PROGRAM INTERDYSCYPLINARNYCH STUDIÓW DOKTORANCKICH WYKORZYSTUJĄCYCH SEKWENCJONOWANIE NOWEJ GENERACJI (NGS) W MEDYCYNIE SPERSONALIZOWANEJ

Program realizowany w ramach Programu Operacyjnego Wiedza Edukacja Rozwój na lata 2014–2020, w ramach działania 3.2 Interdyscyplinarne Programy Studiów Doktoranckich.

Program obejmie listę wykładów i zajęć praktycznych dotyczących projektów badawczych wykorzystujących sekwencjonowanie nowej generacji (NGS) w medycynie spersonalizowanej oraz ćwiczenia ze sztuki prezentacji, pisania grantów i podstaw prawnych komercjalizacji i własności intelektualnej.

Lista wykładów i zajęć praktycznych podzielonych na:

Szkołę wiosenną *From gene to phenotype* z warsztatami z biostatystyki.
Liczba zajęć: 24 x 45 minut

Szkołę letnią *Workshop on visualisation of molecules, interactions and biological processes by molecular methods* połączoną z warsztatami z cytometrii przepływowej i nowoczesnej mikroskopii. Ćwiczenia ze sztuki prezentacji, pisania grantów i podstaw prawnych komercjalizacji i własności intelektualnej.
Liczba zajęć: 24 x 45 minut

Szkołę jesienną *High throughput genomic and transcriptomic technologies in biomedicine* połączoną z warsztatami z izolacji RNA/DNA z tkanek i komórek, oraz zastosowania sekwencjonowania nowej generacji (NGS) w medycynie spersonalizowanej.
Liczba zajęć: 24 x 45 minut

Szkołę zimową *Soft skills workshop.*
Liczba zajęć: 6 x 45 minut

SPRING SCHOOL

FROM GENE TO PHENOTYPE

– ADVANCES IN MOLECULAR BIOLOGY AND BIOMEDICINE

Program wykładów obejmujących diagnostykę molekularną i metody bioinformatyczne w zastosowaniu do badań nad patomechanizmami chorób i diagnostyce molekularnej chorób rzadkich i cywilizacyjnych.
24 godz. zajęć, pierwszy semestr, I rok studiów

Day 1 – DECIPHERING GENOMES AND TRANSLATIONAL MEDICINE

Lecture 1 (45 minutes)

– Breaking the human genome sequence – hopes and challenges

- Origin of the human genome project
- Current state of the human sequencing projects
- Introduction to the application of human sequencing in diagnostics

Lecture 2 (45 minutes)

– Lessons from the studies on the pathogenesis of chronic myeloid leukemia

- Molecular classification of CML
- Molecular mechanisms of CML pathogenesis
- Rational drug design and treatment of CML

Lecture 3 (45 minutes)

– From target to drug: medicinal chemistry approaches

- Evolution of targeted drug design methods
- Target selection and molecular design approaches
- Introduction to drug delivery systems

Lecture 4 (45 minutes)

– From mother to embryo: gene regulation during early embryogenesis

- Animal models to study development
- Genetic modifications that allow for visualization of early embryogenesis
- Modern methods to study genes in development

Lecture 5 (45 minutes)

– Emerging insights into brain tumor pathogenesis and therapy

- Molecular diagnosis and tumor classification
- Emerging trends in brain tumor treatment
- NGS based approaches to evaluate prognosis and monitor modern therapies

Lecture 6 (45 minutes)

– Integrating diverse datasets in functional genomics

- Mathematical tools to analyze and integrate datasets
- Precision functional genomics, an attempt to phenotypically characterize genetic variants
- Tumor genetics coupled with a variant characterization atlas may ultimately guide clinical decisions

Lecture 7 (45 minutes)

– Cellular resource and stress management:

- Molecular bases of stress response
- Medical relevance of studying stress responses
- Mitochondria in stress and diseases

Lecture 8 (45 minutes)

– Animal models to understand brain diseases

- Animal models of neurodevelopmental disorders
- Animal models of neurodegenerative disorders
- Advantages and limitations of animal models of brain diseases

Day 2 – RNA AND DNA WORLD

Lecture 1 (45 minutes)

– Cryo-EM – revolution in structural biology

- The history of Cryo-EM development
- Most important discoveries that were possible thanks to Cryo-EM technology
- The basics of “how it works”

Lecture 2 (45 minutes)

– Eucaryotic gene expression

- The mechanism of RNA Polymerase II transcription elongation
- Mechanism of splicing
- Interconnection between transcription and splicing

Lecture 3 (45 minutes)

– mRNA based gene therapy – dream or reality?

