

The Hebrew University of Jerusalem

Syllabus

Viruses Inducing Cancer - 94628

Last update 06-03-2022

HU Credits: 2

Degree/Cycle: 2nd degree (Master)

Responsible Department: Bio-Medical Sciences

Academic year: 0

Semester: 2nd Semester

Teaching Languages: Hebrew

Campus: Ein Karem

Course/Module Coordinator: Dr. Alexander Rouvinski

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Coordinator Office Hours: Sun-Thurs by appointment

Teaching Staff:

Dr. Leah Baraz,
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Dr. Rouvinski Alexander

Course/Module description:

The course deals with the biology of oncogenic viruses, including viral structure and replication, with special emphasis on molecular mechanisms of cellular transformation, and on the pathogenesis of neoplastic diseases caused by oncogenic viruses.

Course/Module aims:

We aim to provide a mechanistic comprehension of viral oncogenesis in humans and animals, including the mechanisms of action of oncogenes and of tumor suppressors. Through this study, the course aims to provide further insight in the molecular biology of the cell and in the biology of cancer.

Learning outcomes - On successful completion of this module, students should be able to:

1. Classify oncogenic viruses by the nature of their genome and their mode of action.
2. Describe specific RNA and DNA oncoviruses and their mode of oncogenesis in human and animals.
3. Outline the oncogenic mechanisms of oncoviruses.
4. Explain what are oncogenes and tumor suppressors, and describe how they are manipulated by oncoviruses to facilitate host transformation.
5. Compare mechanisms of action of RNA and DNA oncoviruses.
6. Explain how one searches for novel oncoviruses and for their causal relationships with malignancies.

Attendance requirements(%):

none

Teaching arrangement and method of instruction: Lectures with slides

Course/Module Content:

1. Introduction: Development of the notion of oncogenic viruses in the 20th century. Characteristics of normal and of transformed cells in cell culture. Telomerase. Mutations required for cellular transformation (2h).
2. RNA oncogenic viruses. Mechanisms of replication of retro-viruses; reverse

transcriptase, simple and complex retroviruses (2h).

3. Acute oncogenic retroviruses. Rous sarcoma virus. Mechanisms of oncogenes appropriation. Defective retroviruses. Oncogenes found in acutely transforming retroviruses. Mechanisms of v-sis, v-erb, v-src, H-ras, v-myc.

4. Chronic oncogenic retroviruses. How cellular proto-oncogenes are activated. Insertional mutagenesis. Friend leukemia virus: 2-step transformation. MMTV: transmission, endogenous and exogenous virus, structure of the viral protomer, function of the superantigen, activation of wnt, beta-catenin and notch by the virus. How malignancy is promoted. Principles of retroviral vectors. Insertional mutagenesis following gene therapy of SCID-X1 patients. (2.5h)

5. HTLV-1: viral structure, cell-to-cell transmission, spread. Structure of the viral protomer; activation by the Tax protein. Functions of Tax and of HBZ and their involvement in the development of leukemia in humans. (1.5h)

6. HIV-1. Pathogenesis of AIDS. Endogenous retroviruses (ERV) of humans and animals. Physiological roles of endogenous viruses in humans. Possible involvement of HERV in the pathogenesis of germ cell tumors. Mechanism of action of the Rec protein. The APOBEC family of proteins, involvement in the cellular defense against retroviruses and retroelements. (2h)

7. Small DNA tumor viruses. SV40 as a model: genome structure. Replication in permissive and in non-permissive cells. Large T antigen, interaction with p53 and pRb tumor suppressors. Small t antigen and interaction with pp2A/ Conditions conducive to transformation by the virus. Characteristics of viral integration in the host genome. (2h)

8. Human polyoma viruses. BKV and JCV and their possible involvement in human malignancies. Merkel cell polyoma virus (MCPV) – discovery using Digital transcriptome subtraction (DTS). Genome structure, mutations within the T antigen, integration in the host genome, demonstration of causality in Merkel cell carcinoma. (2h)

9. Human Papilloma virus (HPV). Genomic structure, mechanism of replication, dependence on host cell differentiation. Functions of viral proteins E2, E6 and E7. Oncogenic and non-oncogenic strains. Causal link with cervical cancer, oncogenic mechanisms. (2h)

10. Adenoviruses: viral structure, transcription of early genes. Adenoviruses as a model in cell transformation. Functions of E1A and E1B. E4-Orf-3 as a viral oncogene and its role in the inactivation of p53. (2h)

11. Epstein-Barr virus (EBV). Structure, replication. Immune reaction. Latency types. Viral involvement in malignancies: Burkitt's lymphoma (BL), Nasopharyngeal carcinoma (NPC), Hodgkin's lymphoma (HL). (2h)

12. Kaposi's sarcoma-associated herpesvirus (KSHV). Discovery of the virus using representational difference analysis (RDA). Epidemiological evidence for the involvement of the virus in Kaposi sarcoma. Structure of the viral genome. Lytic vs latent infection. Involvement of latent and lytic genes in tumor promotion. Pathogenesis of Kaposi sarcoma. (2h)

13. Hepatitis B virus (HBV) and Hepatitis C virus (HCV). Viral structure, replication, and interactions with the host cells. Association with hepatocellular carcinoma (HCC) and possible mechanisms. (2h)

14. *Conclusions. General characteristics of viral carcinogenesis in humans and animals. Criteria guiding the search for a causal link between virus and malignancy.*
(2h)

Required Reading:

Robert A. Weinberg. *The Biology of Cancer*. 2nd edition. Garland Science, 2014.
Updated research papers on oncogenic viruses.

Additional Reading Material:

One research paper and one review paper will be a part of the final exam.

Course/Module evaluation:

End of year written/oral examination 90 %

Presentation 0 %

Participation in Tutorials 0 %

Project work 0 %

Assignments 0 %

Reports 0 %

Research project 0 %

Quizzes 10 %

Other 0 %

Additional information:

Additional details and slides to be found on the EKMD EduPortal (accessible to registered students and teachers)