Alireza Shafizadeh

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24TH JANUARY

Medical Biotechnology

First Session Report

Introduction

Introduction to Genetics

Introduction to Biotechnology

Useful tips

INTRODUCTION

Section 1

- Professor Arta Fejzullahu
- 13:30 PM - 16:30 PM (Tehran local time)
- 8 international students from different countries and different disciplines background

INTRODUCTION TO GENETICS

Section 2

IN THIS SECTION:

- 13:45 PM - 15:15 PM
- A brief history of genetics
- Types of traits
- Genetics Terms
- Mutation
- Related Trends and Articles

First Session Report

INTRODUCTION TO BIOTECHNOLOGY

IN THIS SECTION:

- 15:30 PM – 16:30 PM
- Definition
- History
- Model organism
- Applications

Section 3

USEFUL TIPS

IN THIS SECTION:

- During class
- Email, HackMD
- Searching for Articles in NCBI, Combined Search
- Article structure, Citation by Mendeley or EndNote, Presentation

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25TH JANUARY

Medical Biotechnology

Second Session Report

Introduction to Biotechnology

Introduction to Genes and Genomics

INTRODUCTION TO BIOTECHNOLOGY

Section 1

- 13:45 PM – 15:00 PM
- Modern Biotechnology products
- Types of Biotechnology
- Prospects for the future of biotechnology and its effects on out life
- Biotechnology Workforce

Second Session Report

INTRODUCTION TO GENES AND GENOMES

Section 2

IN THIS SECTION:

- 15:15 PM – 16:30 PM
- Review of Cell structure
- DNA and Chromosome structure and Karyotype
- DNA replication

Second Session Report

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26TH JANUARY

Medical Biotechnology

Third Session Report

Introduction to Genes and Genomics

Recombinant DNA technology

INTRODUCTION TO GENES AND GENOMES

Section 1

- 13:45 PM – 15:15 PM
- Replication
- Transcription
- mRNA processing
- Translation
- Gene expression regulation
- Polycistron

Third Session Report

RECOMBINANT DNA TECHNOLOGY

Section 2

IN THIS SECTION:

- 15:25 PM – 16:30 PM
- Gene cloning, Recombinant DNA technology, Genetic engineering
- Restriction Enzymes
- Plasmid DNA vectors
- Transformation
- Colony selection/Screening
    - Antibiotic Selection
    - Blue-white selection
- DNA Cloning Vectors

Third Session Report

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27TH
JANUARY

Medical
Biotechnology

The Fourth Session Report

RECOMBINANT DNA TECHNOLOGY

13:35 PM – 16:30 PM

- Vector features that are important: Size, Ori site, MCS, Selectable marker gene, Promoter
- Types of Vectors (Plasmid, Bacteriophage (λ), Cosmid, BAC, YAC, Ti) and their features
    - Homework for Monday: Assume you want to make lots of human insulin using a bacteria expression vector discuss why using human insulin genomic DNA for this coning project would not be advantageous.
- Two types of DNA library (Genomic library, cDNA library) process explanation as two methods that are used for identifying gene
    - Homework for Monday: Assume that a gene involved in increased muscle mass is expressed when the muscle cells are exposed to growth hormone. What would be the source of the cDNA library: muscle cells or muscle exposed to growth hormone? explain your answer.
- Colony Hybridization and PCR process explanation as methods for screening Cloned gene. Home works for Monday:
    - If gene sequence has NOT been cloned in another species but something is known about the protein, what can be done?
    - Assume you want to do 22 PCR cycles to amplify your DNA insert, how many copies of DNA will you have at the end of your PCR?
    - Why can't you use DNA Pol isolated from bacteria that live at 37 ℃?
    - Assume the human genome project was not completed but you wanted to clone growth hormone from humans, what sequence would you use to design PCR primers?
- Laboratory Techniques (Wet-lab techniques):
    - Sequencing and DNA structure: Agarose gel electrophoresis, Restriction mapping (RFLP), Sequencing Techniques (Computer-Automated DNA Sequencing (Capillary electrophoresis, NGS (Next Generation Sequencing) technology
    - Expression analysis: quantitative RT-PCR using TaqMan or SYBR Green, Microarray
- Bioinformatics (Dry-lab techniques): Applications, GenBank, NCBI, BLAST
- Genomics:
    - Whole-Genome Shotgun Sequencing technique, Human Genome Project (HGP)
        - Homework for Monday: Why are there only 20,000 genes coding for proteins when it was predicted that there would be 100,000 genes?
    - As a result of HGP: omics (Proteomics, Metabolomics, Glycomics, Transcriptomics, Metagenomics, Pharmacogenomics and personal medicine, Nutrigenomics), Comparative Genomics, Paleo-genomics.
    - After these: Human epigenomics projects, International HapMap Project (characterization of SNPs for their role in genome variation, disease and pharmacogenomics applications), ENCODE project (Encyclopedia of DNA elements), Personalized genome project, Cancer genome project

During class there were questions that professor asked us (for example about vectors, DNA library and PCR process), but almost all of them were simple for me. So, I answered them. But for other students they were new. As a result, my participation in the class was over 80%.

