DEPARTMENT OF ONCOLOGY-PATHOLOGY

K7F6067, Tumor Evolution in Space and Time, 1.5 credits (hec)

Tumörevolution i tid och rymd, 1,5 högskolepoäng

Third-cycle level / Forskarnivå

Approval

This syllabus was approved by the The Committee for Doctoral Education on 2025-03-07, and is valid from autumn semester 2025.

Responsible department

Department of Oncology-Pathology, Faculty of Medicine

Prerequisite courses, or equivalent

Students should have acquired a foundational understanding of cancer biology, such as by completing the Basic Course in Tumor Biology and Oncology or its equivalent.

Purpose & Intended learning outcomes

Purpose

Cancer is driven by both genetic and epigenetic evolution, alongside interactions with the tumor microenvironment. This combined selection process between tumor intrinsic and extrinsic factors leads to the formation of tumor niches that promote tumor growth while suppressing immune responses. Traditionally, tumor evolution and the tumor microenvironment have largely been studied as separate areas in cancer biology. However, recent advancements in technologies such as single-cell sequencing, spatial profiling, and cell barcoding are bridging these fields. This convergence raises new questions that were previously hard to address, including how the microenvironment affects the selection of tumor subclones, how tumor niches develop over time, and which molecular pathways drive these processes. This course provides an in-depth exploration of tumor evolution across both spatial and temporal scales, including an overview of the key technologies used in such studies and clinically relevant aspects.

Intended learning outcomes

By the end of the course, students will be able to:

Competence and Skills

- Demonstrate the ability to describe the concepts and terminology related to tumor evolution.
- Explain the methods used to track and analyze tumor evolution in both preclinical models and human tissues.
- Design general experimental strategies to study tumor heterogeneity and metastatic spread.

Judgment and Approach

Demonstrate the ability to critically evaluate current tumor evolution models and methodologies.

- Evaluate the implications of tumor evolution research for personalized cancer therapies and clinical applications.
- Assess how novel technologies can improve our understanding of tumor progression across different contexts.

Course content

The main topics covered in the course include:

1. Introduction to tumor evolution and heterogeneity, and experimental techniques

- Basic principles of tumor evolution: clonal selection, genetic vs. epigenetic changes
- Tumor intrinsic heterogeneity
- Lineage tracing to study tumor evolution
- Case study: Tumor evolution in the skin
- Early and late tumor stages: Clinical aspects and approach to the cancer patient

2. Tumor niches, spatial organization, and experimental techniques

- Introduction to tumor (micro)niches
- Spatial transcriptomics and niche characterization
- Defining the tumor microenvironment using proteomics

3. Crosstalk in the microenvironment

- Evolution of tumor-stroma interactions
- Cancer and the immune system

4. Development of metastases with a focus on bone and liver metastases

- Introduction to tumor metastasis
- The bone marrow metastatic niche
- Liver metastases – clinical aspects and metastases-microenvironment interactions

5. Clinical site visits

Students interested in a one-day clinical observership can attend liver metastasis surgery at Karolinska Hospital in Huddinge, the oncology outpatient clinic, and/or pathology workup for cancer specimens (non-mandatory, arranged outside of the course week, depending on clinical schedules).

Forms of teaching and learning

Lectures and interactive workshops.

Language of instruction

The course is given in English

Grading scale

Pass (G) /Fail (U)

Compulsory components & forms of assessment

Compulsory Components
Attendance at all lectures and workshops is mandatory. In cases of absence, the student must submit a summary of relevant literature articles to compensate for missed sessions.

Forms of Assessment

- Brief written report: Mock study design in bullet point format
- Oral presentation: A short presentation summarizing the study design and its relevance to the field of tumor evolution.
- Participation: Active participation in discussions during the course, including providing constructive feedback on peer presentations and discussions with invited external speakers.

To pass, students must demonstrate mastery of the intended learning outcomes through both written and oral assessments.

Course literature

Required reading before the start of the course

Karlsson K, Przybilla MJ, Kotler E, Khan A, Xu H, Karagyozova K, Sockell A, Wong WH, Liu K, Mah A, Lo YH, Lu B, Houlahan KE, Ma Z, Suarez CJ, Barnes CP, Kuo CJ, Curtis C, Deterministic evolution and stringent selection during pre-neoplasia. Nature, volume 618, pages 383–393 (2023). DOI: 10.1038/s41586-023-06102-8

Recommended reading

Forsthuber A, Aschenbrenner B, Korosec A, et al. Cancer-associated fibroblast subtypes modulate the tumor-immune microenvironment and are associated with skin cancer malignancy. Nat Commun. 2024;15(1):9678. Published 2024 Nov 8. doi:10.1038/s41467-024-53908-9

de Visser KE, Joyce JA. The evolving tumor microenvironment: From cancer initiation to metastatic outgrowth. Cancer Cell. 2023 Mar 13;41(3):374-403. doi: 10.1016/j.ccell.2023.02.016. PMID: 36917948.

Lichtenberger BM, Kasper M. Cellular heterogeneity and microenvironmental control of skin cancer. J Intern Med. 2021;289(5):614-628. doi:10.1111/joim.13177

Swanton C, Bernard E, Abbosh C, André F, Auwerx J, Balmain A, Bar-Sagi D, Bernards R, Bullman S, DeGregori J, Elliott C, Erez A, Evan G, Febbraio MA, Hidalgo A, Jamal-Hanjani

M, Joyce JA, Kaiser M, Lamia K, Locasale JW, Loi S, Malanchi I, Merad M, Musgrave K, Patel KJ, Quezada S, Wargo JA, Weeraratna A, White E, Winkler F, Wood JN, Vousden KH, Hanahan D. Embracing cancer complexity: Hallmarks of systemic disease. Cell. 2024 Mar 28;187(7):1589-1616. doi: 10.1016/j.cell.2024.02.009. PMID: 38552609.

Pentimalli TM, Karaiskos N, Rajewsky N. Challenges and Opportunities in the Clinical Translation of High-Resolution Spatial Transcriptomics. Annu Rev Pathol. 2025 Jan;20(1):405-432. doi: 10.1146/annurev-pathmechdis-111523-023417. Epub 2025 Jan 2. PMID: 39476415.

Gulati GS, D'Silva JP, Liu Y, Wang L, Newman AM. Profiling cell identity and tissue architecture with single-cell and spatial transcriptomics. Nat Rev Mol Cell Biol. 2025 Jan;26(1):11-31. doi: 10.1038/s41580-024-00768-2. Epub 2024 Aug 21. PMID: 39169166