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1999
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**FACULTAD DE CIENCIAS EXACTAS Y NATURALES**

**U.B.A.**

**1.- DEPARTAMENTO/INSTITUTO de INVESTIGACIONES BIOQUIMICAS**

2.- CARRERA de: a)Licenciatura en..---.....ORIENTACION:..--- .

**b) Doctorado y/o Post-Grado en Ciencias Químicas y Biológicas**

c) Profesorado en...--- .....

d) Cursos Técnicos en Meteorología..--- .....

e) Cursos de Idiomas...---.....

3.- **2do. CUATRIMESTRE**.....Año**: 1999** .....

4.- Nº DE CODIGO DE CARRERA....**51 y 55** .....

5.- MATERIA "**Terapia Génica del Laboratorio a la Clínica"** .....

Nº DE CODIGO **B 048**

6.- PUNTAJE PROPUESTO **3 puntos** .....

7.- PLAN DE ESTUDIO Año --- .....

8.- CARACTER DE LA MATERIA **Optativa** .....

9.- DURACION **2 Semanas** .....

10.- HORAS DE CLASE SEMANAL:

| | | | |
|---|---|---|---|
| a) Teóricas | **10 hs** | d) Seminarios | **4 hs** |
| b) Problemas | **-- hs** | e)Teórico-problemas | **-- hs** |
| c) Laboratorio | **40 hs** | f)Teórico-prácticas | **-- hs** |

g)Totales Horas **54 hs**

11.CARGA HORARIA TOTAL **108 hs**.....

12.- ASIGNATURAS CORRELATIVAS **Egresados de Cs. Químicas, Ciencias Biológicas, Medicina, Farmacia, Bioquímica, etc.**

13.- FORMA DE EVALUACION**: Examen final y seminario** .....

## 14. PROGRAMA ANALITICO

### ASPECTOS TEORICOS

Introduction and overview: historical aspects of gene therapy. Gene therapy and traditional pharmacology. Highlights and pitfalls on the way to the present situation. General aspects: somatic and germ-line gene therapy. Ex vivo vs. in vivo, rationale of the choice. Autologous vs. heterologous cells. Introduction to the different strategies for gene transfer.

Retrovirus: life cycle, molecular biology, different type of vectors, cell receptors, viral genome, vector design and its improvements, re-targeted vectors, packaging cell lines, vector preparation, production and infection, advantages and disadvantages. Plasmovirus, Retroadenovirus.

Adenovirus: life cycle, molecular biology, viral genome, early and late genes, vector design and improvements , re-targeted vectors, vector preparation, production and infection, advantages and disadvantages, immune response against the vector.

Adeno-Associated Virus and Herpes Virus: general aspects, life cycle, viral genome, vector design and improvements , re-targeted vectors, vector preparation, production and infection, advantages and disadvantages, toxicity of Herpes Virus, Amplicon-based HSV vectors.

Lentiviral vectors (HIV): General aspects, life cycle, viral genome, vector design, preparation, production and infection, advantages and disadvantages, potential applications.

Non-viral strategies:
General view
For in vitro application: calcium phosphate transfection, microinjection, electroporation. For in vitro and in vivo application: particle bombardment; cationic liposomes: formulation, transfection, mechanisms of action, DNA/lipid complex uptake, targeted liposomes.

Antisense technology: oligonucleotides, specificity, triplex formation, chemical modification, ribozymes, Pharmacokinetics of DNA-based therapies.

DNA vaccination: general aspects, different vectors and strategies, application.

Cell based gene therapy: General overview: lymphocytes, endothelial cells, T bodies, tumor cells, dendritic cells, myoblasts, hematopoyetic stem cells, keratinocytes. Special emphasis on dendritic cells.
Transcriptional regulation of transgene expression: progesterone receptor-responsive system, tetracycline-responsive system, ecdysone-responsive system. Tissue-specific expression.

Gene therapy for inherited diseases: organ specific strategies for muscular and skeletal system, nervous system, hematopoyetic system, cardiovascular system.
Therapeutic genes, cell target, choice of the right vector or strategy, studies in animal models and relevance to human disease.

Gene therapy for acquired diseases.

Cancer: melanoma, brain, breast, colon, prostate, lung and others. Vectors used, studies in animal models, different strategies, clinical trials.

Blood and Vascular diseases: induction of angiogenesis, treatment of atherosclerosis and restenosis, hemophilia. Therapeutic genes, cell target, choice of the right vector or strategy, studies in animal models and relevance to human disease. Clinical trials.

Autoimmune diseases: rheumatoid arthtritis, multiple sclerosis, diabetes mellitus. Vectors, different strategies, studies in animal models.

Neurologic and neuromuscular disorders: Parkinson, Huntington Chorea, Alzheimer, Duschenne's muscular distrophy. Vectors, different strategies, studies in animal models.

Perspectives
Biomedical aspects: Human genome project (HUGO). New genes, genetics testing and pre-natal screening. Intra-uterine therapy. New vectors, the "ideal vector". Potential for new health care services. Pharmacogenomics.

**PARTE PRACTICA**

Use of retroviral vectors. Plasmid DNA preparation. Transfection of ecotropic and amphotropic packaging cells. Harvesting of recombinant retrovirus. In vitro trasnduction of murine and human cells. Selection of antibiotic-resistant cells. Gene expression through the use of northern and western techniques. Gene expression through the use of beta- galactosidase and Green Fluorescence protein as reporter genes.
Transduction of cell lines with replication-deficient, recombinant adenoviruses expressing a reporter gene. Analysis of the efficiency of the transduction. Viral DNA extraction by the Hirt method. Evaluation of the incorporation of the transgene in the viral genome by restriction analysis. Biosafety assays: checking the putative presence of replication competent adenovirus by transducing cells unable to transcomplement viral E1 deficiency and detection of E1 sequences by PCR in viral stocks. Cytophatic effects on 293 cells. In vivo transduction of specific brain regions using beta-galactosidase as reporter gene.

**15.- BIBLIOGRAFIA**

Anderson, F. *Human Gene Therapy* **7**, 2201-2202 (1996).
Crystal, R. *Science* **270**, 404-410 (1995).
Revah, F., et al. *Gene transfer into the central and peripheral nervous system using adenoviral vectors* 1-Chapter 7 (John Wiley and Sons, 1996).

FECHA 11/10/99

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