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31ST
JANUARY

MEDICAL
BIOTECHNOLOGY

The Sixth Session Report

16:45 PM – 19:00 PM

- Pre-clinical trials and model organisms as a human disease organism
- 3 phases of clinical trials:
    - Phase I (Safety and pharmacokinetics investigations)
    - Phase II (Effectiveness)
    - Phase III (Effectiveness comparison in patients with different background)
  - Human disease models for research of obesity, apoptosis, cancer, Alzheimer, Lou Gehrig, Huntington, Parkinson, Heart attack mice, HIV small animal model
  - Molecular diagnosis
    - Definition
    - Advantages: Improvement in sensitivity, High specificity, Cost less, Faster analysis time
    - Tests in order to human disease diagnosis: Amniocentesis, Chorionic villus sampling, Hybridization, RFLP (restriction fragment length polymorphisms), Single Nucleotide Polymorphisms (SNPs), Microarray
  - Applications of Medical Biotechnology: Pharmacogenomics and personalized medicine for example for cancer disease based on expression differences detected by Microarray, Improved drug delivery using polymeric targeted N.Ps, Vaccines and Therapeutic Abs
  - Gene therapy definition
    - Two types of methods for this goal: *Ex vivo*, *In vivo*
    - Two types of vectors for this goal: Viral, Non-viral targeted N.Ps like targeted liposome
    - Examples: severe combined immunodeficiency (SCID) treatment by using ADA gene, cystic fibrosis, Transmembrane conductance regulator (CFTR)
    - Challenges: Adverse effects of viral vectors, targeting specific cells, Controlling expression of the therapeutic gene, long lasting therapy
  - Regenerative medicine
    - Tissue engineering definition
      - Applications: Neuron regeneration, Bone regeneration, Blood vessel regeneration
    - Organ transplantation: Autograft and Xenograft
    - Bioprinting definition
    - Stem Cell: Adult, Embryonic, Induced Pluripotent Stem Cells (iPSCs)
    - Therapeutic Cloning and Reproductive cloning

MY PRESENTATION ABOUT COVID-19 VACCINES

19:00 PM – 20:00 PM

- Overview of Vaccination:
    - Definition
    - A brief history (Edward Jenner and Cowpox)
    - Mechanism (Memory lymphocytes)
    - Routs of administration (Injection, Orally, Spray)
- Overview of Vaccine ingredients (Antigen, Adjuvant, Preservative, Stabilizers, Antibiotics, Trace components)
- Overview of the types of vaccines (Definition, Advantages and Disadvantages, Production process and Immune response for each one): Inactivated (Killed), Live Attenuated Vaccine (LAV), Subunit, Toxoid, Virus like Nano particles, Recombinant viral vector vaccines
- Overview of different COVID-19 vaccines (Manufacturer, Platform, Efficiency, Dosage, Storage, Production process, Side effects): Moderna (mRNA 1273), Bharat (BBV152/ COVAXIN), SINOVAC (CoronaVac), Oxford/AstraZeneca (ChAdOx1-s-AZD 1222 (Covishield)), Gamaleya (Sputnik V (Gam Covid Vac) and Sputnik light), Novavax (NVX CoV2373), Sinopharm (BBIBP-CorV), Johnson & Johnson (JNJ-78436735/ Janssen vaccine), Pfizer-BioNTech (BNT162bb2)
    - Other vaccines (Approved Iranian Vaccines): CovIran Barekat, FakhraVac, Soberana 02, Razi Cov Pars, SpikoGen
- Effects of COVID-19:
    - Virus entry to a cell and its life cycle
    - Effects on lung, heart, kidney, liver, bladder and Brain
- Immune response to COVID-19 and Cytokine strom
- Virus escape form immune system
- Overview of Stem Cell therapy for COVID-19 injuries

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1ST
FEBRUARY

MEDICAL
BIOTECHNOLOGY

The Seventh Session Report

CANCER GENOMICS

12:30 PM – 13:30 PM (Because of a meeting)

