

课程大纲

COURSE SYLLABUS

1.	课程代码/名称 Course Code/Title	功能基因组学前沿技术和精准医学 Application of functional genomics tools in Precision Medicine
2.	课程性质 Compulsory/Elective	专业选修课 Elective
3.	开课单位 Offering Dept.	医学院药理学系 Department of Pharmacology
4.	课程学分/学时 Course Credit/Hours	3/48
5.	授课语言 Teaching Language	英文（视学时需要可以部分中文） English (partially in Chinese if needed)
6.	授课教师 Instructor(s)	胡宇慧 Yuhui Hu
7.	开课学期 Semester	春季 Spring Semester
8.	是否面向本科生开放 Open to undergraduates or not	否 Not
9.	先修要求 Pre-requisites	（如面向本科生开放，请注明区分内容。 If the course is open to undergraduates, please indicate the difference.）
10.	教学目标 Course Objectives	<p>（如面向本科生开放，请注明区分内容。 If the course is open to undergraduates, please indicate the difference.）</p> <p>进入后基因组时代，功能基因组学的飞速发展已发明了多种尖端的组学工具，可以系统生物学层面开展人类疾病产生和治疗过程的研究，并同时揭示个体患者之间的巨大差异。尽管机遇与挑战并存，但实现个性化医疗（即精准医疗）（PM）的重要性已得到广泛认可。</p> <p>本课程旨在提供 PM 领域中的两个重要组成模块/部分：功能基因组学中的组学工具，及其在 PM（聚焦药物基因组学）中的应用。</p> <p>模块 1 “功能基因组学、系统生物学和组学技术” 涵盖人类基因组的基本概念和范围、功能基因组学（从基因组到转录组、蛋白质组和代谢组）中的关键分子和术语；相应组学工具的历史、概念、技术和应用，包括用于基因组/转录组等分析的第二代和第三代 DNA 高通量测序，以及蛋白质组学和代谢组学技术；还涵盖了单细胞技术的最新发展，包括空间位置解析的单细胞技术；在简要介绍数据分析工具的基础上，重点讲授每个组学工具获得结果的解释和理解。</p> <p>模块 2 “精准医学（PM）和组学” 涵盖了 PM 的基本概念、研究目标和方法，并聚焦药物基因组学领域，重点讲授对不同个体患者对药物敏感性和药物代谢至关重要的遗传/基因组、和非遗传变异和多态。模块 1 中介绍的关键组学工具和分析方法同样适用于药物基因组学研究，并进行应用场景/特点的讲解。此外，本课程还讲授临床组学工具使用和药物基因组学数据管理涉及的医学伦理。</p> <p>通过本课程学习，学生将熟练掌握功能基因组学的基本概念和知识，以及转录组学/蛋白质组学/代谢组学水平的相关尖端组学工具，并掌握如何用于研究导致疾病发展和治疗反应个体差异的遗传/非遗传性变异。此外，学生可掌握药物基因组学和精准医学的现状、前景、机遇和挑战、伦理等方面的知识，并发表自己的见解。</p> <p>Entering the post-genome era, the rapid advancement in functional genomics have invented multiple cutting-edge omics tools to investigate the human diseases and the therapeutic processes in a systematic way meanwhile disclosing dramatic variations among individual patients. The importance of fulfilling personalized medicine, also namely Precision Medicine (PM), has been widely recognized, albeit possessing both opportunities and challenges.</p> <p>This course aims to deliver two main modules/parts in PM: the omics tools in functional genomics, and their applications in PM with the focus on Pharmacogenomics.</p> <p>Module-1 “Functional genomics, systems biology, and omics technologies” covers the basic concept and scopes of human genome, key molecular terminologies in functional genomics (from genome to</p>

transcriptome, proteome, and metabolome); the history, concept, technique, and applications of cutting-edge omics tools including next-generation sequencing (2nd & 3rd generation) for genome/transcriptome analyses, as well as technologies in proteomics and metabolomics. The most recent development on single-cell technologies, including spatially resolved single-cell technologies are also be covered. The analytic tools are briefly introduced with the focuses on the result interpretation and analyses of each omics tool.

