Nanomedicina, Biomaterials i Enginyeria Tissular 2013/2014

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ECTS Credits: 9

Degree	Type	Year	Semester
4313772 Biotecnologia Avançada	OT	0	1

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Use of languages

Principal working language: anglès (eng)

Prerequisites

Para el seguimiento óptimo del módulo es necesario tener una formación básica en Ingeniería Biológica, Bioquímica, Biología Celular y Molecular y fundamentos de Ingeniería de Bioprocesos y Biorreactores.

Objectives and Contextualisation

El módulo tiene dos partes:

Nanomedicina y Biomateriales:

El objetivo de esta parte del curso es dar una visión general de cómo la nanotecnología está afectando a la medicina y biomateriales. Conceptos básicos breves en nanomedicina y biomateriales serán detallados al inicio del curso. Después de la introducción, el curso se divide en cuatro secciones principales: Nanotoxicology, administración de fármacos, Imaging and Tissue Engineering.

Finalmente se facilitará información de grupos de investigación e instalaciones en este ámbioto en la UAB .

La segunda parte és La Ingeniería Tisular:

El objetivo de esta parte es la de familiarizar al estudiante con las herramientas más importantes utilizadas en la Ingeniería Celular y Tisular y ser capaces de utilizar estas herramientas en la generación de terapias basadas en la utilización de células, biopolímeros y factoresde crecimiento y diferenciación, solos o todas sus combinaciones. Para ello se explorarán, evaluarán, diseñarán, integrarán y optimizarán los procesos de aislamiento, caracterización, expansión y diferenciación celular y la construcción, colonización y caracterización de biomatrices biocompatibles, integrando la producción y determinación de la calidad de procesos y productos y la economia de los mismos. Se tendran en cuenta las regulaciones y normativas de calidad y seguridad en terapias avanzadas reguladas por las agencias Europea y Americana de medicamentos y productos para uso en humanos.

Skills

Biotecnologia Avançada

- Capacitat de síntesi, anàlisi d'alternatives i debat crític.
- Integrar i fer ús deines de biotecnologia avançada per resoldre problemàtiques en àmbits biotecnològics emergents.
- Que els estudiants sàpiguen aplicar els coneixements adquirits i la seva capacitat de resolució de problemes en entorns nous o poc coneguts dins de contextos més amplis (o multidisciplinaris) relacionats amb la seva àrea d'estudi.

- Que els estudiants tinguin les habilitats d'aprenentatge que els permetin continuar estudiant, en gran manera, amb treball autònom a autodirigit
- Tenir coneixements que aportin la base o l'oportunitat de ser originals en el desenvolupament o l'aplicació d'idees, sovint en un context de recerca
- Treballar en un equip multidisciplinari.
- Utilitzar i gestionar de manera responsable informació bibliogràfica i recursos informàtics relacionats amb la biotecnologia.

Learning outcomes

1. Analitzar les diferències entre diferents sistemes dalliberament de fàrmacs.
2. Aplicar els principals mètodes fisicoquímics de preparació i síntesi dels materials i els nanomaterials.
3. Capacitat de síntesi, anàlisi d'alternatives i debat crític.
4. Definir els conceptes de biocompatibilitat i toxicitat de nanomaterials.
5. Descriure com es fa la bioconjugació i per a què serveix.
6. Descriure el concepte de biomineralització i el paper dels diferents components en joc.
7. Descriure els diferents tipus de sensors per al diagnòstic mèdic amb base nanotecnològica i analitzar-ne el mecanisme dacció.
8. Descriure els mètodes dencapsulació de fàrmacs.
9. Descriure els principals materials utilitzats en enginyeria tissular i les seves principals característiques.
10. Descriure i analitzar els aspectes bàsics rellevants en el processos de colonització de matrius per a enginyeria de teixits.
11. Descriure i aplicar les normatives de qualitat, seguretat i regulació dels productes denginyeria cel·lular i tissular i la seva percepció social.
12. Descriure les tipologies de biomaterials partint de la seva composició, estructura i funció.
13. Descriure les tècniques dobtenció de biosensors amb millors prestacions a partir de nanomaterials i nanoelements.
14. Distingir i interpretar els principals tipus de cèl·lules troncals i les seves tècniques de caracterització.
15. Distingir i interpretar les principals fonts de cèl·lules troncals, les seves tècniques dextracció, aïllament i expansió.
16. Identificar les principals aplicacions dels productes denginyeria cel·lular i tissular.
17. Interpretar el paper de les diferents tipologies de nanopartícules en lanàlisi mèdica.
18. Que els estudiants sàpiguen aplicar els coneixements adquirits i la seva capacitat de resolució de problemes en entorns nous o poc coneguts dins de contextos més amplis (o multidisciplinaris) relacionats amb la seva àrea d'estudi.
19. Que els estudiants tinguin les habilitats d'aprenentatge que els permetin continuar estudiant, en gran manera, amb treball autònom a autodirigit
20. Reconèixer el paper de la mida de partícula en la biodisponibilitat.
21. Tenir coneixements que aportin la base o l'oportunitat de ser originals en el desenvolupament o l'aplicació d'idees, sovint en un context de recerca
22. Treballar en un equip multidisciplinari.
23. Utilitzar i gestionar de manera responsable informació bibliogràfica i recursos informàtics relacionats amb la biotecnologia.

