LESSON 1

The Biology and Genetics of Cells and Organisms

1.1 Mendel establishes the basic rules of genetics
1.2 Mendelian genetics helps to explain Darwinian evolution
1.3 Mendelian genetics governs how both genes and chromosomes behave
1.4 Chromosomes are altered in most types of cancer cells
1.5 Mutations causing cancer occur in both the germ line and the soma
1.6 Genotype embodied in DNA sequences creates phenotype through proteins
1.7 Gene expression patterns also control phenotype
1.8 Transcription factors control gene expression
1.9 Metazoa are formed from components conserved over vast evolutionary time periods
1.10 Gene cloning techniques revolutionized the study of normal and malignant cells

The Nature of Cancer

1.11 Tumors arise from normal tissues
1.12 Tumors arise from many specialized cell types throughout the body
1.13 Some types of tumors do not fit into the major classifications
1.14 Cancers seem to develop progressively
1.15 Tumors are monoclonal growths
1.16 Cancers occur with vastly different frequencies in different human populations
1.17 The risks of cancers often seem to be increased by assignable influences including lifestyle
1.18 Specific chemical agents can induce cancer
1.19 Both physical and chemical carcinogens act as mutagens
1.20 Mutagens may be responsible for some human cancers

LESSON 2

Tumor Viruses

2.1 Peyton Rous discovers a chicken sarcoma virus
2.2 Rous sarcoma virus is discovered to transform infected cells in culture
2.3 The continued presence of RSV is needed to maintain transformation
2.4 Viruses containing DNA molecules are also able to induce cancer
2.5 Tumor viruses induce multiple changes in cell phenotype including acquisition of tumorigenicity
2.6 Tumor virus genomes persist in virus-transformed cells by becoming part of host cell DNA

2.7 Retroviral genomes become integrated into the chromosomes of infected cells
2.8 A version of the *src* gene carried by RSV is also present in uninfected cells
2.9 RSV exploits a kidnapped cellular gene to transform cells
2.10 The vertebrate genome carries a large group of proto-oncogenes
2.11 Slowly transforming retroviruses activate proto-oncogenes by inserting their genomes adjacent to these cellular genes
2.12 Some retroviruses naturally carry oncogenes

Cellular Oncogenes

2.14 Can cancers be triggered by the activation of endogenous retroviruses?
2.15 Transfection of DNA provides a strategy for detecting nonviral oncogenes
2.16 Oncogenes discovered in human tumor cell lines are related to those carried by transforming retroviruses
2.17 Proto-oncogenes can be activated by genetic changes affecting either protein expression or structure
2.18 Variations on a theme: the *myc* oncogene can arise via at least three additional distinct mechanisms
2.19 A diverse array of structural changes in proteins can also lead to oncogene activation

LESSON 3

Growth Factors, Receptors, and Cancer

3.1 Normal metazoan cells control each other's lives
3.2 The Src protein functions as a tyrosine kinase
3.3 The EGF receptor functions as a tyrosine kinase
3.4 An altered growth factor receptor can function as an oncoprotein
3.5 A growth factor gene can become an oncogene: the case of *sis*
3.6 Transphosphorylation underlies the operations of receptor tyrosine kinases
3.7 Yet other types of receptors enable mammalian cells to communicate with their environment
3.8 Integrin receptors sense association between the cell and the extracellular matrix
3.9 The Ras protein, an apparent component of the downstream signaling cascade, functions as a G protein

Cytoplasmic Signaling Circuitry Programs Many of the Traits of Cancer

3.11 A signaling pathway reaches from the cell surface into the nucleus
3.12 The Ras protein stands in the middle of a complex signaling cascade
3.13 Tyrosine phosphorylation controls the location and thereby the actions of many cytoplasmic signaling proteins

3.14 SH2 groups explain how growth factor receptors activate Ras and acquire signaling specificity
3.15 A cascade of kinases forms one of three important signaling pathways downstream of Ras
3.16 A second pathway downstream of Ras controls inositol lipids and the Akt/PKB kinase
3.17 A third Ras-regulated pathway acts through Ral, a distant cousin of Ras
3.18 The Jak-STAT pathway allows signals to be transmitted from the plasma membrane directly to the nucleus
3.19 Cell adhesion receptors emit signals that converge with those released by growth factor receptors
3.20 The Wnt-β-catenin pathway contributes to cell proliferation
3.21 G-protein-coupled receptors can also drive normal and neoplastic proliferation
3.22 Four other signaling pathways contribute in various ways to normal and neoplastic proliferation

