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UNIVERSITY OF MYSORE

(Estd.1916)

PROFESSIONAL CERTIFICATE PROGRAM IN PERSONALIZED GENOMIC MEDICINE

Choice Based Credit System (CBCS)

UNIVERSITY OF MYSORE

NEW PROGRAM

Post –graduate Certificate Program:

Professional Certificate Program in Personalized Genomic Medicine

Two Semester Choice Based Credit based Scheme
&
Continuous Assessment of Grading Pattern System

(CBCBS-CAGP SYSTEM)

SYLLABUS

DEPARTMENT OF STUDIES IN GENENTICS AND GENOMICS
MANASAGANGOTRI
MYSURU – 570 006

2017-18

Chairman
Department of Studies in
Genetics and Genomics
University of Mysore
Manasagangotri
Mysore-570 006

PREAMBLE:

The professional certificate program is designed to provide advanced knowledge dissemination in the field of genome sciences, applications and laboratory skills needed for molecular diagnostics and precision medicine procedures conducted in a clinical or research environment. The program is intended for those individuals who wish to enhance their laboratory expertise and knowledge in molecular-based methods.

Precision medicine has the potential to fundamentally change how health care is practiced, but requires a trained health care workforce that understands the complexities of this field. One important component of precision medicine is the use of an individual's genomic information to offer targeted treatment, tailored to the individual. Our course aims to provide participants with advanced knowledge of genomics, an overview of the clinical applications of genomic medicine, the skills to evaluate the clinical validity and utility of new tests, and an appreciation of the associated ethical and social issues inherent in this field.

The course is geared towards individuals with a background in the biological sciences and a basic understanding of genetics. It is designed to be succinct and clinically focused, offering both conceptual and practical information about real-world applications of genomics. The syllabus offers a basic knowledge on genomics relevant to the individual patient as well as to patient populations. Further, the lessons also focus on applications of genomics and present the material as case studies, highlighting the strengths, limitations, and issues that arise in the use of each test.

As technology advances the knowledge base of our scientific workforce needs be in pace for the growing demand. Next-generation sequencing (NGS) has the potential to make genome sequencing an integral aspect of personalized medicine in the near future. The sensitivity and specificity of genetically characterizing mutations in patients has profound implications for treatment choices and predicting potential responses. NGS is arguably one of the most significant technological advances in biological sciences of the last 30 years; we therefore should provide scientific workforce capable of exploiting various NGS platforms to help in advancing the quality of health care.

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Objectives of the course:

a. To impart extensive theoretical and practical knowledge required for genomic personalized precision medicine
b. To create and train scientific workforce to meet the growing pace of Next-generation sequencing (NGS) in clinical genomics
c. To train and conduct research on valid clinical subjects

Number of seats per year: **10**

Mode of selection of students: **National Level Written Test to be conducted by the University of Mysore**

Eligibility for admission

- Post-Graduate in Medical Science (MD)
- Post-Graduate in Basic Sciences in Biotechnology/Genetics/ Applied Genetics/Genomics/Molecular Biology/Biochemistry/ Zoology/Life Sciences or in equivalent areas
- Post-Graduate in Engineering Sciences (e.g. M.Tech in Biotechnology)
- Post-Graduate in Pharmaceutical Sciences (MPS)

Course Format

1. This is a Professional certificate course with 20 credits spanning 6 months including examination.
2. The program consists of lecture-based sessions, hands-on laboratory sessions and research dissertation. Classroom lectures and laboratory sessions are offered based on realistic scenarios. For the certificate, students must complete all credit hours (20) with a 5.5 grade point average.
3. Course is aimed at generating genome analysis specialists in the field of clinical genetic diagnosis.

Internship

Students who successfully complete the above credits will be given opportunities to intern with the below selected companies on the prospect that it will be potentially converted into jobs on their abilities.

1. Xcelris Labs, Ltd, Ahmedabad
2. Genotypic Technologies, Bangalore
3. Strand Life Sciences, Bangalore
4. SciGenom Labs, Cochin
5. Data Genetics Ltd, Mumbai
6. KnowYourGenome Labs, Mysuru
7. X-Code Lifesciences, Chennai
8. Map My Genome, Hyderabad
9. SRL Diagnostics Lab, Gurgaon
10. Molecular connections, Bengaluru

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CREDIT MATRIX FOR

PG Certificate Professional Program in Personalized Genomic Medicine

2017-18

Semester I						
Paper code	Title of the Course	HC/SC	L	T	P	Credit
1.1	Human Genetics and Genomics	HC	4	0	0	4
1.2	Personalized Genomic Medicine	HC	4	0	0	4
1.3	Interactive Session	HC	0	2	0	2
1.4	Major Project	HC	0	2	4	6
1.5	Practical 1	HC	0	0	2	2
1.6	Practical 2	HC	0	0	2	2
					Total Credits	20

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Professional Certificate Program in Personalized Genomic Medicine

