CHARLES UNIVERSITY
First Faculty of Medicine
Department BIOCEV
Průmyslová 595, 252 50 Vestec, Czech Republic
Head: Prof. Tomas Stopka MD, PhD

Title: Biomedicine and biotechnology
B02981 / B82981 / B90275

Summer Team Academic Year 2022/2023

Annotation: This subject focuses on educating students in biomedical research and biotechnologies. It teaches the basis of scientific work, introduction to methodology in biomedicine up to the development of novel diagnostics and therapeutics. Lectures and seminars will contain the insight into modern tools such as transgenic biology or global technologies such as OMICs.

Students are encouraged to read education material ahead of the seminar.

Lectures will be held in **BIOCEV** (Seminary Room U2.020 - Průmyslová 595, 252 50 Vestec) starting **March 2nd 2023** from **4 pm.** In case of questions, please do not hesitate to contact Lucie Vyšatová (lucie.vysatova@lf1.cuni.cz).

Lecture 1 – March 2th, 2023
Prof. Tomáš STOPKA MD, PhD
https://stopka-lab.lf1.cuni.cz/en
Title: **CELL BIOLOGY** : **Stem cell biology versus proliferation and differentiation control**
Regulatory mechanisms in normal cell differentiation including transcription factors and their effector pathways. Biology of stem cells and tissue transplantation. Regulation of cell cycle and its detection.
Study material:

- Kokavec J, Zikmund T, Savvulidi F, Kulvait V, Edelmann W, Skoultchi AI, Stopka T. The ISWI ATPase Smarca5 (Snf2h) Is Required for Proliferation and Differentiation of Hematopoietic Stem and Progenitor Cells. Stem Cells. 2017. Jun;35(6):1614-1623. doi: 10.1002/stem.2604.
- Carvajal LA, Neriah DB, Senecal A, Benard L, Thiruthuvanathan V, Yatsenko T, Narayanagari SR, Wheat JC, Todorova TI, Mitchell K, Kenworthy C, Guerlavais V, Annis DA, Bartholdy B, Will B, Anampa JD, Mantzaris I, Aivado M, Singer RH, Coleman RA, Verma A, Steidl U. Dual inhibition of MDMX and MDM2 as a therapeutic strategy in leukemia. Sci Transl Med. 2018 Apr 11;10(436):eaao3003. doi: 10.1126/scitranslmed.aao3003.
- Yusenko M, Jakobs A, Klempnauer KH. A novel cell-based screening assay for small-molecule MYB inhibitors identifies podophyllotoxins teniposide and etoposide as inhibitors of MYB activity. Sci Rep. 2018 Sep 3;8(1):13159. doi:10.1038/s41598-018-31620-1.
- Decker S, Zwick A, Khaja Saleem S, Kissel S, Rettig A, Aumann K, Dierks C. Optimized Xenograft Protocol for Chronic Lymphocytic Leukemia Results in High Engraftment Efficiency for All CLL Subgroups. Int J Mol Sci. 2019 Dec 12;20(24).pii: E6277. doi: 10.3390/ijms20246277.
- Janku F, Angenendt P, Tsimberidou AM, Fu S, Naing A, Falchook GS, Hong DS, Holley VR, Cabrilo G, Wheler JJ, Piha-Paul SA, Zinner RG, Bedikian AY, Overman MJ, Kee BK, Kim KB, Kopetz ES, Luthra R, Diehl F, Meric-Bernstam F, Kurzrock R.Actionable mutations in plasma cell-free DNA in patients with advanced cancers referred for experimental targeted therapies. Oncotarget. 2015 May 20;6(14):12809-21.
- Behan FM, Iorio F, Picco G, Gonçalves E, Beaver CM, Migliardi G, Santos R, Rao Y, Sassi F, Pinnelli M, Ansari R, Harper S, Jackson DA, McRae R, Pooley R, Wilkinson P, van der Meer D, Dow D, Buser-Doepner C, Bertotti A, Trusolino L,Stronach EA, Saez-Rodriguez J, Yusa K, Garnett MJ. Prioritization of cancer therapeutic targets using CRISPR-Cas9 screens. Nature. 2019 Apr;568(7753):511-516. doi: 10.1038/s41586-019-1103-9.