Content

Parte de Nanomedicina y Biomateriales:

1. Concepts and Generalities in Nanomedicine and Biomaterials:

A general section which will give to the students the basic concepts and methodologies used in Nanomedicine and Biomaterials.

a) Biological modification of surfaces, concepts: Anna Laromaine - 2h

Biological elements of interest in Nanomedicine: DNA, RNA, proteins (antibodies), virus, bacterias and cells .Immobilization of biological elements for the development of novel biomaterials and nanomedicine tools

b) Preparation of materials for nanomedicine and biomaterials: Nora Ventosa - 2h

In order to achieve optimal performance of nanomedicines, a tight control over their structural characteristics at micro, nano, and supramolecular scale isrequired. Concepts related to bottom-up and top-down strategies most commonly followed for the preparation of nanomedicines and biomaterials with defined structural characteristics will be presented. Special emphasis will be given to the scalability and regulatory aspects of the preparation procedures.

Preparation of materials using Biology: Escarlata Rodriguez 2h

Nanomaterials produced in biological systems. Advantages and disadvantages over chemical synthesis. Natural and genetically modified materials. Recombinant proteins as biopharmaceuticals. Eukaryotic and prokaryotic protein expression systems. Cellular inclusions: biolopymers, polymeric nanoparticles, magnetosomes and self assembling proteins.

c) Characterization of materials in nanomedicine: Victor Puntes- 2h

The biological matrix is complex and tracing how nanomaterials evolve in it is key. Characterization fisico-chemical of materials involving techniques as photonic and magnetic probes or mass spectroscopy, and functional characterization describing in vitro , in vivo and clinical tests. Concepts described will be inorganic signatures of nanomaterials and nanokinetics in biological systems.

2. Nanotoxicology Victor Puntes 4h

Does the nanoform of a substance entail an increased toxicity? How the biological activity of nanometarials may become dangerous? How nanomaterials can act as pro-toxins? Which is the balance between intended -primary- and undesirable -side- effects of nanomaterials in medicine? These questions will be addressed in the context ofintended and unintended use of nanomaterials.

3.Drug delivery

Micro and nanostructured materials for drug delivery : Jaume Veciana 2h

A general overview of the main micro- and nanostructured materials used for passive and active drug delivery will be presented. Special emphasis will be given to conjugation of Active Pharmaceutical Ingredients (APIs) to "smart" nanocarriers, which are stimulus sensitive nanocarriers, and to the integration of molecules that bind to over-expressed antigens or receptors on the target cells in structured materials, as a successful strategy for achieving active nanomedicines.

- Case study: Nanocarriers as an emerging platform for cancer therapy:

Nora Ventosa 2h

Cancer remains one of the world's most devastating diseases; with more than 10 million new cases every year. However, mortality hasdecreased in the past two years owing to better understanding of tumors biology and improved diagnostic devices and treatments. Using cancer as a model disease, in this session will be reviewed the recent achievements in the design and synthesis of nanocarriers and molecules that can selectively target tumours. The challenges in translating some of the basic research to the clinic will be highlighted.

