
→ one gene from BT
→ Pest Resistant

BOLLGARD II
2006
→ Two genes from BT
→ Pest Resistant

BOLLGARD III
→ Pest Resistant
+
Herbicide Tolerant
A.K.A [Roundup Ready Flex]
[Not permitted in India] b/c
[Glyphosate] [carcinogenic]

Effective against - Bollworm (Lepidopteran)
[American Bollworm; Pink Bollworm; Spotted Bollworm.]

[2009-10] → Environment Minister, Mr. Jairam Ramesh
→ BT Brinjal → not given permission
grounds → health and env. safety.
→ Red spots on skin, skin cancer → persons working with BT crops
→ Cattle fed on BT-Crop died.
→ All GM crops were banned → later revoked.

[2012] → Parliamentary Committee on Agriculture and Food security.
→ India should stop cultivation of BT cotton → ~~the it has become~~ because pest resistant; [human health concerns]
→ Govt. refused to acknowledge → PIL in SC → appointed Technical Expert committee.

• Recommendation by Technical Expert Committee

① No permission to [Edible GM crops] for next 10 years.
Bl c, Biosafety not proved
Global Benchmark for edible GM crop
- Processing; GM labelling. ×

[2006] → [Food Safety Standards Act] FSSAI
only processed GM food allowed for human consumption
- 2012 → [Ministry of Consumer Affairs] mandatory GM labelling from 1 Jan 2013
→ under C.P. Act 1986
→ Legal metrology (packaged commodities) Rules

GM labelling Debate → Mandatory or Voluntary

Mandatory:
- cost of processing ↑ = cost of product ↑
- absence of food processing industry - labelling uphill task
- Food sector decentralised, unorganised

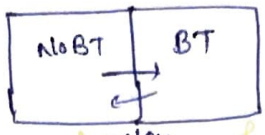
Voluntary:
- commercial aspect might be addressed
- human health will suffer.

- FSSAI → Threshold of GM labelling - 1%

Centre for Science & Env. → found imported food items without GM labelling.

(2) No permission to herbicide tolerant variety (Bollgard III)
→ b/c leads to emergence of superweeds (weeds also become herbicide tolerant)

(3) Crops (centre of origin INDIA) → GM variety not be adopted.
→ legal - CARTAGENA Protocol on biosafety
→ technical → might lead to elimination of food crop
→ endanger food security



pollen transfer → lead to elimination of food crop.

[2016] → 75% BT cotton destroyed → white fly pest
→ MMBL → never promised [resistance against this type]

[2017] → [Yavatmal, Mah.] → [farmers died] → spraying pesticide on BT cotton
b/c BT cotton → became fertile

[2018] → MS Swaminathan, KC Kesvan → Research Paper
→ BT cotton failed to provide sustainable livelihood to farmers
(against abiotic factors)

Bt cotton adoption showed benefits: study

'There has been reduction in insecticide use and its impact on human health'

VIKAS VASUDEVA
CHANDIGARH

Amid the perpetual debate surrounding Bt cotton's positive and negative impacts, a recent study titled – 'Long-term impact of Bt cotton: An empirical evidence from North India' – has said its adoption in Punjab in the past over a decade has resulted in net economic and environmental benefits.

The research was funded by the Agricultural Extension Division of the Indian Council of Agricultural Research under extramural project "Impact evaluation of integrated pest management technologies". The study was jointly done by the Punjab Agricultural University at Ludhiana, the Sher-e-Kashmir University of Agricultural Sciences and Technology in Jammu (SKUAST) and the Noida-based Amity University, and has been recently published in the *Journal of Cleaner Production*.

'Stable cotton yield'

"Since the commercialisation of Bt cotton, there has been reduction in insecticide use by volume and applications, decline in environmental and human health impact associated with insecticide use, more so with the reduction in the use of highly hazardous and riskiest insecticides, and reduction in the expenses associated with insecticide use. Also, cotton yields in the past 13 years have been stable, the only exception being 2015. Yet over the past 13 years, pesticide use has gradually increased in Bt hybrids and reduced in non-Bt varieties, primarily driven by the use of fungicide, which was not applied in cotton in 2003 and 2004.

"Akin to the discovery of synthetic pesticides in the 1940s, which was proclaimed as 'silver bullet technology' by entomologists, the complete reliance on Bt cotton without incorporating it into the integrated pest management (IPM) system led to outbreak of whitefly in northern India and pink bollworm in western India in 2015; thus, resistance to Bt cotton is yet to become a significant problem. Compatibility of Bt with IPM is not a given when we have weaker institutional setting with ad hoc IPM system and the contrarian view that Bt cotton has been a failure in India, in this case Punjab, lacks empirical evidence," professor Rajinder Peshin of SKUAST told *The Hindu*.

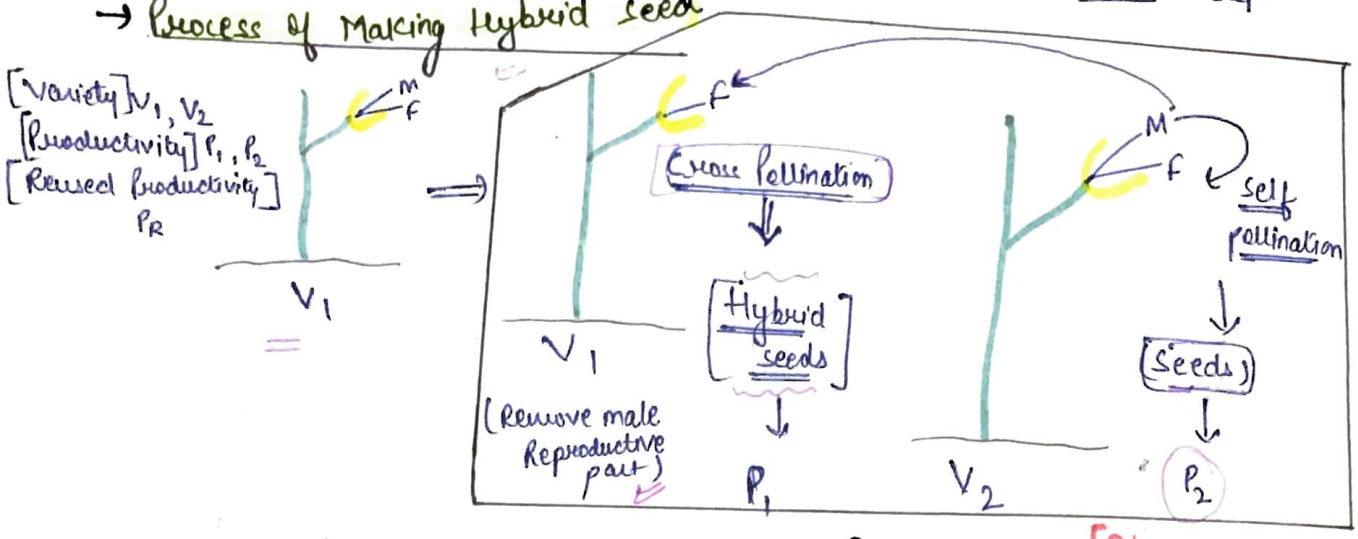
Bt (Bacillus thuringiensis) cotton has been commercially grown in India for the past 19 years. In Punjab, Bt cotton was released for cultivation in 2005.

→ [GM-MUSTARD] → AKA → DMH-11 (Dhara Mustard Hybrid-11)

→ by Deepak Pental

→ [purpose] → increase productivity by developing hybrid variety through [cross pollination] of two varieties of same crop.

→ Process of Making Hybrid seed

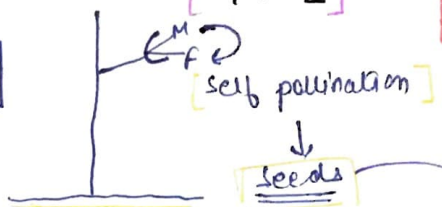


→ Hybrid seeds → [packed & sold to farmer] → [Farmer will sow them]

$P_1 = 1.25 P_2$

$[P_1 > P_2]$

[After making hybrid seed V_2 → Killed]