- The history of first clinical trials
- Molecular mechanisms of mRNA based gene therapy
- Development of the technology

Lecture 4 (45 minutes)

– Tuning protein production using tRNA modifications

- Mechanisms of translation
- tRNA structure and function
- tRNA modifications

Lecture 5 (45 minutes)

– microRNAs in Arabidopsis plants

- How does the microRNA work and how they were discovered
- Differences of miRNA processing between plants and metazoa
- Posttranscriptional regulation of microRNA expression

Lecture 6(45 minutes)

– Mechanisms of RNA decay

- Enzymes involved in RNA decay
- Nuclear RNA turnover
- Cytoplasmic RNA turnover

Lecture 7 (45 minutes)

– Gene silencing – mechanisms and applications

- RNA silencing mechanism
- Application in scientific research
- Application in medicine

Lecture 8 (45 minutes)

– Genome editing, CRISPR technology and beyond

- Basic mechanisms of genome editing
- CRISPR revolution and its use in generation of transgenic animals
- Applications of genome editing in therapy

Lecture 9 (45 minutes)

– Single cell sequencing and its application

- Basic of single cell sequencing
- Application of single cell sequencing to reveal tumor heterogeneity
- Examples of transcriptome analyses by single cell sequencing

Lecture 10 (45 minutes)

– Is personalized medicine a real breakthrough?

- What is a personalized medicine?
- Development of the modern, NGS based diagnostic techniques in biomedicine
- Application of NGS based diagnostic techniques in biomedicine

Day 3 – GENE EXPRESSION AND EPIGENETICS

Lecture 1 (45 minutes)

– How to decipher epigenetic code?

- Writers readers and erasers
- Impact of epigenetic modifications on gene expression
- Modern tools for the analysis of epigenetic modifications

Lecture 2 (45 minutes)

– Chromatin and nuclear architecture remodeling – a new mechanism of epigenetic regulation in the brain

- The structure of chromatin
- Molecular mechanisms regulating nuclear architecture
- Importance for gene expression regulation

Lecture 3 (45 minutes)

– Advances in genetic tools and alternative animal models in biomedical research

- Novel genetic models to study animal development
- *Danio rerio* as a model to study development and human diseases
- Manipulation in *Danio rerio* to model human diseases

Lecture 4 (45 minutes)

– Alzheimer's disease: development of novel models, biomarkers and therapies

- Diagnostics methods and mechanisms of Alzheimer's disease (AD)
- Development of early prognosis markers
- Modern therapies in AD

Lecture 5 (45 minutes)

– Role of microRNAs in human neurodegenerative disorders

- Mechanisms of microRNA action
- Role of microRNAs in muscle regeneration and Duchenne muscular dystrophy
- Duchenne muscular dystrophy as a model for RNA-based therapies

Lecture 6 (45 minutes)

– Computational modeling of 3-D chromatin and nuclear architecture

- Molecular, NGS based methods to collect information about chromatin conformation (3-C, 4-C, HI-C)
- Computational modeling of 3-D chromatin
- Molecular mechanisms regulating nuclear architecture

Workshop on biostatistics

Interactive workshop on biostatistics (personal computers required).

- Introduction to basic methods for determining statistical significance *(45 minutes)*
- Selecting statistical tests for specific studies *(45 minutes)*
- Application of statistical methods to NGS sequencing data analyses. *(45 minutes)*

SUMMER SCHOOL

WORKSHOP ON VISUALIZATION OF MOLECULES, INTERACTIONS AND BIOLOGICAL PROCESSES BY MOLECULAR METHODS

Day 1

Lecture 1 (45 minutes)

– Pluripotent stem cells – introduction

- Characteristics of the pluripotency
- Embryonic stem cells and progenitors
- Pluripotent stem cells in the adult organisms

Lecture 2 (45 minutes)

– Cancer stem cells: biology and therapeutic targeting

- What are cancer stem cells (CSC) and NGS application to demonstrate tumor heterogeneity
- Importance of CSC in cancer development
- Specific targeting of cancer stem cells by modern therapies

Lecture 3 (45 minutes)

– Molecular mechanisms of invasion and cancer cell plasticity

- Cancer invasion and the microenvironment
- Molecular changes underlying switch toward the migratory phenotype
- Plastic changes to adapt to the new microenvironment

Lecture 4 (45 minutes)

– Intracellular trafficking in neurons

- Mechanisms of intracellular trafficking
- Intracellular trafficking of proteins and mRNAs to axons and dendrites
- Human diseases related to dysregulation in intracellular trafficking in neurons

Lecture 5 (45 minutes)

– Epigenetics of the induced pluripotency

- Modern tools for reprograming of the cell to induced pluripotency
- Epigenetic barriers on the way to effective cellular reprograming
- importance in therapy

Lecture 6 (45 minutes)

– Cellular senescence – a dynamic phenotype that influence organismal ageing and age-related diseases.

