Universitat Autònoma de Barcelona

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Vaccines and Drugs

Code: 100900
ECTS Credits: 6

Degree	Type	Year	Semester
2500252 Biochemistry	OT	4	0

Contact

Name: Josep Antoni Pérez Pons
Email: JosepAntoni.Perez@uab.cat

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.) an 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 presented.

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. Cronic 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 nad 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-idiotype 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: monoclonalantibodies, 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.