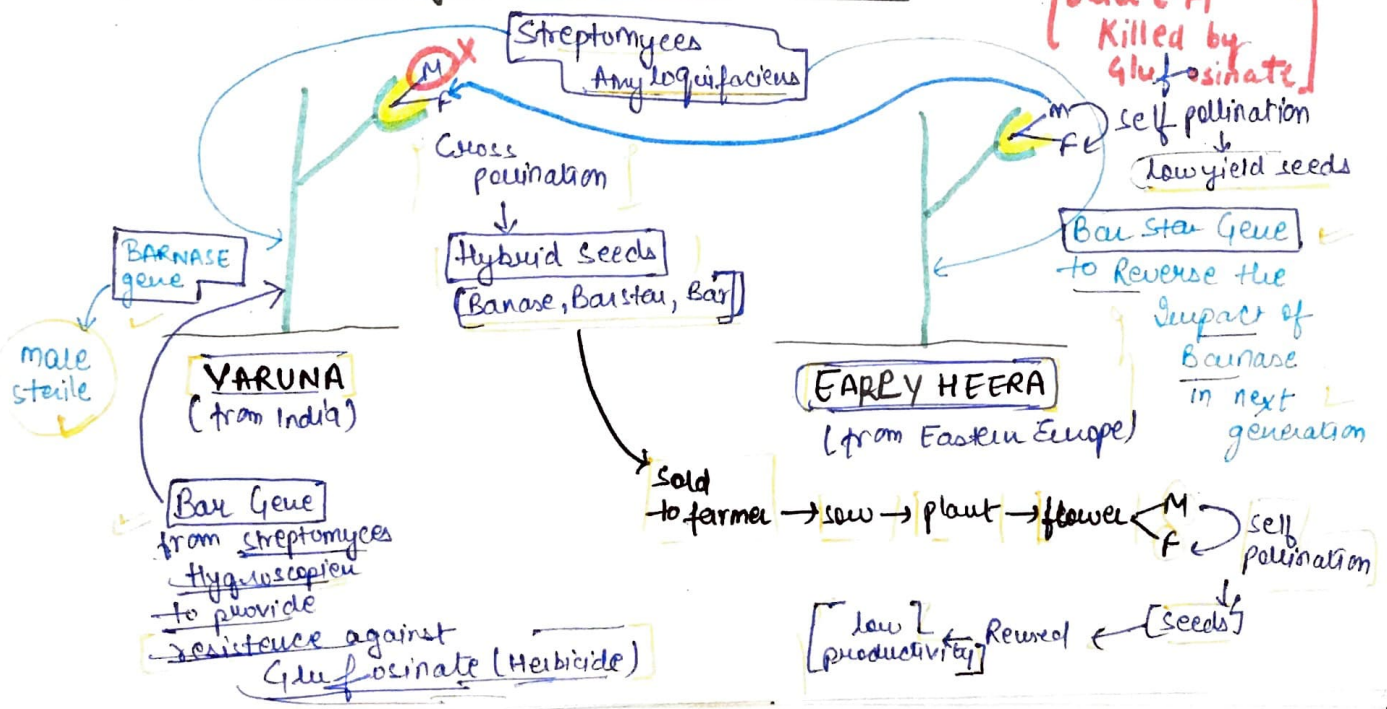
If reused then lead to low Productivity than P_1 → P_R

→ Hybrid seeds if reused are low in productivity.

∴ Farmer has to buy fresh seeds every year to maintain high yield.

$[P_1 > P_R]$

→ Process of Making GM-Mustard (DMH-11)



→ Issues with GM-MUSTARD

① Edible GM crop.
→ Edible GM crops are not yet allowed in India b/c of processing and labelling issues.
→ Biosafety concerns.

② Herbicide Tolerant
→ It will result to superweeds
→ Technical Committee by SC recommended → Not to allow herbicide tolerant variety

③ Genes used in production are Patented by BAYER, Germany but project is public funded
→ Under what condition Bayer has permitted the use of Barnase, Bar Gene, Barstar?
→ Who will control IPR?

④ BAYER has patented Glufosinate, which only can be used as herbicide and no other
→ Consumption of GM Mustard will increase the sale of Glufosinate exponentially.

⑤ Biosafety aspects of Glufosinate missing
→ Biosafety board has explained safety of the three genes but missed aspect of Glufosinate

⑥ Critics → gone too far suggesting → Use of terminator technology (there is Not correct as it is universally banned)

Supporters argue → Ind. → Importing → edible oil from Canada whose crop is transgenic → no example of health Hazard
(But the truth is → Canada have food processing infrastructure that we don't)

⑦ Europe advertises the use of the 3 genes which it itself has completely banned.
→ WHY?
→ Eased out of the market b/c of reluctance of buyers to buy GM labelled food.

NOT ALLOWED IN INDIA B/C OF THE ABOVE ISSUES

→ [GOLDEN RICE] → [Biofortified crop] (increased level of Nutrients)
→ By International Rice Research Institute,
→ purpose → To enhance nutrients → by synthesis of Beta Carotene in grain
→ which forms Vitamin A
Yellow → turns grain Yellow
→ Hence the name. Golden Rice

→ [RICE] → Leaves → Beta Carotene synthesised
→ Grain → No Beta Carotene

[Earlier GOLDEN RICE I was developed]

Daffodil — 1 Gene → RICE → Synthesis of Beta Carotene took place
Erwinia Urdovera
Pantonea Ananatis — 1 gene → RICE
but [only 1.6 microgram/gm.] yielded
very low → Rejected

GOLDEN RICE II

Maize — gene → RICE → Beta Carotene [37 microgram/gm]
Erwinia Urdovera — 1 gene → RICE
(Pantonea Ananatis)
→ Permitted in Bangladesh (first to permit), along with BT Brinjal

---

→ [GM-RICE] → By MS Swaminathan Research Foundation
→ to make crop climate change resilient
→ To develop Rice which can grow in saline conditions

Mangroove Plant (in Marshy area) — gene → RICE → capability to survive in saline conditions

---

→ [TRANSGENIC RICE] By → Lucknow Based CSIR lab → National Botanical Research Institute
→ To reduce arsenic content

Westerdykella aurantiaca (fungus) — gene → RICE
(WAARS-M)
aka Arsenic Methyl Transferase
This gene converts Arsenic into Volatile organic compound
→ Expelled from leaves
→ makes Rice crop Arsenic free

→ [BT BRINJAL] → Effective against fruit and shoot Borer (pest responsible for holes in Brinjal)
aka Leucinodes Orbonalis

↓

[CATEGORY I] → By [Monsanto Mahyco]

[[CRY1AC] gene from BT ⟶ [BRINJAL]]

- Banned by Ministry of Environment and Forest on following grounds—
  1. Impact on Human health & Bio diversity
  2. ∪ ∪ local variety
  3. Biopiracy

[CATEGORY II] → BSS 793 and JANAK
→ By National Research Center for plant Biotechnology under Indian Council for agricultural Research
+
[Beej Sheetal ltd, Maharashtra]

[CRYFa1 gene from BT ⟶ BRINJAL]

Permission for field trials in WB, ODISHA, BIHAR, JHARKHAND, MP, Chattisgarh, TN, KARNATAKA

- Reasons for concern
  1. GM labelling will not be possible
  2. Pest will became Resistant → b/c [Monophagus (only live on Brinjal) → overexposure ↓ Resistence]
  3. Loss to Bangladesh farmers
     → Initially BT Brinjal able to reduce damage by 95%. → overproduction ↓ [prices went very low]

→ [GENETIC USE RESTRICTION TECHNOLOGY (GURT)] —

To prevent farmers from [re-use]

To ∪ patenting the seeds like India have (IPA, 1970 §3c, 3)

→ Protection of Plant Varieties and farmer Rights Act

↳ Right to seed (Use, [Re-use], sell, exchange etc)
Consume, exchange

To prevent this

[TERMINATOR SEED] by Delta & Pine Land (American Co.)

seed → sold to farmer → fertile
∪ → harvested → infertile.

→ Terminator seeds are fertile for only one generation.

- Banned by Convention on Biological Diversity (CBD) on following grounds :-

(1) Gene flow may result in situation where other vegetation will also be producing infertile seeds.

(2) Homogenisation of Agriculture → narrow gene pool

(3) Exploitation of farmer increase.

→ TRAITOR SEEDS → By UK based Zeneca ltd.

→ AKA → Dirty seeds / Addicted seed

→ To control expression of traits

→ Rat gene → plant → seeds → sold to farmer → sow → plant growth will be slowed down.

→ Restore the growth → farmer have to spray the chemical → also patented by Zeneca.

→ Argument → by breeder company → they will include multiple attributes in a single seed to activate a particular feature farmer have to spray specific Chemicals.

GM-RUBBER

World's first GM rubber sapling planted in Assam

Institute says it is tailored for the climate of the northeast

make freshnotes on GM Rubber

SPECIAL CORRESPONDENT
GUWAHATI

A Rubber Board research farm on the outskirts of Guwahati now sports the world's first genetically modified (GM) rubber plant tailored for the climatic conditions in the Northeast.

The GM rubber has additional copies of the gene MnSOD, or manganese-containing superoxide dismutase. Inserted in the plant

• INTELLECTUAL PROPERTY RIGHTS (IPR)

→ [legal] exclusive rights which are [transferrable], [intangible] in nature.
→ B/c of unique intellectual ability of individual/organisation
(created)

→ [PATENT] → To promote Innovation → Incentivise Technology → Economic Growth → B/c of technology export
→ [Monopoly for 20 years.]

→ All developed economies → {efforts of corporates towards innovation}
e.g. → US → more than 2% of GDP → [for Innovation]

• Condition for patent

① Novelty → always for innovation (~~FIT~~ [New])
② Must have industrial/commercial use
③ Non-obvious → not a modification of a preexisting product.

→ Under ministry of commerce → [Department of Industrial Policy and Promotion]

[Controller General of Patent and Trade Mark Office] → Delhi, Mumbai, Kolkata, Chennai

[Patent takes 5-7 years] → included in 20 year (monopoly period)

→ [TWO TYPES OF PATENT]

[PROCESS PATENT]

→ [INDIAN PATENT ACT, 1970]
→ 1970 → India decided
→ Medicine will get → [Process patent]
→ [Method used in making medicine]

Same med. can be made using diff. mechanism

→ To control prices of medicine

India → called "Pharmacy of Developing world" - By NGO Doctors without Borders
→ [60%] of world's ~~Generic~~ Generic Drugs
→ [Every 7th person in world uses Indian medicine.]

