

Vaccines and Pharmaceutical Products

Code: 101003
ECTS Credits: 6

Degree	Type	Year	Semester
2500502 Microbiology	OT	4	0

Contact

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Use of Languages

Principal working language: catalan (cat)
Some groups entirely in English: No
Some groups entirely in Catalan: Yes
Some groups entirely in Spanish: No

Teachers

Jaume Piñol Ribas

Prerequisites

There are no official prerequisites but knowledge of Biochemistry and Molecular Biology, Genetics, Microbiology, Cell Biology, Recombinant DNA Methods, Genomics and Proteomics, and Bioinformatics are assumed.

Objectives and Contextualisation

The first biotechnological drugs were simply "substitution molecules". These drugs were substances from human or animal organisms (hormones, etc.), which were available in very limited quantities, and that the recombinant DNA techniques allowed to obtain in large amounts. The current paradigm of the application of biotechnology to the design of vaccines and drugs is based on the prior identification of vaccine targets (genes / proteins related to pathogenicity, virulence or immunogenicity) and pharmacological targets (enzymes, receptors, whole metabolic pathways related to pathology, etc.) and then obtain the corresponding vaccine or drug by a rational design. The different "omics" (genomics, transcriptomics, proteomics, interactions, metabolomics, systems biology ...) represent key methodologies to identify the targets. In fact, these methods have allowed the emergence of so-called "reverse vaccination" (where a "silico" genome can be obtained by obtaining a vaccine) and the rational design of drugs from the three-dimensional structure of proteins. "Omics" have also generated new concepts in drug design such as "druggable genome / proteome / targetome" or "diseasome".

This course is aimed to describe the main procedures to identify vaccine and therapeutic targets. Methods and strategies to develop vaccines and to design organic molecules to modulate the biological activity of a therapeutic target will also be presented.

Competences

- Apply microorganisms or their components to the development of products of interest in health, industry and technology.
- Design experiments and interpret the results

- Identify the molecular mechanisms of pathogenesis and relate them to the response to infection in order to design and develop strategies for diagnosing and combating diseases caused by microorganisms.
- Obtain, select and manage information.
- Use bibliography or internet tools, specific to microbiology or other related disciplines, both in English and in the first language.
- Work individually or in groups, in multidisciplinary teams and in an international context.

Learning Outcomes

1. Design experiments and interpret the results
2. Identify viral elements that are useful for the design of antigens, immunogens and vaccines.
3. Identify viral elements that are useful for the design of diagnostic reagents.
4. Know the molecular bases of viral invasiveness and virulence and recognise the value of attenuated viral variants in vaccine design.
5. Know the molecular processes of the viral cycle and identify the potential targets of antiviral drugs.
6. Obtain, select and manage information.
7. Use bibliography or internet tools, specific to microbiology or other related disciplines, both in English and in the first language.
8. Use omics techniques for identifying target genes and proteins related to pathogenicity and virulence, and usable in the design of vaccines and antimicrobial compounds.
9. Work individually or in groups, in multidisciplinary teams and in an international context.

Content

Lesson 1. Introduction. History of vaccines. Generations of biotech vaccines. Diseases and orphan vaccines/drugs. *Blockbuster* vaccines/drugs. General characteristics, benefits and issues of vaccines.

Lesson 2. Economical and social interest of vaccines. Vaccines world market. R_0 -index of contagious diseases. Origin of infectious diseases: zoonosis. Relationship infection-disease-genes-evolution. Chronic diseases and infection. Pathogenicity and virulence. Pathogenicity factors.

Lesson 3. Vaccine development. Concept of Safety, Immunogenicity, Efficacy, and Effectiveness. Side effects. Risk/Benefit ratio. Development stages (Stage 0, I, II, III, and IV). Timeline and costs; Vaccine production. Main control tests. GLP and GMP regulation.

Lesson 4. Identification and characterisation of vaccine antigens. Mechanisms of genetic diversity and virulence. Pathogenomics and omics applications: surfomics, comparative and differential proteomics, immunomics, protectomics. Analysis of virulence genes activation: TraSH, STM, IVET, DFI, *RNAi-mediated knockdown*. Bioinformatics resources. Reverse vaccinology. Structural vaccinology. MALDI-Imaging and BioTyping; Immune response. *Vaccinomics*.

Lesson 5. Types of vaccines. Classic vaccines: inactivated; autovaccines; attenuated. Modern vaccines: subunits and conjugated; peptide-based; recombinant-live (SAVE, DISC, and DIVA vaccines); nucleic acids vaccines; anti-idiotypic vaccines; structure-based vaccines; therapeutic vaccines and cancer; carbohydrate-based vaccines.

Lesson 6. Adjuvants. Immune-enhancers. Delivery systems. New adjuvants. Nanovaccines. Adjuvant characteristics and modes of action. Vaccine administration. VIOLIN database (*The Vaccine Investigation and Online Information Network*).

Lesson 7. Drugs and Biopharmaceuticals. Concept and history of biopharmaceuticals. Different generations of biotechnological drugs. New paradigms for drug development. Pharmacoeconomics. Analysis and validation of the purity of biopharmaceuticals. Key concepts of pharmacological analysis: Pharmacokinetics, Pharmacodynamics and ADME. Key parameters in pharmacology. Biotransformation. Toxicity. Phases of the development of a drug: preclinical and clinical stages.