- Cancer as a multifactorial genetic disease
- Comparison between different types of cancers based on incidence and Mortality
- Types of Cancer based on incidence factors: Hereditary Cancer, Familial Cancer, Sporadic cancer
- Two Hit Hypothesis definition
- Tumour Suppressor genes (Gate keeper and Caretaker, Protooncogenes and Oncogenes)
- Different types of mutagens: Initiation, Promotion, Progression
- Metastasis process: Primary tumour -> pre-malignant state -> Malignant progression -> Invasion and dissemination -> Metastatic colonization
- Most common mutated genes in cancer
- Different results of low-level mutation and high-level mutation for a cell
- Cancer Genomics Projects definition and its applications:
    - Finding new cancer genes (cancer drivers)
    - Finding new therapeutic targets
    - identify molecular signatures to stratify tumors
    - Move towards personalized cancer treatment

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2ND FEBRUARY

MEDICAL BIOTECHNOLOGY

The Eight Session Report

EPIGENOMICS, PHARMACOGENOMICS

13:30 PM – 15:30 PM

- Epigenetic definition and its difference with Genetics
- Epigenetic molecular mechanisms and their effects on gene expression: DNA methylation, Chromatin modification (Histon acetylation, Histon methylation, Histon phosphorilation), non-coding RNAs (lnRNA, microRNA)
    - Examples: X inactivation, Epigenetic Changes Associated with Cell Differentiation, Genomic imprinting (Igf2 gene, H19 gene), Epigenetic effects in monozygotic twins

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- Pharmacogenetics definition and definition and features of two important parts of it:
    - Pharmacokinetics: Absorption, Distribution, Metabolism, Excretion
    - Pharmacodynamics: Receptors, Ion channels, Enzymes, Immune system
- Goals of Pharmacogenomics:
    - Maximize drug efficacy
    - Minimize drug toxicity and its side effects
    - Predict patients who will respond to intervention
    - Aid in new drug development
- TPMT gene product and 6MP drug as an example
- Different stages of enzyme activity in pharmacogenomics for drug metabolism:
        - EM (Extensive metabolizer): Normal enzyme activity -> Need Normal dose of drug
        - PM (Poor metabolizer): low enzyme activity -> Normal dose of drug can be toxic and dangerous because of its side effects. So, they need decreased amount of drug
        - IM (Intermediate metabolizer)
        - UM (Ultra-rapid metabolizer): Need more dose of drug
- Pharmacogenomics challenges:
        - Paucity of studies -> Still much to be learned
        - Needs Genome sequencing

CLASSMATE PRESENTATIONS

15:30 PM – 16:00 PM

- A brief description about COVID-19, Its symptoms and spread
- Immune response to COVID-19
- Structure of SARS-CoV-2 (Spike protein, Nucleocapsid protein, Membrane protein, Envelope protein, RNA viral genome)
- SARS-CoV-2 life cycle
- Proposed treatment: Vaccines
    - Components of vaccines
    - Different types of vaccines
- COVID-19 diagnosis assays: qRT-PCR, ELISA test strip, CT-scan

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15:30 PM – 16:00 PM

- Two types of psychological treatment:
    - Psychosocial treatment
    - Psychobiological treatment
- Different types of Brain neuroimaging technology as a necessary tool for psychobiological treatment: MRI, dMRI, fMRI, EEG/MEG, ECoG, Modeling
- Depression definition
- Biological viewpoint of depression: GABA (Gamma amino butyric acid) Neurotransmitter receptor dependent signaling pathway -> Point mutation in hippocampus (learning and memory area of the brain) for studying its role -> After activation can't inhibited by picrotoxin (A chemical compound that blocks chloride channels to inhibit receptor activity) -> Activating receptors has Antidepressant effects for example serotonin is an antidepressant.
- Epigenetic regulation: in neurogenesis, neural plasticity, depression formation and memory of depression for example: related heritable DNA methylation and Histon modification (Histon acetylation/deacetylation, Chromatin remodeling) and ncRNA
    - For example:
        - Hypomethylation and over expression of SLC6A4 gene -> depression.
        - BDNF gene, NR3C1 gene methylation -> depression
    - Signaling pathways about epigenetic role in depression