[PRODUCT PATENT]

→ WTO formed in 1995 → Process Patent was replaced with [Product Patent.]

[Monopoly to sale of med]
2000 → Developed countries given deadline
2005 → Developing " "

[CRITICISM] → Disincentivised the investment in R&D by Indian Pharma Co.'s

→ Pharmas like Pfizer, Merck & Co., Novartis, Sanofi — captured Indian pharma market.

→ [GENERIC MEDICINE] / [GENERIC DRUGS]

→ Name of Chemical of the medicine
→ Branded Generics are also available in market.

→ Required to fulfill following Norms.

- Must have same salt
- Must be equally effective
- Cannot use Brand Name
- Fillers / Binding agents should be different

→ Need of Generic Medicine / significance

- To achieve affordable and universal healthcare
  - acc. to National sample survey office (NSSO) :-
    - medical Trap of poverty
      - 39-94 million people fall below poverty line b/c of health care expenditure, every year.
    - Urban area — 72% of total healthcare expenditure is on buying medicines
    - Rural Areas — 68%
- → Govt have emphasized → Govt hospital Doctors should prescribe generic medicine
- → To Break nexus b/w Big Pharma companies and doctors.

Couldn't replace

→ Issues with Generic Drugs

- Absence of active pharmaceutical agent which was shown on wrapper.
- Actual Quantity much less than dose specified.
- Hygiene
  - Some pharma units
    - biological agents which can contaminate drug.
- Lack of Data Integrity
  - many serious Ques. regarding reliability of Information.
- Fixed Dose Combination
  - making one medicine by mixing other med.
    - sometimes very high
      - Antibiotic Resistance.

→ [COMPULSORY LISCENCE] → Patent suspended without consent of patent holder.

→ Domestic manufacturer asked to make that medicine available, under two conditions:—

↓ Price to be determined by govt.

↓ IPR holder should be paid royalty

→ Conditions for issuance of Compulsory Liscence

- U/s 84 of Indian Patent Act, 1970

(1) Unreasonable Prices or (2) Not able to meet the demands

or (3) Patent has not been worked upon in India. (no manufacture, no import)

- U/s 92 of IPA, 1970

(1) National health Emergency or (2) Request of some other country

e.g. Bayer → NEXAVER (Anticancer medicine)

Bayer patent → Cost of one month dose → (120 tablets) → 2,88,000 Rs

→ Unreasonable price → Patent suspended (U/S 84 IPA)

permission given to Nacto Pharmaceuticals

Price → ₹ 8,800

soft power.

Brazil → (HIV) → National health emergency → (patent suspended U/S 92 IPA)

↓ approached India for med. → Ranbaxy, Cipla

[FREE GENERIC DRUG POLICY -2012]

→ Govt. hospital doctor → mandatory prescription of Generic Drugs

→ If not → liscence cancel

→ Target to cover 52% population.

[PMJAY/PMBJY]

→ Target 3000 Jan Aushadhi stores all over India.

[TRIPS AGREEMENT] Plus

[Trade Related IPR]

→ Developed countries insisting developing countries → adopt same IPR as their policy → [Top priority to IPR]

→ Developing countries → [Refused to comply] → b/c it will hurt developmental process.

In case of health care TRIPS PLUS has 3 issues

① [DATA EXCLUSIVITY] → when a co. is looking to introduce a drug.

→ has to approach [Drug Controller]

↳ He will ask for data collected in form of [clinical trials]

→ clinical trial → [lengthy] → expensive [any incompetency at any stage] → [process restarts]

[INDIA] → Manufacturers of Generic Drugs → exempted from clinical trials

→ Tested on the basis of info. submitted by patent holder → for [Affordability & Availability]

No Data Exclusivity

[WTO exempted Developing Countries till 2030]

[USA, EUROPE] → Data Exclusivity exist

→ Manufacturer of medicine → can ask the drug controller → Not share info. with competitor for [Next 5 years] will continue even after Patent expires

Want same arrangement in INDIA → opposed b/c will hurt

[b/c they might invoke D.E in final year of patent]

[2007] S. Reddy Committee

↳

→ No Data exclusivity for allopathy

→ suggest " " [for traditional medo, agrochemicals.]

② [EXTENSION OF PATENT] → b/c Long time in issuing patent → loss in company → Recover damages

→ WTO exempted developing nations till 2030,

→ Extend the duration for Patent → 5 years (one time extension)

→ should be no change in original product

→ INDIA under pressure by [developed nations]. (Refused)

③ [EVERGREENING OF PATENT] A.K.A. Incremental Innovation.

→ Big Pharma companies use → to continue monopoly.

→ Develop salt → Patent

→ Add functional group to that salt → properties change (Chemical composition change)

→ Develop Derivatives → multiple → choose one showing desired property

Properties like → ① Bioavailability (soluble in blood)
② Absorption by tissues
③ Thermokinetic stability

→ get patent again

GLIVEC OF NOVARTIS (Anticancer Drug.)

Salt used → Imanitib Mesylate (1991)

[1991] → Novartis had salt → IMATINIB
but (India → Process Patent)

[1995] → WTO → Replace process patent with Product Patent
→ only to those items created on/after 1 Jan 1995

[1997] → Novartis developed derivative → Imanitib Mesylate
→ [US/EUROPE → Patent Granted] 30% more bioavailability

[2005] → IPA, 1970 → amended → to move from process patent to product patent
→ Also amended → sec 3(d) of IPA (to stop evergreening)

"If property of pre existing substance being altered by altering chemical composition, but no correlation b/w change and improved therapeutic efficacy → No Patent"

[2006] → Applied for Patent in India → Application Rejected by Chennai Patent Office
→ Appeal in Madras HC → Rejected
(b/c IPAB wasn't there yet)

[2013] SC → Basic condition → innovation → not fulfilled
→ No patent acc to Sec 3(b) and 3(d) of IPA, 1970

[Implication of verdict]

1. Refined norms of patent
2. Defined what is patentable and what not
3. many countries → inspired by this verdict changed their respective laws → [US demanding to remove S[3(d)] → IND → [GO to WTO]
4. Never implies that no medicine will be granted patent → Pharmaceutical innovation duly recognised

[If they say we will remove]

● [GENOMICS]

→ study of Genome. Genome → [collection of genes.]
→ Gene is that part of [DNA] which determines Character by determining protein synthesis.
→ [HUMAN GENOME PROJECT] → Path breaking project in the field of Genomics.
→ started in [1990] completed in [2003]
→ 3 Bn Base pairs were studied [A–T], [C–G]

Objective → to find out no. of genes in human Genome. (25000 Genes)
→ to determine the function of gene
→ to " " location of gene

→ Report Published [2003] → there are [~25000 Genes] (46 chromosomes)
→ location and func. of most genes also known.

[2009] → India became 6th country to sequence human genome

[INDIGENE PROJECT] → [CSIR] → To determine population characteristics
→ Took DNA of [1000 rural youths] → they were sequenced, Youth were given USER ID and PASSWORD.
→ Whenever they experience ailment → Doctor will access the whole genetic structure → prescribe medicine accordingly.
This is called Pharmacogenomics.

e.g. [Three Parent Baby] → UK case → lady had problem with her Mitochondrial DNA (comes from mother) → (If not → baby will not have nervous tissue → will survive only 2 years → Leigh Syndrome)

They replaced the mitochondrial DNA with donors DNA.

e.g.2 Designer Baby → Parents approach gene therapist for child with certain characteristics.

e.g.3 Gene Test → to determine probability of a disease

→ Implications of Genomics

- Pharmacogenomics
- Gene Therapy
- Gene Doping
- Gene Patent
- Synthetic Genome
- Genome Editing

① [PHARMACOGENOMICS] → Pharmaceuticals + Genomics

→ Personalised Medicine

→ Basis of this approach → "No two individual will react to the same stimulus in same manner, everyone's response may be/will be different"

→ Treatment on the Basis of Genetic information.

→ Medicine should be given according to an individual's response to such medicine b/c of genetic instruction.

[Issues with Pharmacogenomics]

1. Genomic Analysis of whole population requires huge resource as well as time.
2. Cybersecurity Issue
3. Pharma companies will have to come up with multiple dosages of same medicine.

② [GENE DOPING]

Doping → use of Banned substance and method to enhance performance

→ Monitored by WADA (World Anti-Doping Agency)

→ Introduced WHEREABOUTS clause recently.

[Every week dope test twice] Every olympic athelete has to give there location twice every week; if they test +ve for banned substance → they will be put under suspension.

* Gene Doping (explained after) → Non Therapeutic use of gene therapy so as to increase rate of formation of some substances for improving performance.

* Blood Doping → AKA Autotransfusion.

e.g. → German Cyclist Ullrich → Doctor took out one unit Blood, → saved RBCs (can survive separately for 70 days).

→ RBC again transfered to his body.

RBC carry oxygen → More RBC → More oxygen → Better performance.

→ He was caught.