- Definitions and methods to study cellular senescence
- Metabolic changes in the cell during senescence
- The role of senescence in organismal ageing and age-related diseases

Practicals in neuronal/flow cytometry

Day 2

Lecture 1 (45 minutes)

– Xenopus as tools for understanding gene regulation and function

- Introduction into Xenopus based research
- Xenopus eggs as a “living tube” to study the molecular basis of development
- Application of genome editing in Xenopus to model human diseases

Lecture 2 (45 minutes)

– Adult stem cells in tissue specific regeneration

- Sources of adult stem cells and methods of their detection
- Applications of stem cells in tissue specific regeneration
- Considerations of the safety of the regenerative therapies based on adult stem cells

Lecture 3 (45 minutes)

– Multidisciplinary approach to tissue reconstruction and regeneration

- Methods and materials for tissue reconstruction
- Modern approaches to tissue reconstruction and regeneration
- Growing 3-D organs in vitro and their application in biomedicine

Lecture 4 (45 minutes)

– Circulating tumor cells and circulating tumor DNA

- Introduction to methods for detection of circulating tumor cells and circulating tumor DNA
- Role of circulating tumor cells in metastasis

- Importance for early patient prognosis and determination of appropriate tailored treatments

Lecture 5 (45 minutes)

– Neutrophil extracellular traps in autoimmunity

- Molecular mechanisms of generation of extracellular traps
- Methods of detecting and analyzing neutrophil extracellular traps
- Role of neutrophil extracellular traps in autoimmunity

Practicals in neuronal cell cultures/confocal microscopy

(3 x 45 minutes)

Day 3

Lecture 1 (45 minutes)

– Mechanisms of tumor immune evasion

- Basic mechanism of immune surveillance
- Understanding the molecular mechanisms of tumor immune evasion
- Mechanisms of tumor escape from immune surveillance

Lecture 2 (45 minutes)

– Advances in immunotherapy

- Development of immunotherapeutic approaches
- Check point inhibitors and CAR T cells in anticancer therapy
- Personalization of immunotherapy treatment

Lecture 3 (45 minutes)

– Visualization of synaptic remodeling

- Modern techniques to visualize neurons in vivo and in vitro
- Visualization of the single synapses on the dendritic spines
- Synaptic remodeling in the response to neuronal stimulation

Lecture 4 (45 minutes)

– Extracellular vesicles – a new tool for tissue repair

- Visualization of extracellular vesicles (EVs)
- EVs as biomarkers in joint diseases

- EVs as a new tool in tissue regeneration

Lecture 5 (45 minutes)

– Visualizing functions of mitochondria

- Functions of mitochondria in the cell, beyond ATP synthesis
- Methods to study mitochondrial metabolism
- Visualizing of functional mitochondria in the cells

AUTUMN SCHOOL

HIGH THROUGHPUT GENOMIC AND TRANSCRIPTOMIC TECHNOLOGIES IN BIOMEDICINE

Program obejmuje metody sekwencjonowania DNA i RNA za pomocą NGS oraz metody bioinformatycznej analizy w zastosowaniu do badań nad patomechanizmami chorób i diagnostyce molekularnej chorób rzadkich i cywilizacyjnych.

Liczba zajęć: 24 x 45 min.

Day 1 – NEXT GENERATION SEQUENCING IN GENOMICS, TRANSCRIPTOMICS AND EPIGENOMICS

Lecture 1 (45 minutes)

– Tumor heterogeneity and stemness across tumor types

- NGS in dissecting interpatient and intrapatient heterogeneity
- The significance of antitumor heterogeneity and its effect of microenvironment
- Heterogeneity and stemness of particular tumor types

Lecture 2 (45 minutes)

– Immune tumor evasion mechanisms in lymphoma

- Immune tumor evasion mechanisms of classical Hodgkin lymphoma
- Hodgkin lymphoma as an example of targeted treatment
- New immunotherapy approaches.

Lecture 3 (45 minutes)

– Discovering novel rare mutations with NGS

- Sequencing of genomes in different populations, determining mutation frequencies and polymorphisms
- NGS – early and current techniques to identify genomic alterations

- Correlation genotype-phenotype

Lecture 4 (45 minutes)

– Reproducibility in science – power and limitations of RNA-Seq

- Big data analysis, advantages and problems
- Building of mathematical models on big data analysis
- Experimental validation of the data

Lecture 5 (45 minutes)

– Predicting synthetic lethality in cancer

- A concept of synthetic lethality in cancer
- Predicting cancer-specific vulnerability via data-driven detection of synthetic lethality
- Validation of synthetic lethality in cancer