LESSON 4

Tumor Suppressor Genes

4.1 Cell fusion experiments indicate that the cancer phenotype is recessive
4.2 The recessive nature of the cancer cell phenotype requires a genetic explanation
4.3 The retinoblastoma tumor provides a solution to the genetic puzzle of tumor suppressor genes
4.4 Incipient cancer cells invent ways to eliminate wild-type copies of tumor suppressor genes
4.5 The *Rb* gene often undergoes loss of heterozygosity in tumors
4.6 Loss-of-heterozygosity events can be used to find tumor suppressor genes
4.7 Many familial cancers can be explained by inheritance of mutant tumor suppressor genes
4.8 Promoter methylation represents an important mechanism for inactivating tumor suppressor genes
4.9 Tumor suppressor genes and proteins function in diverse ways
4.10 The NF1 protein acts as a negative regulator of Ras signaling
4.11 Apc facilitates egress of cells from colonic crypts
4.12 Von Hippel-Lindau disease: pVHL modulates the hypoxic response

pRb and Control of the Cell Cycle Clock

4.14 External signals influence a cell's decision to enter into the active cell cycle
4.15 Cells make decisions about growth and quiescence during a specific period in the G_1 phase
4.16 Cyclins and cyclin-dependent kinases constitute the core components of the cell cycle clock

4.17 Cyclin-Cdk complexes are also regulated by Cdk inhibitors
4.18 Viral oncoproteins reveal how pRb blocks advance through the cell cycle
4.19 pRb is deployed by the cell cycle clock to serve as a guardian of the restriction point gate
4.20 E2F transcription factors enable pRb to implement growth-versus-quiescence decisions
4.21 A variety of mitogenic signaling pathways control the phosphorylation state of pRb
4.22 The Myc oncoprotein perturbs the decision to phosphorylate pRb and thereby deregulates control of cell cycle progression
4.23 TGF-β prevents phorphorylation of pRb and thereby blocks cell cycle progression
4.24 pRb function and the controls of differentiation are closely linked
4.25 Control of pRb function is perturbed in most if not all human cancers

LESSON 5

P53 and Apoptosis: Master Guardian and Executioner

5.1 Papovaviruses lead to the discovery of p53
5.2 *p53* is discovered to be a tumor suppressor gene
5.3 Mutant versions of p53 interfere with normal p53 function
5.4 p53 protein molecules usually have short lifetimes
5.5 A variety of signals cause p53 induction
5.6 DNA damage and deregulated growth signals cause p53 stabilization
5.7 Mdm2 and ARF battle over the fate of p53
5.8 ARF and p53-mediated apoptosis protect against cancer by monitoring intracellular signaling
5.9 p53 functions as a transcription factor that halts cell cycle advance in response to DNA damage and attempts to aid in the repair process
5.10 p53 often ushers in the apoptotic death program
5.11 p53 inactivation provides advantage to incipient cancer cells at a number of steps in tumor progression
5.12 Inherited mutant alleles affecting the p53 pathway predispose one to a variety of tumors
5.13 Apoptosis is a complex program that often depends on mitochondria
5.14 Two distinct signaling pathways can trigger apoptosis
5.15 Cancer cells invent numerous ways to inactivate some or all of the apoptotic machinery

Eternal Life: Cell Immortalization and Tumorigenesis

5.17 Normal cell populations register the number of cell generations separating them from their ancestors in the early embryo
5.18 Cancer cells need to become immortal in order to form tumors
5.19 Cell-physiologic stress impose a limitation on replication
5.20 The proliferation of cultured cells is also limited by the telomeres of their chromosomes
5.21 Telomeres are complex molecular structures that are not easily replicated
5.22 Incipient cancer cells can escape crisis by expressing telomeres
5.23 Telomeres plays a key role in the proliferation of human cancer cells
5.24 Some immortalized cells can maintain telomeres without telomerase
5.25 Telomeres play different roles in the cells of laboratory mice and in human cells
5.26 Telomerase-negative mice show both decreased and increased cancer susceptibility
5.27 The mechanisms underlying cancer pathogenesis in telomerase-negative mice may also operate during the development of human tumors