(2) Gene Doping → A gene is transferred to Athelete's body.
→ Due to which secretion of some substance increases.
e.g. → [Erythropoietin] EPO → Increases the rate of formation of RBC in human Blood.
MORE RBC → GREATER OXYGEN TRANSPORT → more energy → improved performance.

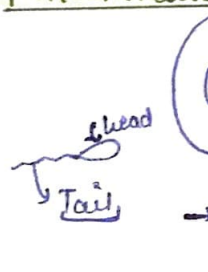
[After RIO OLYMPICS]
[WADA and International Olympic committe Medical Association]
Said → some Athletes are using Gene Doping but b/c of ethical and legal reason they cannot be identified.

Why? - There is no law in any country to declare Gene Doping as a crime.
- To identify such gene - 3 persons needed
Athelete and his parents (biological)
- Genetic material of parent → difficult to get b/c of privacy related issue. → Unethical.

Implications → Gene Doping
→ Not Biological parents → (identity crisis)
- Another Ethical Aspect → Gene Doping can be used in animals which are part of modern commercial sports.

(3) [THREE PARENT BABY] → First country to legalise → Britain
→ refer the example of (Leigh Syndrome)

Mitochondrial DNA always comes from mother. Why?



→ [Mitochondria of sperm is in tail]

When Reproduction takes place, only head of sperm enters ovum, tail is left behind, so there is only one Mitochondrial DNA i.e, from Mother.

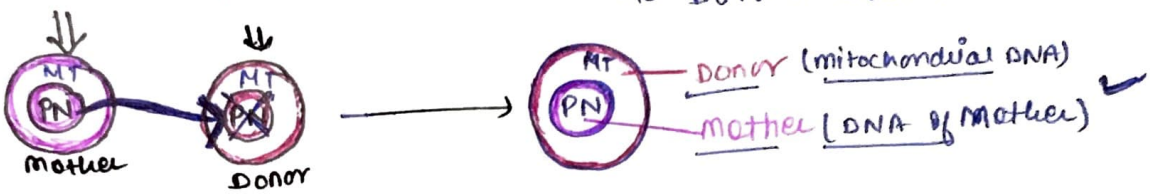
→ If the mitochondrial DNA is having mutation → results in [Leigh's Syndrome.] → Concept of Three parent Baby has come up to rectify it.

Methods for having 3 parent Baby
- Pro-Nuclei Transfer (June 2020)
- Spindle Transfer
- Cytoplasmic Injection.

[PRO-NUCLEI TRANSFER] → Str. formed immediately after fertilisation

→ Two ovum are taken → one from [mother] and one from [donor]
→ Both are fertilised → To allow formation of pro Nuclei.

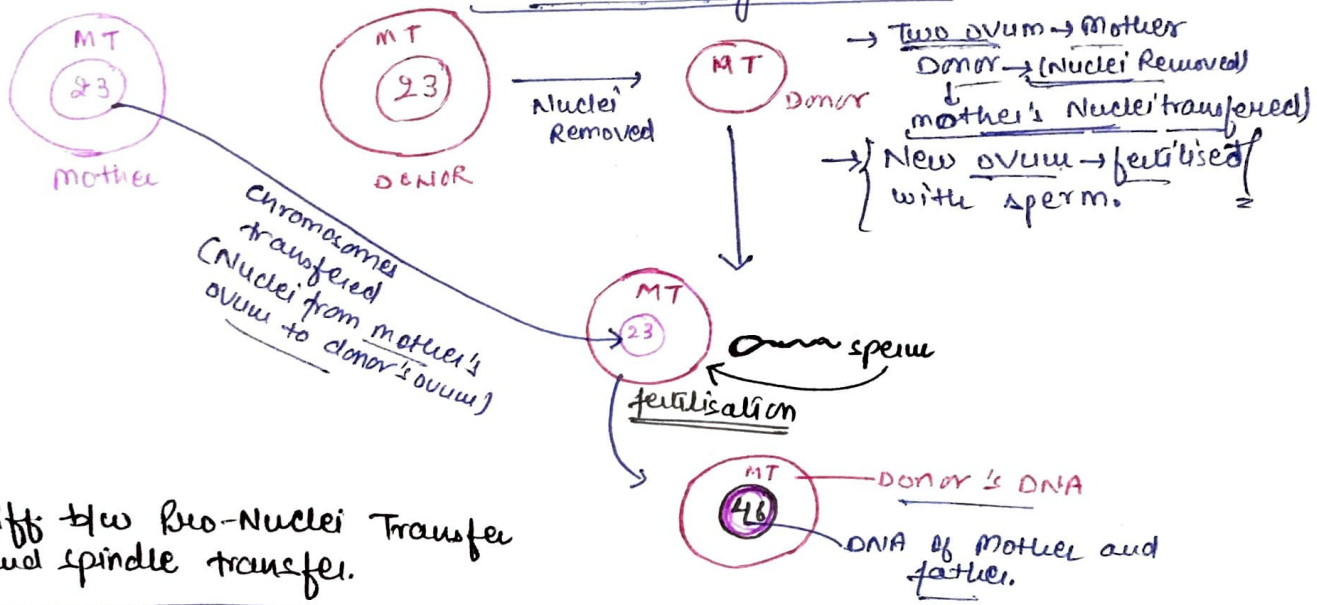
→ PRONUCLEI of Donor is Removed and Pro Nuclei of mother is transfered to Donor's ovum.



→ [Stage where chromosomes of mother and father are about to merge to form spindle.]

[SPINDLE TRANSFER]

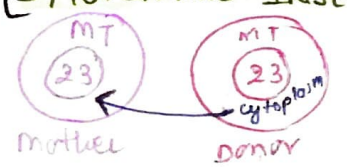
Spindles are microstructures found in the nuclei and function is to move the chromosomes during cell division.



Diff b/w Pro-Nuclei Transfer and spindle transfer.

Pro Nuclei Transfer	→ Fertilisation	before	Rearrangement
Spindle Transfer	→ 〃	after	〃

[CYTOPLASMIC INJECTION]



→ Cytoplasm of Donor's ovum extracted and transfered into the mother's ovum.
→ Obsolete approach → B/c both DNA will be present. So, there remains a chance that mother's DNA will express itself.
→ Not used anymore.

(4) **SYNTHETIC GENOME** → Human Genome Project (HGP) → 1990 was called HGP Read

→ After sucess of HGP → HGP-write came up.

Human Genome Project-Write → synthesizing human DNA in the lab with specification which can be employed for disease treatment, Vaccine development etc.

→ like designer baby → difference being Designer baby took gene from other people → Outside but in Synthetic Genome desired gene being made in the lab.

→ It was not allowed for humans but allowed for other species.

e.g. J. Craig Venter Institute (JCVI) annonced → that they developed world's first self Replicating Synthetic cell.

→ Bacteria Mycoplasma Capricolum and Mycoplasma Mycodis

Took DNA and copied it

→ Synthesised DNA took control of Mycoplasma Capricolum and was still dividing despite that fact that it was an artificially synthesised DNA.

→ Synthesised a DNA which was almost same as DNA of Mycoplasma Mycodis

Transfered that DNA to Mycoplasma Capricolum.

This was named **MYCOPLASMA MYCODIS JCVI SYN 1.0**

→ But many scholars complained that they created synthetic cell, they could've better called it Synthetic Genome.

Applications of Synthetic Genome

(a) Bacteria that will inhale CO_2 and cover it into Biofuel

(b) Vaccines → We can have vaccines which can produce proteins that can be produced by virus/pathogen. By synthesizing Genome we will recognise which of those proteins will be injected to activate/develop immunity.

(c) Combat oil spill — Plastic Consuming Bacteria → Anand Mohan Chakraborty was working on bacteria → Pseudo-monasputrida. Genetically modified it and sprayed over crude oil, it consumed crude oil.

(d) **Biological Weapon** → where no medicine can work
e.g. for COVID vaccine m-RNA approach.

(e) **Minimal Genome** → least no. of genes required for survival of the cell.

→ Took a bacteria **Mycoplasma Genitalium** → 543 genes.
→ they took out the DNA and reduced the no. of genes → and after every reduction → ~~No. of~~ genes was transfered to host cell.

In the end it was found 473 genes are needed for survival of the cell. → Described as **SYN3.0** (3rd synthetic cell)

543 genes —3→ 540 (placed in Mycoplasma genitalium) (dividing)

Reduced to 530 (Dividing)

This will help us in understanding evolutionary pattern/process

473 (U) → 472 (not dividing)

Man and Chimpanzee share 99% of DNA

(5) **GENOME EDITING** → [CRISPR Associated]

Tool → **CRISPR | CAS9**
(Clustered Regularly Interspaced short palindromic Repeats)

→ Invented by **Charpentier and Doudna** (Nobel Prize – 2020)
~~discovered~~ discovered while forming a **bacteria** showing resistance against viral infection.

→ They took DNA of that **Bacteria** → **Streptococcus** → found that DNA was showing a pattern

P-DNA – U_1 – P-DNA – U_2 – P-DNA

→ There was Palindromic DNA → frequently repeating

or P-DNA

→ Unique DNA also (U_1), (U_2)

U_1 → RNA 1 (Cas 1)
U_2 → RNA 2 (Cas 2)

Linked with Enzyme Cas

Complementary RNA
[for every unique section]

NOTE

* COMPLEMENTARY RNA

$U_1 \longrightarrow RNA_1$ → This is Complementary RNA.