Paper 1: Human Genetics and Genomics — 64 Hrs

Unit I & II — 16 Hrs

i) Introduction to Human Genetics: Introduction to human genetics, human chromosomes, karyotyping, chromosome structure, function and implications for disease, human genome organization, gene organization, gene expression and regulation- at chromatin level, transcription and translational levels, epigenetics and epigenomics.

ii) Tools in Human Genetics: Pedigree analysis, Patterns of Inheritance, Mendelian inheritance and exceptions; Human genome mapping methods: Genetic mapping: Linkage analysis (RFLP/MS/SNP); Genome-wide association studies, Gene identification using positional and functional cloning approach, Physical mapping: DNA markers, Fluorescence in situ hybridization, comparative genome hybridization, long range restriction mapping, high resolution mapping STS/EST/MS/SNP/sequencing; Applications of mapping in normal and disease genomes; SNP Genotyping: Massarray-Snapshot technique, Axiom genotyping, Sequenom MassARRAY iPLEX Platform.

Unit III & IV — 16 Hrs

ii) Genomic variations: Single Base Variations (Synonymous, Nonsynonymous, Stop gain, read through, splice site, promoter and TFBs mutations/polymorphisms), Multi Base Variations (Insertions, Deletions, Frame shift), Copy Number Variations (Duplications, Deletions), Gross mutations (Translocations, Inversions).

iii) Genetic Diseases and Disorders: Monogenic disorders, Complex genetic diseases and disorders, Syndromes.

Unit V — 8 Hrs

i) **Genome projects:** The Human genome project, HapMap Project, The 1000 genome project, and The ENCODE Project, Human Epigenome Project.

ii) **Epidemiology:** Diseases in Populations, population specific diseases and protection, Minor allele frequency, genome architecture between populations, adaptive evolution of human genome.

Unit VI — 8 Hrs

iii) **Structural genomics:** (a) Assembly of a contiguous DNA sequence, whole – genome shotgun sequencing. (b) Understanding a genome sequence: locating the genes in a genome sequence, determining the functions of individual genes.

iv) **Functional genomics**: Study of transcriptome (By RNAseq, and Microarray analysis) and Proteome (Interacting proteins by phage display and Yeast two hybrid system, In vitro translation).

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UNIT VII & VIII — 16 Hrs

i) Human-Microbial Genomics: Introduction to Metagenomics, Comparative Microbial Genomics: From Sequence to Significance, Infectious Diseases, Emerging Infectious Diseases, Immunology of Infectious Diseases, Metagenomics - Microbial gut flora, Gut-Brain axis, Molecular Phylogenetic Techniques.

ii) Applications of Genetics: Gene therapy (Viral and Non-viral methods), Stem cell genetics, Stem cell therapy, RNAi: RNAi in treatment, miRNAs in cancer: tumor suppressors and oncogenes.

Paper 2: Personalized Genetic Medicine — 64 Hrs

Unit I & II — 16 Hrs

Genomic Tools 1:

i) Genome Structure and Sequence: Whole Genome Sequencing (WGS) (Illumina, Ion, PacBio, MinION), Whole Exome Sequencing (WES) (Agilent capture kits, Illumina-Truseq, Nextera), Targeted Sequencing, Disease specific panels (Cardiac, Brain, Lung diseases), Cancer panels (all onco panels), and Nutri-genomics panel to identify mutations.

ii) Transcriptome: Real-Time RT-PCR, Microarray, and RNAseq of Disease Cells Vs Normal Cells and Tumor cells Vs Normal Cells.

iii) Proteome: Human Protein Atlas, Human Proteome Map, Protein Networks: String and GeneMANIA Proteome: Co-expression, Co-localization, Physical Interactions, Genetic Interactions, Pathways and Shared Protein Domains of proteins, Tools to understand LC-MS, MS and 2D.

iv) Biological pathways: Ingenuity Pathway Analysis, Elsevier Pathway Studio, Biocyc, KEGG, WikiPathways, Pathway Commons, and networks based pathway builder.

Unit III & IV

Genomic Tools II: — 16 Hrs

i) Cancer Genome: Identifying driver and passenger gene mutations using CRAVAT and other tools, Identifying translocations (balanced and unbalanced) and inversions, Identifying enhancer elements near translocations and inversions.

ii) Regulatory regions: Identifying transcription factors for a coding gene using Transcription Factor Databases like PAZAR and others. Identifying enhancers in the human genome and annotating them to identify mutations in genome. Identifying promoters and transcription factor binding sites for genes.

iii) miRNA genome: Identifying gene targets for miRNAs (miRdb and others), identifying regulatory miRNA's for coding genes, identifying miRNA-mRNA binding sites, Understanding the role of 3'UTR mutations and miRNA gene mutations in altered miRNA-mRNA pairing using BiBiServ-RNA Hybrid.

iv) Role of mutations in Translational Regulatory regions: 5'-cap, secondary structures, multiple uAUGs (up-stream AUGs), IRESs (internal ribosome entry sites), positioning of AUG sequence in Kozak's context, polyadenylation signals and motifs,

such as IREs (iron-responsive elements), and Ribosome Binding Sites using MIRVAS and other tools.