Gene therapy: Esther Vazquez 2h

Definition of gene therapy. Different strategies for the transport of nucleic acids. Nucleic acid binding. Specific entrance into the cell. Endosomal escape. Intracellular trafficking. Transport into the nucleus. Factors to consider in designing a vehicle for gene therapy. Case Study: Design of a protein nanoparticle directed to metastatic cells in colorectal cancer.

4. Biosensors for Diagnostic

From Macro-micro to nanosensing devices in nanomedicine- Josep Puigmartí 4h

Micro- and nanostructuration methods are widely used in a broad number of research fields including sensor

development and diagnosis. In this section, special attention will be given to micro- and nanosensing devices employed in nanomedicine. Apart from presenting common fabrication techniques, a wide number of systems employed in today's live will be analysed and described.

Case study and visit to the Molecular Chirality, Surfaces and Nanomaterials Group lab at ICMAB: Josep Puigmartí (2h)

Fabrication and performance of single and multilayer microfluidic PDMS platforms described in the previous section will be shown in a practical case.

5. Tissue Engineering 4h

Biomaterials for Tissue Engineering Ana Lopez

The objective of this course is to provide an insight into the area of biomaterials and tissue engineering. It will be show the importance of the preparation of these materials in the nanoscale.

This course will include the study of the chemical nature of the biomaterials, from inorganic to organic, as well as polymeric materials. Thus, it will be show an introduction to biomineralization, bioceramics and bone generation, giving examples such as generation of nano-hydroxyapatite.

From the point of view of polymeric biomaterials, it will be study the chemical composition and function of synthetic biodegradable and no-biodegradable polymers.

Regarding the development in biomaterials, special attention will be focus on Tissue engineering, where it will be explained the direct use of a material within a biological system. It will be describe the need and general aspects of the topic. It will include the study of the biomaterials used for tissue engineering (natural and artificial). Introduction to the term scaffold, properties and characteristics of scaffolds and principles of scaffold design, scaffold architecture, and techniques of fabrication.

- Case study and visit totheBiomaterial Processing and Nanostructuring Unit of CIBER-BBN at the ICMAB of CSIC: Santi Sala (1h) Ana Lopez (1h)

Practical examples of preparation of nanomaterials using compressed fluids will be presented.

Preparation of a polymeric scaffold of PMMA using supercritical CO2 as solvent and porogenic agent.
The aim is to show how scCO2 can be used as an advantageous method for scaffold preparation since the pore size can be easily controlled and the scaffold obtained is solvent free, so no further processing is needed.

6. Imaging

Fundamentals to diagnostics imaging modalities:Anna Roig 3h

Fundamentals to diagnostics imaging modalities (Positron Emission Tomography, Computed Tomography, Magnetic Resonance Imaging, Optical Imaging, Ultrasound). Basic working principles and comparision of the medical imaging modalities. Magnetic nanoparticles as contrast agents and cell tracking.

Nanomaterials as contrast agents and multimodal imaging probes

Facilities at the UAB and CIBER BBN platforms for Nanomedicine and Biomaterials: 2h Silvia Lope

Visit to the NMR facility at the UAB. Basic magnetic resonance imaging (MRI) concepts for detection of MRI contrast agents will be explained and images of a prepared phantom composed of contrast agents at different concentrations will be obtained in a Bruker BioSpec 7 tesla MR scanner.

Case Study MRI and visit to MRI facility: Silvia Lope 2h

7. Nanomedicine and Biomaterials conclusions. 1h

Nanoparticles in translational medicine;diagnosis, therapy and biological barriers.

Antonio Villaverde

Types and chemical nature of nanoparticles of biomedical value. Applications in diagnosis and imaging. Therapeutic potential in drug delivery. Pharmacokinetics, biodistribution, clearance and biological barriers. Toxicology concerns at organic and environmental levels.

Parte de Ingeniería Tisular:

1. Tipos celulares y su caracterización. Células madre embrionarias, células madre adultas, células iPS. Principales técnicas de caracterización. Citometria de flujo. Cariotipado. Capacidad de diferenciación. Expresión génica. Bioquímica.