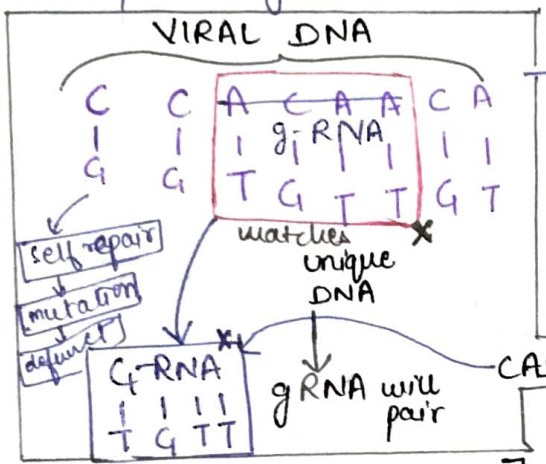
A - T ⟶ A
C - G ⟶ C
A - T ⟶ A
A - T ⟶ A

• Arrangement of Nitrogenous bases of RNA is determined by the arrangement of N_2 bases in DNA.

* gRNA - Guide RNA - most vital part → guides CAs

→ Whenever there is a viral infection, DNA is pushed by infection causing agent inside bacterial cell (target cell).

→ If a part of a viral DNA matches the unique DNA (same sequence) then Complementary/Guide RNA will come and pair with it. (Complementary RNA)



→ Cas will come and remove that ~~Entire~~ part of Viral DNA.

→ DNA has property of self healing → Viral DNA will try to repair itself → but will go through mutation → will get disabled/defunct (non-functioning)

(change in Base pair)

→ Bacteria then incorporates the excised DNA into ~~but~~ its existing genome - to counter future infections.

[Viral D → match U_1 → gRNA pair → CAs will cut → self healing → mutation → defunct]

→ In Genome Editing (in a lab setting) →

To Remove this part

A A C C C A A
T T G G G T T

→ A guide RNA will have to be made → inserted along with Cas in the Target cell to remove the part and add another part → This is genome editing.

~~found~~ used by He Xiankui → to impart resistence against HIV

→ Implications → Crop resistent against virus
→ Hepatitis
→ Designer Baby
→ lethal biological weapon
→ Developmental Biology
→ COVID-19 diagnosis < SHERLOCK (USA) - Sp Cas9
FELUDA (IND) → fn Cas9 (more accuracy)

GENE PATENT

→ one of the most controversial areas associated with modern Biotech.
→ Thousands of patents has been issued for various genes.
→ Purpose of patent to promote innovation → No patent → No investment in R&D (means denying modern medical techniques)

backdrop:
- e.g. ₹ 16,00,00,000 for one dose (Zolgensma) → In news.
  - crowdfunding
  - child was ill.
  - couple raised money
- costly b/c of patent
  - govt. have option of compulsory licence

CONDITIONS TO GIVE PATENT TO GENE

① Novel ; ② must involve an inventive step ; ③ must have commercial use.

HOW ITS DONE?

→ Gene is extracted from human body → modified so that it can be used for
- (a) Diagnostic Purpose, or
- (b) Therapeutic Purpose

→ Gene which is given patent called → Expressed Sequence Tag (EST) or (cDNA). Complementary DNA to Messenger DNA

+Negative Aspect

→ Gene patents are classified as GATEKEEPER Patents b/c patent holder will allow the use if the user is willing to pay royalty.
→ ∴ They are used to block ideas rather than promoting the innovation.
→ Patents are used in drug designing that will lead to increase in cost. (against public health care)
→ Restrict proliferation of modern therapeutic approaches towards weaker sections of society.

CASE STUDY → USA

→ BRCA 1 & 2 (Breast Cancer 1&2) → by Myriad Biotech, Utah, USA
→ used for diagnosis for Breast Cancer & ovarian Cancer.
→ Challenged by American Civil Liberty Union.
→ US Supreme Court declared these patents illegal.
- "Natural Processes and natural laws, natural products cannot be patented". b/c they are the Basis of technological development.
- "These patents hinder the proliferation - - - - -.
- "mere discovery of a use of a gene is not something which will allow to get you a patent."
- "But there is no ↓ discovery → was discovered by human Genome Project.

Last -ve

CASE STUDY → INDIA

→ Sec 3(c) and 3(j) of Indian Patent Act have ruled out possibility of gene patent.
- Sec 3(c) → any substance, living or non-living found in nature cannot be patented
- Sec 3(j) → Neither a complete plant or complete animal nor any part of plant or animal can't be patented.

→ Positive Aspects

→ It is an incentive for Bio pharma companies to develop new approaches for treatment and diagnosis.

→ Create Next generation jobs.

→ Establish Knowledge based economy.

Note Guidelines issued by Deptt. of Biotechnology, 2013

- Guidelines were not very clear
- If conflict b/c law and and guideline then the priority will be given to law.

GENE THERAPY

→ Used for treatment of Genetic Disorders

- Mutation - Sickle cell Anemia, colour blindness (- Courtsea primary colour), Thalessemia, Phenylketona, Cystic Fibrosis, Haemophilia.
- Chromosomal Abnormality - Downs Syndrome,

→ In mutation → no. of chromosomes will remain same but there will be slight defect which is responsible for abnormality

→ Chromosomal Abnormality → no. of chromosomes are not complete

→ In Gene therapy, target cell is identified (say someone has colour blindness)

gene will be carried by vector → and transferred in the target cell.

gene will increase → abnormality cured.

e.g. Haemophillia → Blood doesn't clot.

protein responsible not synthesised either → gene is not present or " " working.

Can be Corrected by Gene Therapy.

CBD → CONVENTION ON BIODIVERSITY

→ Adopted in 1992, came into force in 1993.
→ It has defined Biodiversity.
→ Explained the types of → Ecosystem, Species, Genetic diversity
→ Identified issues with Biodiversity → Biopiracy.
→ Adoption of Protocols → Cartagena Protocol, Nagoya Protocol.

BIOPIRACY

- Rice Tech USA → patented Basmati → Genome editing → Texmati
- Turmeric was patented
- Neem was patented.

→ Acc to WTO → Neither Traditional Knowledge, biological resources nor Geographical Indication can be patented.
→ When items in above categories are appropriated by way of patent, consequently, local stakeholders are denied commercial benefit → i.e. Biopiracy.
→ Two types of patent issues
  - WRONG PATENT → issued by violating norms set by WTO.
    → when challenged → They were cancelled.

→ MECHANISM TO PREVENT BIO-PIRACY

(i) • TRADITIONAL KNOWLEDGE DIGITAL LIBRARY, initiative of; CSIR, Ministry of Ayush, Ministry of S&T
→ Document traditional knowledge has been converted into digital form.
→ On the basis of this database, thousands of patents were challenged in diff. countries and 20% of them were cancelled.
→ Later it was declared as open source; means the medicinal formulations can be used for commercial purposes but, two conditions

(ii) — (1) Prior Informed Consent
(iii) — (2) Access Benefit sharing

↳ KANI TRIBE EXPERIMENT
- Nomadic Tribe
- medicine made by their traditional knowledge
- some part of profit was shared with the tribe.

(N) BIODIVERSITY ACT 2002
→ 3 Tier system.
→ National Biodiversity Authority in Chennai
- To ensure → "Biodiversity should benefit all"
  i.e, No patents in GI, BR, TK.
→ Quasi Judicial power → power to cancel patents falling in category of Biopiracy. e.g. BT Brinjal.
→ Permission necessary to use indegenous genetic resources for commercial purpose.
→ No role in granting/denying permission for cultivation of GM crops.

→ State Biodiversity Board – same function @ state level.
→ Biodiversity Management Committee @ dist level.
→ compilation of Biodiversity Register in dist known as "Peoples Biodiversity Register."
→ Wayanad is the first distt to prepare this.

(vi) SUI GENERIS MECHANISM

Self evolved

→ When TRIPs was formulated all rules were made acc to interests of Developed economies. (IPR)
→ Developing economies said 'what about our IPR?'
→ TRIPs ⟶ Gave discretionary Power to developing economy → If you feel like a sector is vulnerable.
→ use these powers to formulate your own rules / ~~Acts~~ Laws / mechanism

- GI Protection Act 1999 → b/c Texmati Case in 1997
- Protection of Plant Varieties & Farmers Rights Act → Right to seeds, Rights to compensation

→ Right to seed → Rajji V. Gujrat Potato Farmers
→ Bowman V. Monsanto
- Round up Ready
- No reuse

→ Doctrine of Patent Exhaustion.
→ Rights of Patent holder gets extinguished after Patent exhaustion.

→ Monsanto V. Nuziveedu → Process & Product Patent for BT cotton.
→ Nuziveedu sells BT cotton seeds under license from Monsanto.
→ In India we don't give patent for seeds (part of plant), patent given for method, product patent given to monsanto was for toxin and the other for method.
→ GOI set the MRP of cotton seeds, then Nuziveedu approached Monsanto to reduce royalty amount (license amount), they said no and cancelled license but farmers had Right to seed, hence they could continue producing seeds, under sec 3(j) of IPA (1970) ⟵ Part of plant cannot be patented.