Module-2 “Precision Medicine (PM) and Omics” covers the basic concept, goals, and approaches of PM with particular focus on **Pharmacogenomics**, which discovers genetic/genomic and non-genetic variations critical to drug sensitivity and metabolism for individual patient. The key omics tools and analytical methods introduced in Module-1 are also discussed for pharmacogenomic studies. Moreover, the ethics to use omics tools and management of pharmacogenomic data are also discussed in the course.

Within this course, the students are expected to get familiar to basic concepts and knowledge in functional genomics and relevant cutting-edge omics tools at transcriptomic/proteomic/metabolomic level to study genetic/non-genetics variations responsible for disease development and therapeutic responses. Through the course learning, the students are expected to grasp the knowledge on the status, perspective, opportunities and challenges, as well as ethics of pharmacogenomics and precision medicine, and also to deliver their own opinions.

11. 教学方法

Teaching Methods

(如面向本科生开放, 请注明区分内容。 If the course is open to undergraduates, please indicate the difference.)

本课程以英文为主(视学生掌握情况辅以中文补充解释说明)进行教学, 采用课堂讲授功能基因组学和多组学技术理论知识、基本原理、实际运用、实验设计和流程, 并紧扣精准医学中的临床前和临床研究实例进行数据分析和结果讨论; 针对特定的组学技术, 提供相应仪器设备进行现场介绍和讲解。课程学习过程中将学生进行分组, 针对具体科研和临床实例利用口头汇报的形式进行深入探讨和考查, 最后利用综述论文形式全面培养和考查学生对功能基因组学、多组学技术发展、精准医学理论实践和伦理等的掌握程度。

This course is mainly taught in English (supplemented by Chinese explanations depending on the students' English skill). Through the course lectures, students can grasp the core components in functional genomics and multi-omics technology including theoretical knowledge, basic principles, practical applications, experimental design and process, as well as the case-studies in Precision Medicine with suitable data analysis and result discussion; for certain omics technologies, the corresponding instruments are provided for on-site introduction and explanation. During the course, the students are required to present oral talks to demonstrate their understanding on specific omics tool and clinical relevance. Finally, through writing a review article, the students can achieve the comprehensive understanding of functional genomics and omics tools, as well as the practice and ethics of precision medicine.

12. 教学内容

Course Contents

(如面向本科生开放, 请注明区分内容。 If the course is open to undergraduates, please indicate the difference.)

<p>Section 1 (1 hrs) (1 学时)</p>	<p>Lecture 1, (1 hr): Introduction of the course, scope & overview 课程概述</p> <ul style="list-style-type: none"> • Overview of Functional Genomics and Precision Medicine 功能基因组学和精准医学 • Contents of the course 课程内容介绍
<p>Module-1</p>	<p>Functional genomics, systems biology, and omics technologies 功能基因组学、系统生物学、多组学技术发展</p>
<p>Section 2 (2 hrs) (2 学时)</p>	<p>Overview of Genomics and Systems biology 基因组学和系统生物学概述</p> <p>Lecture 2, (2 hrs): Introduction of Human Genome 人类基因组</p> <p>1) Important Molecules in Molecular Biology 分子生物学重要分子和</p>