LESSON 6

Multi-Step Tumorigenesis

6.1 Most human cancers develop over many decades of time
6.2 Histopathology provides evidence of multi-step tumor formation
6.3 Colonic growths accumulate genetic alterations as tumor progression proceeds
6.4 Multi-step tumor progression helps to explain familial polyposis and field cancerization
6.5 Cancer development seems to follow the rules of Darwinian evolution
6.6 Tumor stem cells further complicate the Darwinian model of clonal succession and tumor progression
6.7 A linear path of clonal succession oversimplifies the reality of cancer
6.8 The Darwinian model of tumor development is difficult to validate experimentally
6.9 Multiple lines of evidence reveal that normal cells are resistant to transformation by a single mutated gene
6.10 Transformation usually requires collaboration between two or more mutant genes
6.11 Transgenic mice provide models of oncogene collaboration and multi-step cell transformation
6.12 Human cells are constructed to be highly resistant to immortalization and transformation
6.13 Nonmutagenic agents, including those favoring cell proliferation, make important contributions to tumorigenesis
6.14 Toxic and mitogenic agents can act as human tumor promoters

6.15 Chronic inflammation often serves to promote tumor progression in mice and humans
6.16 Inflammation-dependent tumor promotion operates through defined signaling pathways
6.17 Tumor promotion is likely to be a critical determinant of the rate of tumor progression in many human tissues

Maintenance of Genomic Integrity and the Development of Cancer

6.19 Tissues are organized to minimize the progressive accumulation of mutations
6.20 Stem cells are the likely targets of the mutagenesis that leads to cancer
6.21 Apoptosis, drug pumps, and DNA replication mechanisms offer tissues a way to minimize the accumulation of mutant stem cells
6.22 Cell genomes are threatened by errors made during DNA replication
6.23 Cell genomes are under constant attack from endogenous biochemical processes
6.24 Cell genomes are under occasional attack from exogenous mutagens and their metabolites
6.25 Cells deploy a variety of defenses to protect DNA molecules from attack by mutagens
6.26 Repair enzymes fix DNA that has been altered by mutagens
6.27 Inherited defects in nucleotide-excision repair, base-excision repair, and mismatch repair lead to specific cancer susceptibility syndromes
6.28 A variety of other DNA repair defects confer increased cancer susceptibility through poorly understood mechanisms
6.29 The karyotype of cancer cells is often changed through alterations in chromosome structure
6.30 The karyotype of cancer cells is often changed through alterations in chromosome number

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VISTO:

la nota del Dr. Norberto Iusem Director del Departamento de Fisiología, Biología Molecular y Celular, mediante la cual eleva la información del curso de posgrado **Biología Tumoral**, que será dictado en el primer cuatrimestre 2012 (entre el 5 y el 16 de marzo), por el Dr. Jorge E. Filmus

El CV del Dr Jorge E. Filmus

CONSIDERANDO:

Lo actuado en la Comisión de Doctorado de esta Facultad el 25/10/2011,
lo actuado por la Comisión de Enseñanza, Programas, Planes de Estudio y Posgrado,
lo actuado por este cuerpo en Sesión Ordinaria realizada en el día de la fecha,
en uso de las atribuciones que le confiere el Artículo Nº 113º del Estatuto Universitario,

EL CONSEJO DIRECTIVO DE LA FACULTAD DE
CIENCIAS EXACTAS Y NATURALES
R E S U E L V E:

Artículo 1º: Autorizar el dictado del curso de posgrado **Biología Tumoral** de 25 horas de duración.

Artículo 2°: Aprobar el programa del curso de posgrado **Biología Tumoral** obrante a fs 4 a 10 del expediente de la referencia.

Artículo 3°: Aprobar un puntaje máximo un (1) punto para la Carrera del Doctorado.

Artículo 4º: Aprobar un arancel de 20 módulos. Disponer que los montos recaudados serán utilizados conforme a lo dispuesto por Resolución CD Nº 072/03.

Artículo 5°: Comuníquese a la Dirección del Departamento de Fisiología, Biología Molecular y Celular, a la Biblioteca de la FCEN y a la Subsecretaría de Postgrado (con fotocopia del Programa fs 4 a 10 incluídas). Comuníquese a la Dirección de Alumnos (sin fotocopia del Programa) Cumplido archívese.

Resolución CD Nº 3020

SP/med/01/11/2011

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