→ It was a clear example of "Neo colonialism"
→ There is a classic contrast b/w USA and India's Right to seed.

no organised marketing
use | Reuse | Sell | Exchange | consume

⇒ PROTOCOLS UNDER CBD

① CARTAGENA PROTOCOL / BIOSAFETY PROTOCOL

→ Deals with r-DNA and GMO (Genetically modified organism)
→ " " Regulation of GM
→ Member countries have to fulfil following requirements.

(i) PRIOR INFORMED CONSENT (Permission before such movement) for + transboundary movement of the living modified organism.

(ii) GM LABELLING

(iii) Regulatory mechanism → MS Swaminathan Committee recommended (but still not)

(iv) If a country is a centre of origin for a certain crop then it should not allow GM variety.

(v) There is bio safety clearing house and all the members are required to give the details of GMOs developed by them

* REGULATION OF GMO

• Environment Protection Act 1986 –
Defined "Hazardous substances".
- Bio Medical Waste
- Hazardous Chemicals
- GMO – 1989 → MoEF & DBT drafted GMO Rules, 6 Committies Constituted.

a • Genetic Engineering Appraisal Committee
under MoEF & CC → Regulating GMO
→ Allows for commercial release of GM crops.

b • r-DNA Advisory Committee → MS&T
– advises the ministry for the adoption of GM crops.

c • Review Committee on GM → MS&T
– Decision on whether

d • DLC –

e • IBSC – Indian Biomedical Skill Consortium
To prevent accidental relase of GM crops etc

→ CP Act 1986 – GM labelling } Edible Crops.
→ FSSDA – 2006

(2) NAGOYA PROTOCOL

→ Adopted in 2010 ✓

→ Includes - (a) ABS → Access Benefit Sharing (Kani Tribe)
(b) Aichi Targets → were to be acried by 2020.

* AICHI TARGETS

→ Mainstreaming the biodiversity accross the govt and administration.

- First priority should be given to the assessment that how a developmental project will work

e.g. Great Indian Bustard died b/c of solar Projects in Rajasthan
SC ~~Govt~~ → go for underground line
Company → but cost will go up by 20%.

e.g. Western Ghats Ecological Expert Panel (Gadgil Panel)
- To identify ecologically sensitive areas as per EPA.
- declare 1,20,000 sq. km to be declared as protected area.

e.g. Kerala Floods
If Gadgil Panel was listened to, consequences of floods would've been less severe.

→ Reducing the pressure on biodiversity i.e. allow the Nature to replenish itself.

e.g. [Illegal Sand mining] → sand is lungs of a river ✓
sand mining may cause water pollution

→ Supporting Biodiversity
- 10% of marine Area
- 17% of terrestrial Area
] should be declared as protected area.

→ Biodiversity should benefit All.
e.g. Biopiracy should be banned

→ Adopt Participatory Approach for conservation of Biodiversity
e.g. People's Biodiversity Register - BMC - BDA - 2002.

ANTIBIOTIC RESISTANCE

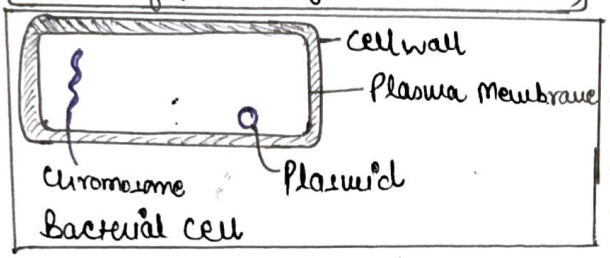
e.g. NDM-1, MCR-1, DR-TB, MRSA

→ Antibiotics are medicinal formulations used for treatment of infections like Viral, bacterial, fungal, protozoa.

→ Classification → Narrow spectrum
on range → Broad spectrum
→ Bacterio static

→ Classification on Mode of Action.

• Mode of Action of Antibiotics (AB)



→ Some Antibiotics work by targeting cell wall
→ " " " target Protein synthesis
→ " " " inhibit DNA synthesis
→ " " " " RNA "
→ " " " " Metabolic "

- Beta lactans → largest class of AB → target cell wall
- Carbapenemes → target cell wall
- Polymixine → " " "

- Antibiotic Resistence → AB fails against the bacteria.
- Antimicrobial " → when bacterial/fungi/virus change over time and no longer respond to medicines making infections harder to treat.

NDM-1

Cancer carried a Research —

"B/c of Irrational use of Antibiotics in India there is an emergence of a superbug showing resistence against Beta lactams."
– "It is b/c of the gene NDM-1 (New Delhi Metallo Beta Lactamase-1)"
→ Any bacteria having NDM-1 → against that Beta lactam will not work.

Reasons for ABR

- Irrational use → over the counter sale and purchase of medicine
- ~~Use of Anti~~ → Non human use of human antibiotics
  → Poor hygine and sanitation
  → Community Bathing
  →

MCR-1 – Mobilised Colistin Resistence

→ In China, A bacteria has been found which is showing ~~res~~ ABR against Colistin (most powerful AB) – AB of last Resort!!
→ This bacteria was initially found in gut of a pig, later in humans.
→ It was called as "Antibiotic Apocalypse"
→ Found in Europe, SA, NA, Africa, Asia (same places including India.

→ **STEPS TAKEN**

→ Drugs & Cosmetics Act 1945 – amended to bring AB in Schedule H.
- It cannot be sold without prescription.
- Prescription to be Xerox by Chemist (shop) → atleast for 2 years.
- Red line campaign
- National action plan, State Action Plan (MP, Delhi, Andhra)
- Chennai Declaration – Prevent Non human use of Antibiotics.

→ Manufacture and use and sell of Colistin – banned for poultry industry.

→ WHO → AWARE strategy – Access watch & Restrict categorization of Antibiotics.

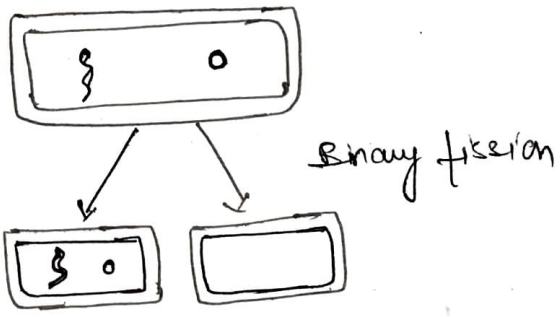
→ **MECHANISM FOR SPREAD of ABR**

HORIZONTAL GENE TRANSFER

→ Gene responsible for ABR develops on plasmid, when it is transfered from one species to other.

VERTICAL GENE TRANSFER

→ Gene passed from one generation to other within same species.



DRUG RESISTANT TB

→ TB is caused by a Bacteria Mycobacterium Tuberculosis in Aerosolic form.

→ Symptoms → Fever mild, cough for two weeks, weight loss, tiredness, chest pain.

→ India is having highest no. of TB patients, about 25% of global drug resistant TB cases are here.

→ For every 1 lakh of population, no. of TB patients in 2014. Target set to eradicate TB by 2025.

→ Acc to WHO if no. of TB patient per million of population is less than 1

→ then the country will be declared as TB free.

→ WHO defined TB as a disease of poverty but b/c of poor treatment, poor follow up and poor drugs there is emergences of Drug Resistant TB which is of three types.

→ Latent TB → No symptom but carrying bacteria.

→ If immunity gets compromised by Biomedical factors like diabetes, /HIV/stress/malnutrition → bacteria will get released - TB ——— why TB increase?

Reason for Spread of TB

- or by Air Pollution (Env. pollution)
- or socio economic issues
- or lack of push and pull factor
  - pull factor → govt convince people for treatment
  - push factor → from family
- or long duration of treatment

→ **TYPES OF DR-TB**

- MDR (Multi Drug Resistant TB) → If resistance against two most common medicine of 1st line → Rifampicine, Isoniazid. Mortality rate 30%.
- XDR (Extensive Drug Resistant TB) → All first line medicine not working and in second line Flouroquinolones not working. Injection not working one of 3 → Amikasin, Kanamycin, Capreomycin. 60% mortality Rate
- TDR (Totally Drug Resistant TB) → 1st & 2nd line medicine not working. Mortality Rate 100%.

WHO Protocol for TB

1st Line Medicine

IInd Line Medicine

→ **STEPS | MEASURES TAKEN**

- **NATIONAL TB CONTROL PROGRAM** (1960s) → later **Revised NTCP** (1990s)
  - DOTS Directly Observed Treatment Short Course
  - now named as National TB Eradication Program

- In 2012 National Plan was started **First Phase** (2012-2017)
  - A system → eNikshay to collect the information in a centralised manner.
  - → TB was declared notifiable Disease.

Second Phase 2017-25 → It is working on four diff. aspects i.e., Detect, treat, Prevent, Build and Focussing on strategic areas i.e. ensure participating of private sector, plug the leakages in the TB care Cascade, Target Key populations, areas like slums, refugee, night shelters,

JAPNESE ENCEPHALITIS

→ Viral infection spread by Culex Mosquito
→ 200+ distt in 14 states where this disease in endemic.
→ humid conditions → culex grow (stagnated water)

↳ swelling in these membranes → J E.