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4TH
FEBRUARY

MEDICAL
BIOTECHNOLOGY

The Ninth Session Report

BIOINFORMATICS

13:30 PM – 16:30 PM

- Bioinformatics definition and its related fields
- Comparison between Bioinformatics and Computational biology
- Bioinformatics brief history (DNA, Protein)
    - Edman peptide sequencing and its disadvantage
    - The first bioinformatic software
    - Paleogenetic and evolutionary genetics
    - Multiple sequence alignment (MSA)
    - Sanger sequencing and Maxam-Gilbert sequencing
- Bioinformatics advantages and applications:
    - Storage and Organization
    - mRNA processing data
    - Gene expression analysis
    - Proteome (Prediction of Function and Structure)
    - Big data and meta-analysis
    - Health and drug discovery
    - Tool development
    - Algorithm and Statistic development
- Characterization of Bioinformatician:
    - Maths: Statistics, Artificial Neural, Network, Algorithm, Data analysis, Regression analysis, Scatter charts, Modeling
    - Life sciences: Epigenetics, Genetics, Protein, Biology, Molecular Biology, DNA, RNA
    - Programming: Python, R, Bash, Java, JavaScript, C/C++
- Biological databases:
    - Primary databases:
        - Nucleotide sequence databases: NCBI, EMBL, DDBJ
        - Protein sequence databases: Swiss-Prot, PIR, Uniprot, PDB (Structure)
    - Secondary databases: Prosite, Print, Blocks, Profiles, Pfam
    - Other databases: KEGG, GEO, dbSNP, Reactome, OMIM, …
- Bioinformatic skills: PubMed, Gene database, GeneBank, FASTA, Infevers database, Nucleotide database, BLAST, Primer designing by NCBI, Ensemble, CCDS, Uniprot, Genome browser, Primer BLAST

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4TH
FEBRUARY

MEDICAL
BIOTECHNOLOGY

The Last Session Report

CLASSMATE PRESENTATIONS

17:30 PM – 19:00 PM

- CRISPR-Cas9:
    - Introduction and Definition
    - Development process
    - Main Principle and How it works
- Comparison between different CRISPR systems (Why Cas9?)

- Cancer Immunotherapy:
    - History of cancer immunotherapy (Dr. William Coley's mixed bacterial toxin)
- Immunosurveillance, Immunotherapy and Cancer immunotherapy definition
- Immune system function
- Types of immunotherapies:
    - Dendritic cell vaccines
        - Examples: Sipuleucel-T, ProstVac,
    - Antibody therapy:
        - Types of Ab: Naked/ Conjugated
        - Based on source: Murine/ Chimeric/ Humanized/ Human
        - Mechanism
        - Examples: Nivolumab, Rituximab,
    - Immunomodulator (Cytokine) therapy (IFN-α, IL-2)
    - Adoptive T cell therapy:
        - Tumour-Infiltrating Lymphocyte (TIL) therapy
        - Engineered T-Cell Receptor (TCR) therapy
        - Chimeric Antigen Receptor (CAR) T cell therapy
        - Natural Killer Cell therapy
    - Checkpoint inhibitor therapy
    - Combined therapy: Coincubation of Herceptin (Trastuzumab (Targets ERBB2)) and NK Cells

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- Pharmacogenomics of Anti-Platelet Intervention (PAPI): Variation in Platelet response to Clopidogrel and Aspirin
    - Pharmacogenomics definition
    - Study protocol and intervention
        - Review of personal and family history, Measurement of blood pressure and its cell counts, kidney and liver function test, Measurement of TSH level, Smoking history
        - Platelet aggregation tests: Before Clopidogrel administration, Post Clopidogrel, (Post Dual Anti-Platelet Therapy) DAPT

19:15 PM – 19:30 PM
GENE THERAPY and CRISPR/Cas9

- Comparison of *Ex-vivo* gene therapy and *In-vivo* gene therapy
- Clinical trials based on Years, advances, Geographical Distribution, Vectors, Diseases
    - Examples: Edited T cells by CRISPR/Cas9 for Cancer immunotherapy, Wolframs Syndrome Treatment, β-Thalassemia Treatment, SMA Treatment, Motor Neuron Diseases Treatment, β-cell malignancies treatment, Type 1 Diabetes Treatment
        - In Turkey: Useful for treatment of different heritable disease because in Turkey marriages usually are between relatives.
- Top 30 CRISPR companies
- A Book and Documentary about it: THE CODE BREAKER, ~~un~~natural selection

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19:30 PM – 19: 40 PM
Ethics in Medical Biotechnology

- Ethics Definition,
- Ethical Decision: Statistic probability / Risk assessment
- Moratorium: After Recombinant DNA technology -> A temporary but complete stoppage of any research in this field until its safety and possible consequences assessed.
- Ethical issues about GMO
- Cloning Human and other animals for any reason
- Genetic information
- Biotechnological doping

19:30 PM – 20: 40 PM
Human Genome Project

- The Race to sequence the human genome between H.G.P (Shotgun sequencing using BAC) and CELERA (Shotgun sequencing)
- Review of difference between genetics and genomics
- Sequencing applications: SNPs, Cloning gene and animal, …
- DNA Sequencing methods: Discovery of DNA structure and function -> Early DNA sequencing methods (Sanger chain termination method (Classic and Modern (Capillary electrophoresis)) and Maxam-Gilbert sequencing method) -> Large scale sequencing methods (Shotgun sequencing, NGS (Next generation sequencing)) -> NGS data analyzing and alignment and its bioinformatical challenges