	<p>概念</p> <p>2) The Human Genome Project 人类基因组项目</p> <p>3) The structure of human genome 人类基因组结构组成</p> <p>4) From Genes to Phenotypes 从基因到表型</p>
<p>Section 3</p> <p>Section 3-1: (6 hrs) (6 学时)</p>	<p>Omics Technology—Measuring Nucleic Acids (Genomics tools) 组学技术—核酸定量技术（基因组研究工具）</p> <p>Section 3-1: Methods for DNA sequences 确定 DNA 序列方法 polymerase chain reaction, Sanger sequencing, microarray for gene expression profiling, next generation sequencing PCR、Sanger 测序、DNA 芯片、新一代 DNA 高通量测序</p> <p>Lecture 3, (1 hrs): DNA sequence determination methods 确定 DNA 序列方法</p> <ul style="list-style-type: none"> • PCR and Sanger sequencing PCR 和 Sanger 测序 • Microarray technology <p>Lecture 4, (3 hrs): DNA sequence determination methods (continued)—2nd generation sequencing 二代基因组测序技术</p> <ul style="list-style-type: none"> • 2nd-generation sequencing techniques 二代基因组测序技术介绍 • The type of second-generation sequencing methods 二代基因组测序种类 • The principle of second-generation sequencing methods 二代基因组测序原理 <p>Lecture 5, (2 hrs): DNA sequence determination methods (continued)—3rd generation sequencing 三代基因组测序技术</p> <ul style="list-style-type: none"> • 3rd-generation sequencing techniques 三代基因组测序技术介绍 • Nanopore, • PacBio, • Linked Read Sequencing – 10X Genomics Chromium Technology
<p>Section 3-2 (6 hrs) (6 学时)</p>	<p>Section 3-2: Applications of Next-Generation Sequencing (NGS) DNA 高通量测序技术的应用</p> <p>Lecture 6, (3 hrs): Whole-genome sequencing; Exosome sequencing 全基因组测序、外显子测序</p> <p>Lecture 7, (3 hrs): Transcriptome sequencing (RNA-seq) 转录组测序</p> <ul style="list-style-type: none"> • Techniques of RNA-seq: 转录组测序方法分类 poly(A) mRNA-seq; 3' mRNA-seq; rRNA-depleted RNA-seq • Definition, advantage/disadvantage of each 各技术的定义和优势 • Applications of RNA-seq 转录组测序应用
<p>Section 4</p>	<p>Omics Technology— Mass Spectrometry-Based Proteomics &</p>

<p>(6 hrs) (6 学时)</p>	<p>Metabolomics 组学技术—基于质谱的蛋白组、代谢组定量技术</p> <p>Lecture 8, (3 hrs): Basic principle of Proteomics, Techniques & applications, Results Analysis 蛋白组学基本概念、原理、应用、结果分析</p> <p>Lecture 9, (3 hrs): Basic principle of Metabolomics, Techniques & applications, Result analysis 代谢组学基本概念、原理、应用、结果分析</p>
<p>Section 5 (3 hrs) (3 学时)</p>	<p>Lecture 10, (3 hrs): From Genome to transcriptome to proteome & metabolome 从基因组、转录组、到蛋白组调控</p> <ul style="list-style-type: none"> • From genome to transcriptome 基因组到转录组 • Sequence variations in coding region affect gene & protein expression 影响转录组和蛋白组的表达谱的基因组编码区序列变异 • Sequence variations in non-coding region affect gene expression 影响转录组的表达谱的基因组非编码区序列变异
<p>Section 6 (6 hrs) (6 学时)</p>	<p>Single-cell technology—Detection of cell heterogeneity at diverse level. 单细胞技术—多层次检测单细胞异质性</p> <p>Lecture 11-12, (6 hrs): single cell Omics (scRNA-seq, scATAC-seq, scRNA proteomics) 单细胞多组学（单细胞转录组、染色质开放、蛋白组）</p> <ol style="list-style-type: none"> 1. Single-cell transcriptomics (2 hrs) 单细胞转录组 <ul style="list-style-type: none"> • Aim & history of single-cell technology development 单细胞技术发展历史和目的 • Techniques and applications of single-cell RNA-seq 单细胞转录组技术和应用 2. Single-cell multi-omics (1 hr) 单细胞多组学 <ul style="list-style-type: none"> • Principles & Techniques for single-cell epigenomic & proteomic information 单细胞表观组学和蛋白组学原理和技术 3. Spatially resolved single-cell transcriptomics (3 hrs) 单细胞空间转录组学 <ul style="list-style-type: none"> • Principle & aim of spatial transcriptomics 空间组学原理和目的 • Techniques to gain spatial gene expression 基因表达空间信息技术 • Applications of spatial single-cell transcriptomics 单细胞空间组学应用
<p>Section 7 (3 hrs) (3 学时)</p>	<p>Module-1 summary & Mid-term assessment: 3 hrs 模块 1 总结和期中考查</p> <p>Lecture 13, (3 hrs)</p>