→ Acute Encephalitis Syndrome → infection reaches brain
→ Majority of victims 1-15 years of Age
→ Mortality rate - 25%; Phy. & Mental Disability - 40% = 60%.
→ Focus should be on prevention and rehabilitation.

[Culex] → [virus] → [pig] —culex→ [human]
↳ Intermediate Host.

→ Focus on Sanitation → to prevent stagnated water.
→ Vaccination → Indradhanush Programe
→ Rehabilitation → Cpl. Schools
→ Monthly relief Amount

COVID - 19

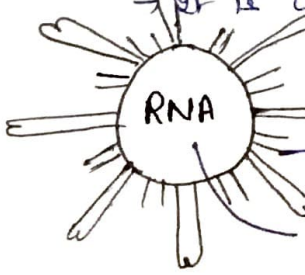
- CORONAVIRUS
- TESTS
- VACCINES

⇒ CORONAVIRUS [SARS-COV-2]

→ Retro Virus
→ Belongs to SARS family → Severe Acute Respiratory syndrom.
→ First Outbreak was in china (2003) - controlled, China said → Civet cat from
→ 2nd " " " 2012 West Asia - MERS (Middle East Respitory Syndrom)
- Came from Camel.

2019 → SARS-COV-2

→ said to have come from Bat
→ It is a zoonotic Disease.



- Doctors recommended AntiRetroviral medicine
- Plasma Therapy

⇒ COVID-19 VARIANTS

Alpha Variant - UK
Beta " - SAfrika
Gamma " - Brazil
Delta " - India

Varients of Concern defined by WHO

→ 3 criteria of classifying a mutant of virus into VOC.
① Increased transmissibility
② " virulence (ability to cause infection)
③ Collapse of Healthcare system.

→ Nomenclature done by International Committee on Taxonomy of Viruses

Varient of Interest

① Found in multiple countries.
② WHO has identified it as VOI.

⇒ Mutation of SARS-COV-2 · WHY MUTATION IS SO HIGH?

→ ~~COVID-19~~ is RNA Virus, less stable, rate of spread is very high.
→ Tries to save itself from the immunity

⇒ WHAT WE COULD'VE DONE IN 2020?

→ Massive Testing
→ closing of International flights.

WHERE THE PROBLEM LIES?

→ Inflamation of internal organs, lung fibrosis (lungs lose elasticity), ...
↳ (Cytokine storm) [Interstitial lung disease]

⇒ VACCINES FOR COVID-19

→ Purpose of vaccine is to activate the immune system.
→ Immune system works in two ways.

Cellular Mechanism → (Phagocytosis)
When the WBCs directly engulf the pathogen

Humoral Mechanism → based on Antibody.

→ Most of the vaccines work on humoral mechanism. eg. OPV (weak) (attenuated polio virus)

How HM works? → 2 types of WBC

T-Cell → IB of body, look for pathogen, and identify pathogen through Antigen.
→ After identifying, T cell generates the signal when these signal Reach B-cell

B-cell → Produce Antibodies and these antibodies kill the pathogen.
→ B cell has memory

→ **TYPES OF VACCINES**

① **NUCLEIC ACID VACCINE** → Pfizer etc.

DNA | RNA

•DNA BASED VACCINES

→ We take a gene of the **Pathogen** and inserted it into **Plasmid** (small circular DNA).

→ Injected in muscles

→ There will be synthesis of Pathogen protein → T-cell → signal → B-cell → Antibody → Kill pathogen

• RNA BASED VACCINE

→ RNA is of 3 types

- mRNA → Carries information for protein synthesis
- t RNA → mobilises the amino acids
- r-RNA → binds the amino acid to form protein

encapsulated by nano particles → enter cell → result in the synthesis of spike protein → will be identified by T-cell → signal → B cell → antibody → attack spike protein.

→ most advanced technique. Pfizer vaccine is of this type

→ Requires [-20 to -80 °C]

② **WHOLE VIRUS VACCINE**

• INACTIVATED VIRUS VACCINE

e.g. COVAXIN by Bharat Biotech ltd.

e.g. Inactivated Polio Vaccine

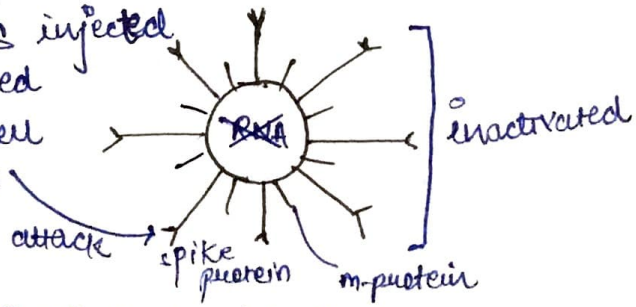
→ Virus is taken and this virus is inactivated by destroying its genetic material. (by chemicals / radiations)

→ Inactivated virus is injected

→ T-cell will recognised

→ send signal to B cell

→ B-cell → antibody



→ will be more effective on Mutants of coronavirus.

- ATTENUATED VIRUS VACCINE

→ Virus is weak e.g. Oral Polio Vaccine

③ VIRAL VECTOR VACCINE

- REPLICATING – Virus will multiply.
- Non-REPLICATING – Virus will not multiply e.g. Sputnik V, Covishield. (Oxford-AstraZeneca) → Serum Institute

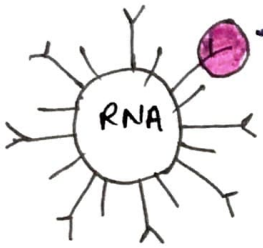
Adeno Virus → common cold

→ DNA as the genetic material

→ gene of corona is added to DNA of Adeno Virus

→ This entire Virus is injected.

④ PROTEIN SUB UNIT



Took a particular part of a DNA → that part is injected.

→ will be recognised by T-cell → signal → B-cell → antibodies → attack pathogen

⇒ TESTS FOR COVID-19

① RT PCR (90%)
② Antigen Test (70%)
③ Rapid AB Test
④ Truenat Test / CBNat
⑤ Feluda
⑥ SHERLOCK
⑦ DETECTR

⑤⑥⑦ → CRISPR / CAS 9

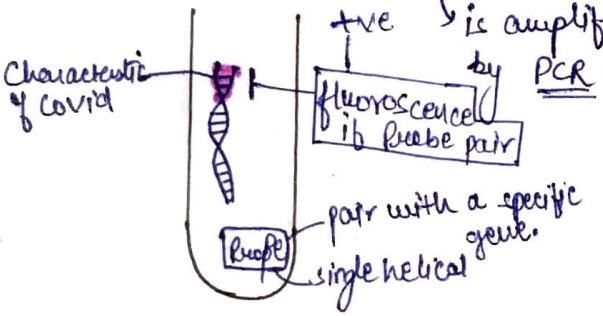
① RT-PCR – Reverse Transcription – Polymerase Chain Reaction (90%)

→ Nasal Swab, Throat Swab is taken, Virus is taken.

→ from Virus RNA is taken.

→ RNA converted into DNA – This is Reverse Transcription.

→ is amplified (Quantity Increase) by PCR → to make infinite copies of DNA.



② RAPID ANTIGEN TEST (70%) → 15% false negatives chances

→ Swab is taken → into solution.

→ Put one @ strip containing Antibodies (bind with Spike Protein) → 2 Red lines (+ve test)

→ If No Corona → 1 Red line (–ve)

③ **RAPID ANTIBODY TEST**

→ Not to detect coronavirus
→ But to run a sero-surveillance to find out that how many persons have formed antibodies.

→ Blood is taken → put on a strip containing coronavirus.
→ If Blood blood has antibody → they will react with Coronavirus
→ 2 Red strips → they had recovered from COVID
→ 1 Red strip → they never had COVID.

④ **TRUE NAAT | CB NAAT** → TB | DR-TB

NAAT → Nucleic Acid Amplification Test

RNA → Amplified → we took **RdRp** gene → (RNA dependent RNA Polymerase)
↳ multiplication of the virus

⑤ **FELUDA**

→ Based on CRISPR/Cas9
↳ Francisella Novicida
→ Developed by CSIR and IGIB (Institute of Genomics and Integrative Biology)
→ RNA → DNA → Amplification
↳ guide RNA → Binds with specific sequence of viral DNA.
→ We put viral DNA + guide RNA + Cas9 in the mixture

⑥ SHERLOCK, DETECTR (CRISPR/Cas 9)

GENE SILENCING → 2019 prize

→ Natural mechanism ~~involve~~ evolved in eukaryotic organisms.
→ works against viral infections.
→ AKA RNA interference
→ Fire & Mello → Nobel in medicine
→ Silencing → genes associated with Hepatitis, Cancer, HIV, Macular Atrophy, Huntington disease (neural disorder)
→ Based on micro RNA → miRNA
→ Pre miRNA comes from nucleus into cytoplasm
→ In cytoplasm there is an Enzyme – DICER → Produces miRNA from Pre-miRNA
→ miRNA joins RISC (RNA Induced Silencing Complex)
→ miRNA takes the RISC towards complementary m-RNA.
→ RISC will chop m-RNA → no protein synthesis.