2. Aislamiento, expansión y diferenciación de células troncales. Principales fuentes de células madre en los tejidos. Extracción, selección y purificación. Aspectos básicos que regulan el proceso de expansión celular y la diferenciación a los distintos linajes celulares. Cinéticas. Caracterización del producto final.

3. Sistemas de cultivo de células troncales. Tipos debiorreactores. Aspectos más relevantes para su operación y monitorización.

4. Moléculas utilizadas en medicina regenerativa e ingeniería celular y tisular. Citoquinas: Interleuquinas, factores de crecimiento, quimioquinas.

5. Biomateriales y Bioingenieria. Principales tipos de materiales utilizados para ingeniería tisular y sus características básicas: estructura, resistencia, porosidad, elasticidad, biocompatibilidad, biodegradabilidad.

6. Fenómenos de transporte en ingeniería tisular. Difusión molecular de sustratos y productos. Subministro de oxígeno. Colonización celular. Adherencia.

7. Calidad, seguridad y regulación de los productos obtenidos por ingeniería celular y tisular. Aspectos sociales, éticos, de percepción pública y comunicación.

8. Aplicaciones clínicas. Etapas necesarias para desarrollar un producto de terapias avanzadas. Ensayos preclínicos y clínicos. Principales empresas en el campo de la ingeniería celular y tisular. La protección de la Propiedad Industrial e Intelectual. Elementos clave para el desarrollo delsector. Estudio de casos.

Methodology

Clases magistrales/expositivas

Seminarios (normalmente presentados por investigadores o empresas activas en algunos temas específicos de la asignatura)

Estudio de casos. Realizado en grupos reducidos de alumnos. Análisis de aplicaciones específicas, en base a los conocimientos adquiridos en el curso y de artículos científicos, y presentación pública al resto del grupo

Activities

Title	Hours	ECTS	Learning outcomes
Type: Directed			
Clases magistrales	53	2.12	1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23
Type: Supervised			
Preparación y exposición artículo investigación	50	2	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23

Type: Autonomous			
Estudio autónomo	110	4.4	1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23

Evaluation

Examenes teóricos (40%)

Presentación oral de trabajos científicos (40%)

Intervenciones en clase (20%)

Evaluation activities

Title	Weighting	Hours	ECTS	Learning outcomes
examen escrito y/o multirespuesta	40	2	0.08	1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23
exposicion oral trabajos	40	8	0.32	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23
participación en clase	20	2	0.08	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23

Bibliography

La bibliografía necesaria para el seguimiento del módulo se podrá consultar a través del campus virtual. Además el alumno tendrá que realizar búsqueda y consulta bibliográfica específica para la elaboración de su trabajo en grupo, contando con el asesoramiento del profesorado. A continuación se muestra parte de la bibliografia de la primera parte de nanomedicina y biomateriales:

Preparation of materials using biology:

Rodríguez-Carmona E, Villaverde A. (2010) Nanostructured bacterial materials for innovative medicines. Trends Microbiol. 9:423-30.

Ferrer-Miralles, N. et al. (2009) Microbial factories for recombinant pharmaceuticals. Microb. Cell Fact. 8, 17.

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Pilar Rivera Gil, Günter Oberdörster, Alison Elder, Vctor Puntes,Wolfgang J. Parak. Correlating Physico-Chemical with Toxicological Properties of Nanoparticles: The Present and the Future. ACS Nano 2010 4(10), 5527-5531.

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Frasconi M, Mazzei F, Ferri T. Protein immobilization at gold-thiol surfaces and potential for biosensing. Anal Bioanal Chem. 2010;398(4):1545-64.

Lu B, Smyth MR, O'Kennedy R. Oriented immobilization of antibodies and its applications in immunoassays and immunosensors. Analyst. 1996;121(3):29R-32R.

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Jong Bum Leea, Michael John Campolongo, Jason Samuel Kahn, Young Hoon Roh, Mark Richard Hartman and Dan Luo. DNA-based nanostructures for molecular sensing. Nanoscale, 2010, 2, 188-197

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