	<p>Team work: literature research and presentation “the omics technology most relevant to individualized therapy” 分组讨论和口头汇报 “功能基因组学技术与个性化医疗”</p>
Module-2	Precision Medicine (PM) and Omics 精准医学和组学
Section 8 (11 hrs) (11 学时)	<p>Pharmacogenomics and Personalized Medicine 药物基因组学和个性化治疗</p> <p>Lecture 14, (2 hrs): Genomics & diseases; Applicable Omics tools 基因组和疾病；组学技术应用 Genetic/genomic and non-genetic variations in Disease development 基因（组）遗传和非遗传变异与疾病发生</p> <ul style="list-style-type: none"> • Monogenic diseases 单基因疾病 • Complex diseases 复杂疾病 • Cancer 癌症 <p>Analytical methods in Pharmacogenomics 药物基因组分析方法</p> <p>Lecture 15, (3 hrs): Pharmacogenomics and personalized medicine 药物基因组和个性化医疗</p> <ul style="list-style-type: none"> • Introduction of Pharmacogenomics 药物基因组背景介绍 • Drug metabolism & Variability in drug response 药物效应和代谢差异 • Genetic/genomic and non-genetic variations in drug response and metabolism 药物效应和代谢差异中的遗传和非遗传变异 <p>Lecture 16, (6 hrs): Pharmacogenomics Case study 药物基因组实例分析 Pharmacogenomics in Oncology, Neurodegenerative Disease, Cardiovascular drugs, etc. 肿瘤、神经退行性疾病、心血管疾病等中的药物基因组学</p>
Section 9 (1 hr) (1 学时)	<p>Lecture 17, (1 hr): Ethics in Precision Medicine 精准医学伦理 New Technologies and Personalized Medicine: Opportunities and Challenges 个性化医疗新技术：机遇与挑战</p>
Section 10 (3 hrs) (3 学时)	<p>Lecture 18, (3 hr): End-term assessment 期末考查</p> <ul style="list-style-type: none"> • Summary of the course 课程总结 • Guidance for writing a review about “Omics & Precision Medicine (Opportunities and Challenges in your own opinion)” 综述《组学和精准医学机遇与挑战》撰写指导
48 hrs in total 共计 48 学时	48 hrs in total 共计 48 学时

Course Assessment

(① 考核形式 Form of examination; ②. 分数构成 grading policy; ③ 如面向本科生开放, 请注明区分内容。
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出勤 Attendance 10%; 期中小组口头报告 Mid-term oral presentation 40%; 期末综述 Review 50%

14. 教材及其它参考资料

Textbook and Supplementary Readings

- 1) Human Genetics and Genomics, 4th Edition, Bruce R. Korf, Mira B. Irons, ISBN: 978-0-470-65447-7
 - 2) Pharmacogenomics, Challenges and Opportunities in Therapeutic Implementation, 2nd Edition, 2018, Yui-Wing Francis Lam, Stuart Scott ISBN: 9780128126271
 - 3) Clinical Genomics, 1st Edition, 2014, Shashikant Kulkarni, Somak Roy, ISBN: 9780124047488
 - 4) A First Course in Systems Biology, 2nd Edition, By Eberhard Voit, ISBN 9780815345688
- Supplementary readings: assigned literatures along with lectures.
以及课堂添加的最新文献进展。