GM-MOSQUITOS

→ To control outbreak of chickenguinea, Dengue, Zika, → Singapore has permitted use of GM-Mosquitos.

→ In India, the trial was planned by oxitech and GBIT (Gauja Bishan Bhikulal Investment Trust → in Jalna dist of Maharashtra.

→ Male Aedes Aegypti is taken, lethal gene is transfered into it.

→ They will be released in the environment.

→ They will mate with normal female Aa → lay eggs → eggs then hatch into larvae but the larva dies.

Criticism

→ Not sustainable in nature, these mosquitos have to be released after few days.

→ The gene from the mosquitos will be part of food chain. Consequences of which are not known.

→ One person will require 800 mosquitoes.

Alternatives to GM mosquito

→ • Use of Wolbachia Bacteria → found in the gut of the insects.
  • This prevents the growth of virus.
  • But Wolbachia is not found in mosquitos.
  • Male Aa is infected with Wolbachia and Released then mate — eggs will not be hatched.
    ↳ same issue of sustainability
  • female Ae infeted with Wolbachia → Release → eggs → larvae → mosquito (will have Wolbachia in gut → No virus)

↳ this is sustainable and a reliable option.
→ B/c problem is not with mosquito ~~not~~ but with the virus.

SURROGACY (womb on Rent 'literal meaning')

→ A Broader term includes ART (Assisted reproductive Technology)

→ 3.1 Billion Dollar Industry.
→ 2000 surrogacy births take place in India.
→ Boon for child less couples
  e.g. A lady in Pune. Her only child (son) died. She asked Doctors to preserve sperm of her son. She got her grandchild by surrogate services.

→ Families of surrogate mothers flourished.

CONS

→ Eg. Japnese couple came to India. By surrogate child they wanted a baby. Got divorced. India doesn't recognise single parent's right for surrogacy. Child was stateless.

→ e.g. Surrogate mother died in India.

→ e.g. Australia a surrogate baby came out with down's syndrome. They blamed it on surrogate mother.

→ It we support it is improving the condition of poor women. It can't be the only solution to eradicate poverty.

→ women (surrogate) may face exploitation.

COMMERCIAL SURROGACY

→ Surrogate services in return of financial consideration.

ALTRISTIC SURROGACY

→ Surrogate services without any consideration.

⇒ **SURROGACY BILL, 2020**

→ Ban commercial surrogacy

→ Permission of Altristic surrogacy.

→ Allows PIOs & Resident Indians, NRIs, OCI to avail the services.

→ No permission for foreigners

→ Defined minimum and maximum age for couples looking for services.
[Female - 23-50 ; males 26-55] → (Commissioning parents)

→ Surrogate mother should be any willing women. (Age 25-35 years)

→ " " " " married and must have 1 child.

→ No financial consideration.

→ Condition for commissioning parents → childless
→ physical/mental disability / some fatal disease.

→ widowed and divorcees are also permitted to have a child through surrogacy.

→ If there is a provision of any provision → Imprisonment for 10 years/ 10 lakh Rupees.

⇒ **WHAT CAN BE DONE?**

→ This should be a sunset clause. In remaining period govt. should address concerns of affected people and then child adoption policies should be eased.

HUMAN DNA BASED TECHNOLOGIES (USE & REGULATION) BILL

⇒ **DNA FINGERPRINTING** → Concept was given by Sir Alec Jaffry.

→ 99.99% of DNA of any individuals is same and remaining 0.01% is different.

→ 0.01% of DNA :- There is a particular combination of base pairs found in all but frequency of repetition is unique for every individual.

→ There is a particular combination of base pairs found in all but its frequency of repetition is diff. for diff. individuals.

→ Purpose of DNA Fingerprinting is to find out the frequency of appearance of the base pairs per unit Unit length of DNA.

Note → In India DNA fingerprinting is not a primary evidence.

→ No one can be convicted only on basis of fingerprints. Additional evidence is needed in criminal trial.

→ This is called DNA profiling. In this we only determine that this fingerprint belong to a particular person or not.

2003 Department of Bio-tech. asked GOI to pass a law to give legal backing to DNA Fingerprinting.

2005 CrPC was amended to allow DNA fingerprints as an evidence in the court of law.

Later Tamil Nadu Amended Identification of Prisoners Act to include DNA fingerprinting.

2007 Since 2007 multiple bills have been Drafted and the Human DNA Based Technologies (Use and Regulation) Bill was the work of Law Commission of India.

As per this Bill

① There will be a national DNA Profiling Board, the chairperson of Hydera-bad based Centre for DNA fingerprinting and diagnostic will be the exoffico chairman.

Role → To define protocol of DNA profiling, to give accredition to the labs, to determine the use of the stored DNA.

② There will be National DNA Data Bank and Regional data Bank to store DNA under 5 diff. indexs :-

(a) Offender Index → DNA will not be removed

(b) Undertrial/ Suspect Index → can be removed if acquitted.

(c) Missing Index → DNA removed if found.

(d) Crime Scene Index → Can be removed.

(c) Unknown Dead person Index → cannot be removed.

(3) Consent of accused, if someone is charged with offence where punishment is > 7 years → consent Not required.
< 7 years → Consent is required.

(4) If accused gave illogical reason for denial then DNA can be collected on order of magistrate.

(5) If someone is found to be responsible for the misuse of stored DNA, then there is imprisonment for 3 years and a penalty of upto 1 lakh.

(*) DNA fingerprint is not a deterministic technology, it is a probabilistic one.

(*) In case of Identical twins it can fail → Not fullproof.

(*) Those who have undergone bone marrow transplantation → not fullproof

(*) Some people having same DNA naturally, it will fail.

STEM CELLS

→ These are unspecialised cells capable of forming all the specialised cells of body, they are found in multicellular organisms.

→ e.g. A girl in USA, had problem in her windpipe.
They took stem cell (skin cell) and made her a new windpipe transplanted in her body.

→ e.g. Japanese woman lost eyesight. skin cell taken. Retina developed and transplanted.

→ Stem cell therapy is used against degenerative disease.
is AKA Regenerative Therapy.

⇒ CLASSIFICATION

→ ON THE BASIS OF CAPACITY TO DECIDE

① Totipotent Stem cell → Capacity to divide totally.
Total capacity to divide
→ Capacity to form all the cells of the body including placenta.

② Pluripotent Stem cell → capacity to form 'almost' all the cells of the body.
→ Not all the cells

iPSC → Induced Pluripotent stem cell
Imparting a character which was not there

Skin cell (specialised cell) → transformed into pluripotent stem cells
↳ any tissue/organ can be made.

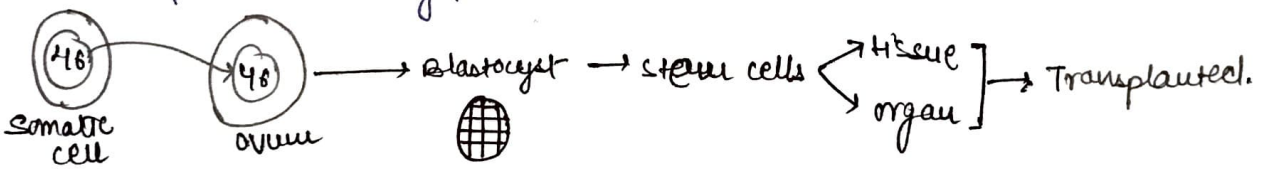
→ **ON THE BASIS OF THE SOURCE**

① **Embryonic stem cell** – pluripotent, obtained from umbilical cord and Blastocyst (easy to obtain)
– no. is also significant → popular among the researchers.
→ b/c of this Embryonic stem cell, an ethical debate started b/w pro lifers who oppose the stem cell research, and pro researchers.
→ A/C to pro lifers → whenever a stem cell is extracted there is termination of human life which is unethical
→ A/C to scientists → They are not creating embryos for stem cell rather they are collecting them from the fertility clinics.

② **Adult stem cells** – found in Bone marrow, fatty tissues, Adibos tissue, liver.
– they have less pluripotency.
– their no. is less and difficult to extract.

→ **ON THE BASIS OF METHOD**

① Theraputic Cloning (AKA Regenerative medicine)
→ object is to develop the organ or tissue in the lab by extracting stem cells from the blastocyst.



② iPSC → developed by John Gurdon and Yamanaka, they transformed the specialised cell into an ~~unspecified~~ unspecialised pluripotent stem cell through genetic reprograming.
→ Genese which were manipulated are named as Yamanaka Genes.

It is important that now the dependence on embryonic stem cells will be reduced, there will be no need to store the stem cells, it will broadbase the scope of therapeutic cloning and stem cell therapy by providing the treatment for degenative disease like Parkinson, Dementia, even cancer.

⇒ **APPLICATIONS OF STEM CELL**

① To develop the organoids
② To test the drugs
③ To Revive organs and the tissue
eg. LV Prasad Eye Institute Hyd → for Acid Attack Victims.
④ Artificial blood.
⑤ NAC – SRT → Research.
↳ National Apex Committee for Stem Cell Research Techniques.