Unit V & VI

Personalized Genomic Medicine I: **16 Hrs**

i) **Using WGS/WES**: NGS Raw data FASTA Sequence alignment, Genome assemblies of NCBI and UCSC, Variants calling, .VCF files, .VCF annotations, Pipelines for disease specific and traits specific mutation identification, mutation annotation (wANNOVAR, SG-ADVISER and others), gene enrichment analysis, disease gene and candidate gene identification strategies, gene-protein and protein-protein network construction, gene-based drug selection (PharmGKB, DrugBank, DGIdb, Druggable Human Proteome), Building pathways using genes bearing mutations, strategies for identifying both known and novel genes for diseases, strategies for identifying both known and novel mutations/polymorphisms in genes, disease risk and protection assessment.

ii) **Nutrigenomics**: Identifying good and poor metabolizers.

iii) **Genotype based**: drug toxicity estimation, drug response efficacy, and drug dosing recommendations. Personalized Genomic Medicine map creation, clinical development of drugs and biologics, drug repositioning, personalized report preparation, strategies for deciding treatment options, counseling patient and family members, ethics and conversing with clinicians and healthcare personnel.

VII & VIII

Personalized Genomic Medicine II: **16 Hrs**

i) **Microarray Transcriptome**: Clinical & molecular diagnostics using microarray, microarray based gene expression in cancer cells for personalized treatment, identifying molecular targets for cancer, tumor profiling for targeting cancer treatment and the use of blood-based gene expression profiles in cancer prognosis.

ii) **Next Generation Sequencing:** The use of next-generation sequencing for solving diagnostic dilemmas, Methods used in patient populations to uncover associations between genome variation and common diseases, Predictive tests for common, complex diseases.

iii) **Drug Development:** Pharmacogenomic testing for drug selection, dosing and predicting adverse effects of commonly prescribed drugs, drug-drug interactions.

Paper 3: Interactive Session **32 Hrs**

Paper presentation, Counseling skills and Discussion of utility of NGS in clinical diagnostics and personalized medicine

Paper 4: Major Research Project 6x2x16= 192 Hrs

Case Studies - Addressing a scientific issue using experimental tools and submission of the report.

Paper 5: Practical -1 16X 4 = 64 Hrs

1. Visit to (a) genetics and genomic diagnostics company, (b) Institution of Excellence, Vijnana Bhavan, University of Mysore for whole Genome/Exome Sequencing demonstration using NGS.
2. Isolation of DNA from Human Blood by phenol-chloroform extraction method.
3. DNA amplification by PCR method and cloning by TA cloning method (Ligation, competent cell preparation and Transformation).
4. Isolation of recombinant DNA, Restriction digestion, and electrophoresis.
5. Isolation of mRNA from blood, cDNA conversion and quantification of expression of any gene of interest.
6. CNV duplication mapping and Deletion Mapping techniques
7. Whole genome expression analysis using microarray, integrating expression data with variant annotations, enrichment analysis, and eQTL regulatory protein relationships.
8. Whole genome expression analysis using RNASeq.
9. Methylation detection using Bisulfite sequencing using PCR.

Paper 6: Practical -2 16X 4 = 64 Hrs

1. Processing .fastq/.bam/.vcf files in several genome aligning programs to perform genome alignment using NGS PROGRAMS: StrandNGS, SVS Golden Helix, Genome Browser, CLC Genomics Workbench, and NCBI Workbench.
2. Performing genome alignment, Whole genome/exome sequence analysis, variant annotations of SNP, InDels and CNVs (VeP, wANNOVAR, SG-ADVISER, IVA etc.), pathway and network establishment.
3 Whole genome/exome sequence analysis, variant annotations of SNP, InDels and CNVs using Variant Analysis Programs: customized pipelines, Ingenuity Variant Analysis, wANNOVAR, Ensembl-VeP (Variant effector Predictor), and regulomeDB.
4. Whole Genome Scans using Microarray based Genome-Wide SNP 6.0 chip.
5. SNP Data Analysis using Golden Helix program and Affymetrix Genotyping Console and CNV Association Software, Genome-wide Association study, CNV studies and CNV annotation.
6. Integrating NGS and expression data in Ingenuity Pathways Analysis and Ingenuity Variant Analysis to identify upstream and downstream targets.
7. Whole Genome sequence analysis to identify structural variations (Gene, Mutations, and Polymorphisms) and their enrichment analysis.

8. Genome-wide Hot-spot detection using HD-CNV and Circos plot generation.
10. Expression and Enrichment analysis: GenespringGX, Affymetrix Transcriptome Analysis Console, WebGestalt, EnrichR, Gorrila, and DAVID.
11. Protein Interaction Network Programs: Cytoscape-GeneMANIA, Ingenuity Pathway Analysis (IPA), Pathway Studio, KEGG and Wikipathways, and Pathway Commons.
12. In silico protein modelling, drug target prediction, 3D drug molecule structure and drug-protein docking

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