Lesson 8. Drug discovery. Therapeutic targets. Estimates on therapeutic targets from genomics and proteomics. Classification of therapeutic targets. Systems biology and network pharmacology. Concept of pharmacophore. Strategies for the identification of new therapeutic targets. Drugs and novelty.

Lesson 9. Drug development. Methods and rationale to validate pharmacological targets. Validation of hits and leads. Lipinsky rules. Methods for obtaining and improving leads: combinatorial chemistry, fragment analysis and click chemistry. Techniques to identify interactions between hits and targets: SPR-Biacore, NMR, mass spectrometry, double and triple hybrid, protein complementation assay. Structure-Function relationships. SAR and QSAR: descriptors and equations. Rational design of new drugs and structure-based drug design. Some examples of rational design. Design of anti-interaction drugs. Tools for attenuation of HERG polypharmacology.

Lesson 10. Discovery and development of antimicrobial drugs. Specificities and problems when developing new antimicrobial drugs. Pharmacoeconomics of antimicrobials. Main pharmaceutical targets. Strategies for the development of antimicrobials: specialized libraries, rational design, "iChips", silent operons, polyketides, antimicrobial peptides synthesized by ribosomal and non-ribosomal pathways, virulence factors and quorum sensing. New strategies for phage based therapies.

Lesson 11. Biopharmaceuticals of first and second generation. Biopharmaceuticals against a pharmacological target: monoclonal antibodies, peptides and antisense and interference RNAs. Biopharmaceuticals in replacement therapies: hormones, growth factors, cytokines and interleukins, regulatory microRNAs. Humanization, industrial production and stabilization of monoclonal antibodies. Drug-Antibody conjugates. Main monoclonal antibodies used in therapy. Design and modifications of interference RNAs.

Methodology

The course consists of theoretical lectures and laboratory practices.

Theoretical lectures:

The teacher will develop the contents of each topic with the support of powerpoint presentations that will be posted on Virtual Campus (Moodle classroom). These presentations constitute the most important piece of the study material and it is strongly recommended that students attend lectures with a printed form of them. The use of specialized bibliography is also encouraged.

Laboratory practices:

Three sessions (4 hours each), in which some basic proteomic techniques, applied to the design of vaccines and drugs, are illustrated and performed. The assistance to the practical sessions is required.

Activities

Title	Hours	ECTS	Learning Outcomes
Type: Directed			
Theoretical lectures	40	1.6	5, 4, 1, 2, 3, 7, 8
Type: Supervised			
Laboratory practices	12	0.48	1, 2, 3, 6, 9, 7, 8
Type: Autonomous			
Study, recommended readings	94	3.76	5, 4, 1, 2, 3, 6, 9, 7, 8

Assessment

The theoretical contents will be assessed continuously through two partial exams (multiple choice test) corresponding to the Vaccine and Drugs parts of the course, respectively. The weight of each exam on the global score is a 40%. A score equal or greater than 4.0 in the partial exam allows to pass the corresponding part of the subject.

Laboratory practices will be evaluated by means of an individual exam consisting of two or three questions related to the work carried out in the lab (weight 15%), plus the student's attitude and performance during the practical sessions (weight 5%). As described for theory exams, a score equal or greater than 4.0 allows to pass this part of the subject.

Those students who have not passed either theory and practices exams as a result of the continuous evaluation must attend a final exam in order to reassess any of the parts previously scored below 4.0. Moreover, the access to the final exam will only be allowed to the students who have previously been evaluated in a set of activities whose weight equals to a minimum of two thirds of the total grade of the subject.

On the other hand, those students who have passed the subject per course as a result of the continuous evaluation can also go to the final exam to improve their grades in any of the previous exams. In this case, the score obtained in the former exam will be preserved if greater.

The students will obtain the qualification of "Not Evaluable" if the number of their assessment activities is less than 67% of the programmed ones for the subject.

To pass the course a global score equal or greater than 5.0 must be attained.

Assessment Activities

Title	Weighting	Hours	ECTS	Learning Outcomes
Laboratory practices exam	20%	2	0.08	6, 9, 7, 8
Partial Exam 1 (part: Vaccines)	40%	1	0.04	5, 4, 1, 2, 3, 6, 9, 7, 8
Partial Exam 2 (part: Drugs)	40%	1	0.04	5, 4, 1, 2, 3, 6, 9, 7, 8

Bibliography

- "Biopharmaceuticals: Biochemistry and Biotechnology". Walsh G. Ed. John Wiley & Sons, 2^a ed. 2004
- "Pharmaceutical Biotechnology": Fundamentals and Applications. D. J. A. Crommelin, R. D. Sindelar & B. Meibohm. Springer, 4^a ed, 2013
- "Vaccine Design". R. Rappuoli & F. Bagnoli eds. Ed. Caister, 2011
- "Proteins. Biochemistry and Biotechnology". Walsh G. Ed. John Wiley & Sons, 2^a ed, 2002
- "Real World Drug Discovery". R.M. Rydzewski. Ed. Elsevier 2008
- "Development of Vaccines: From discovery to clinical testing". Editors: M. Singh & I.K. Srivastava. Ed Wiley 2011