DEPARTMENT OF ONCOLOGY-PATHOLOGY

K7F5541, Overview course in Cancer Drug Discovery, 1.5 credits (hec)

Introduktionskurs i läkemedelsutveckling inom onkologi, 1,5 högskolepoäng

Third-cycle level / Forskarnivå

Approval

This syllabus is approved by the The Committee for Doctoral Education on 2023-12-11, and was last revised on 2024-01-31. The revised course syllabus is valid from autumn semester 2024.

Responsible department

Department of Oncology-Pathology, Faculty of Medicine

Prerequisite courses, or equivalent

Students must have aquired a basic understanding of cancer biology, for example by having participated in the Basic course in tumor biology and oncology or equivalent.

Purpose & Intended learning outcomes

Purpose

This course describes the steps, processes and approaches needed for drug discovery with a focus on oncology. Through lectures and interactive workshops, the students will learn about current drug discovery techniques, from screening for hit discovery to the synthesis of the final drug candidate through lead optimization. Aspects of clinical testing and precision medicine will also be addressed.

In this five-day course, students will attend lectures by prominent scientists from academic and industry active in the fields of drug screening, drug library design and logistics, disease models, drug development, medicinal chemistry, image analysis, chemoinformatics, precision medicine, and clinical trials. The students will also participate in a group-based learning project to design their own screening strategy, and site-visits to drug discovery companies based in Stockholm, as well as the screening platform at SciLifeLab Chemical Biology Consortium Sweden.

At the end of the course, the students should have a good overview and understanding of the

drug discovery workflow in cancer research, allowing them to pinpoint potential career directions for their own scientific paths.

Intended learning outcomes

At the end of the course the students are expected to be able to:

Knowledge and understanding

Describe, define and understand the different drug discovery approaches used in both academia and industry. In addition students should be able to show a familiarity of the drug discovery process through to clinical implementation. This includes topics such as high throughput screening, the different stages in the drug discovery and development pipeline, recent trends and new modalities.

Competence and skills

Design experiments, explain screening concepts, and evaluate strategies for drug discovery and development in cancer. Understand the different screening strategies and the associated benefits and shortcomings. Describe the concepts and terminology of drug discovery in cancer. Describe and understand how a compound can become a drug and explain its clinical implications.

Judgement and approach

Demonstrate the ability to understand the concepts of drug discovery. Evaluate how a drug discovery campaign can be used to discover new anti-cancer drugs. Evaluate how drug discovery techniques can be currently used in a clinical setting for precision medicine. Judge the challenges and risks associated with drug discovery and development projects. Judge the broader societal impact, including ethical considerations, of a drug discovery and development process.

Course content

The main blocks of the course include:

Drug discovery in pharma and academia: a perspective
-ChemoInformatics
-Drug Library design
-Model systems

Drug discovery strategies:
-Target-based in vitro screens
-Cell-based phenotypic screens
-Virtual screens
-High-throughput phenotypic screening
-High content imaging
-Image analysis

-Multi-parametric analysis

Target identification:
-Thermal Shift (CETSA and others)
-CRISPR
-Transcriptomics

Lead optimization and Medicinal chemistry:
-Journey from compound to drug
-ADME and toxicity

Clinical trials and patient stratification:
-Diagnostics
-Drug repurposing in personalised cancer medicine

Workshop: design your screening strategy to target one of the hallmarks of cancer.

Forms of teaching and learning

Lectures, workshops and site-visits.

Language of instruction

The course is given in English

Grading scale

Pass (G) /Fail (U)

Compulsory components & forms of assessment

Compulsory components

Attendance to all lectures and workshops is compulsory. Attendance will be compensated through verbal summaries of relevant literature reviews or case studies with one of the course organizers or lecturer.

Forms of assessment

The examinations will consist in a written (2 pages) and short oral presentation of a mock drug discovery project that is well motivated in background of the current state of knowledge/lack of knowledge in the cancer research area of choice or their own scientific path. Each student should actively participate (ask questions or comment) the other students's presentations at the final session of the course. One needs to show that all intended learning outcomes are reached for a pass.

Course literature

Required reading:

Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144(5):646–674. doi:10.1016/j.cell.2011.02.013 (https://www.ncbi.nlm.nih.gov/pubmed/21376230)

Swinney DC, Anthony J. How were new medicines discovered?. Nat Rev Drug Discov. 2011;10(7):507–519. Published 2011 Jun 24. doi:10.1038/nrd3480 (https://www.nature.com/articles/nrd3480)

Hughes JP, Rees S, Kalindjian SB, Philpott KL. Principles of early drug discovery. Br J Pharmacol. 2011;162(6):1239–1249. doi:10.1111/j.1476-5381.2010.01127.x (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3058157/)

Recommended reading:

Arrowsmith CH, Audia JE, Austin C, et al. The promise and peril of chemical probes. Nat Chem Biol. 2015;11(8):536–541. doi:10.1038/nchembio.1867 (https://www.nature.com/articles/nchembio.1867)

Blagg J, Workman P. Choose and Use Your Chemical Probe Wisely to Explore Cancer Biology . Cancer Cell. 2017;32(1):9–25. doi:10.1016/j.ccell.2017.06.005 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5511331/)

Boutros M, Heigwer F, Laufer C. Microscopy-Based High-Content Screening. Cell. 2015;163(6):1314–1325. doi:10.1016/j.cell.2015.11.007 (https://www.cell.com/cell/fulltext/S0092-8674(15)01487-7?rss=yes)

Jones LH, Bunnage ME. Applications of chemogenomic library screening in drug discovery. Nat Rev Drug Discov. 2017;16(4):285–296. doi:10.1038/nrd.2016.244 (https://www.nature.com/articles/nrd.2016.244)

Feng Y, Mitchison TJ, Bender A, Young DW, Tallarico JA. Multi-parameter phenotypic profiling: using cellular effects to characterize small-molecule compounds. Nat Rev Drug Discov. 2009;8(7):567–578. doi:10.1038/nrd2876 (https://www.nature.com/articles/nrd2876)

Horvath P, Aulner N, Bickle M, et al. Screening out irrelevant cell-based models of disease. Nat Rev Drug Discov. 2016;15(11):751–769. doi:10.1038/nrd.2016.175 (https://www.nature.com/articles/nrd.2016.175)