Lecture 6 (45 minutes)

– Deregulation of epigenetics in cancer

- Targeted sequencing in discovery of deregulation of epigenetics in cancer
- Molecular mechanisms of deregulation of epigenetics in cancer – the mutated IDH1/2 case
- Molecular mechanisms of deregulation of epigenetics in cancer – histone variant mutations

Lecture 7 (45 minutes)

– NGS data analysis to identify differences in pathogenesis of leukemia/lymphoma among patients with inherited DNA repair defects

- NGS in discovering pathogenesis of leukemia/lymphomas
- NGS as a diagnostic tool in the identification of molecular identity of tumors
- Inherited DNA repair defects in leukemia/lymphomas

Lecture 8 (45 minutes)

– NGS data analysis to identify alterations in pathogenesis of brain tumors

- Application of targeted sequencing to unravel pathogenesis of gliomas
- NGS as a tool for more accurate diagnostics
- Potential applications of NGS in personalization of brain tumors treatment

Wet lab workshop on isolation of RNA/DNA from tissue samples; measuring quality of RNA/DNA; preparing libraries for sequencing *(3 x 45 minutes)*

Day 2 – MOLECULAR DIAGNOSTICS

Lecture 1 (45 minutes)

– Deciphering genetic disorders: human genome sequencing and results follow-up.

- The history of research on genetic disorders, autosomal recessive, autosomal dominant and X linked disorders
- Genome sequencing as a diagnostic tool
- Understanding the role of mutation and correlation with the disease symptoms

Lecture 2 (45 minutes)

– The role of microRNAs in shaping tumor microenvironment

- The complexity of tumor microenvironment
- The effect of microRNAs
- The potential utility of secreted microRNAs in diagnostics and treatment

Lecture 3 (45 minutes)

– Bioinformatics tools for analysis and prediction of post-transcriptional RNA modifications

- Modeling post-transcriptional RNA modifications
- Predicting their effect on RNA structure and function
- Exploring databases post-transcriptional RNA modifications

Lecture 4 (45 minutes)

– Structural basis of immunotherapy by PD-1/PD-L1 checkpoint inhibition

- Modeling PD-1/PD-L1 checkpoint interactions
- Designing compounds interfering with PD-1/PD-L1 checkpoint interactions
- Validation of compounds interfering with PD-1/PD-L1 checkpoint interactions

Lecture 5 (45 minutes)

– Criteria of excellence and grants for research teams and leading scientists

- Definition of excellence of research teams and leading scientists
- Carrier in science advice
- Funding agencies and grants for research teams and leading scientists

Day 3 – Bioinformatics in genomics and epigenomics

Lecture 1 (45 minutes)

– New approaches to epigenome profiling

- New sequencing methods for epigenome profiling
- Molecular assays for epigenome profiling
- Application of NGS into single cell epigenome profiling

Lecture 2 (45 minutes)

– Unveiling informative DNA methylation sites and gene expression profiles that contribute to glioma patients survival

- Role of DNA methylation in cancer patient
- Databases of DNA methylation in cancer patient
- Integration of information about DNA methylation sites and gene expression profiles that contribute to patient's survival

Lecture 3 (45 minutes)

– Identifying functional non-coding elements on the genome scale

- Wet lab techniques for identifying non-coding DNA sequences
- Methods of identifying non-coding DNA sequences
- Computational models to discover function of noncoding DNA

Lecture 4 (45 minutes)

– Human Genome in Three Dimensions

- Three-dimensional organization of the genome
- Chromatin interactions
- Role chromatin structure in gene expression

Lecture 5 (45 minutes)

– Scenarios of cancer progression – computational analyses

- Mathematical tools to model cancer progression
- Computational tools to interfere with cancer progression
- Computational tools to study clonality and tumor evolution

Lecture 6 (45 minutes)

– A framework for cell-type specific annotations for predicted motifs of transcription factors across the human genome

- Wet lab techniques for identifying transcription factors binding DNA sequences
- Computational methods of identifying transcription factors binding DNA sequences
- Predicting putative motifs for transcription factors from ChIPseq data.

Introduction of basic computational analyses for detecting DNA alterations and copy number alterations in genomic data (training with data analyses). Gene ontology analyses of transcriptomic data. *(3 x 45 minutes)*

WINTER SCHOOL

SOFT SKILL WORKSHOP

Lecture 1 (45 minutes)

– Intellectual properties rights

Lecture 2 (45 minutes)

– Procedures of patenting

Lecture 3 (45 minutes)

– Ethics in science

Lecture 4 (45 minutes)

– Art of presentation of the scientific data

Lecture 5 (45 minutes)

– Writing papers and grant proposals

Lecture 6 (45 minutes)

– Animal experimentation regulations