Lecture 2 – March 16th, 2023

Mgr. Peter Dráber, PhD

https://biocev.lf1.cuni.cz/draber-laboratory

Title: **The role of cell death in tissue homeostasis and autoimmune disorders**

Cell death is necessary for removal of damaged cells and tissue renewal. However, aberrant cell death can lead to severe autoimmune disorders. The molecular pathways triggering cell death in physiological settings and pathological conditions will be discussed.

Study material:

- Lafont E, Draber P, Rieser E, Reichert M, Kupka S, de Miguel D, Draberova H, von Mässenhausen A, Bhamra A, Henderson S, Wojdyla K, Chalk A, Surinova S, Linkermann A, Walczak H. TBK1 and IKKε prevent TNF-induced cell death by RIPK1 phosphorylation. Nat Cell Biol. 2018 Dec;20(12):1389-1399. doi: 10.1038/s41556-018-0229-6.
- Newton K, Wickliffe KE, Dugger DL, Maltzman A, Roose-Girma M, Dohse M, Kőműves L, Webster JD, Dixit VM. Cleavage of RIPK1 by caspase-8 is crucial for limiting apoptosis and necroptosis. Nature. 2019 Oct;574(7778):428-431. doi: 10.1038/s41586-019-1548-x.
- Lalaoui N, Boyden SE, Oda H, Wood GM, Stone DL, Chau D, Liu L, Stoffels M, Kratina T, Lawlor KE, Zaal KJM, Hoffmann PM, Etemadi N, Shield-Artin K, Biben C, Tsai WL, Blake MD, Kuehn HS, Yang D, Anderton H, Silke N, Wachsmuth L, Zheng L,Moura NS, Beck DB, Gutierrez-Cruz G, Ombrello AK, Pinto-Patarroyo GP, Kueh AJ,Herold MJ, Hall C, Wang H, Chae JJ, Dmitrieva NI, McKenzie M, Light A, Barham BK,Jones A, Romeo TM, Zhou Q, Aksentijevich I, Mullikin JC, Gross AJ, Shum AK,Hawkins ED, Masters SL, Lenardo MJ, Boehm M, Rosenzweig SD, Pasparakis M, Voss AK, Gadina M, Kastner DL, Silke J. Mutations that prevent caspase cleavage of RIPK1 cause autoinflammatory disease. Nature. 2020 Jan;577(7788):103-108. doi:10.1038/s41586-019-1828-5.

Lecture 3 – March 30th, 2023

RNDr. Kristýna Pimková, Ph.D.

https://stopka-lab.lf1.cuni.cz/en

Title**: Redox Biology**

Reactive oxygen and nitrogen species are not just harmful by-products that cause damage to macromolecules and ultimately cell death. They are essential signaling molecules that play a role in basic biological processes, so-called "redox signaling". The basic principles of redox signalling, its role in physiological cellular processes and in cancer will be discussed.

Study material:

- Georgiou G. How to flip the (redox) switch. Cell. 2002 Nov 27;111(5):607-10. doi: 10.1016/s0092-8674(02)01165-0. PMID: 12464172.
- Paulsen CE, Carroll KS. Cysteine-mediated redox signaling: chemistry, biology, and tools for discovery. Chem Rev. 2013 Jul 10;113(7):4633-79. doi: 10.1021/cr300163e. Epub 2013 Mar 20. PMID: 23514336; PMCID: PMC4303468.
- Aebersold R, Agar JN, Amster IJ, Baker MS, Bertozzi CR, Boja ES, Costello CE, Cravatt BF, Fenselau C, Garcia BA, Ge Y, Gunawardena J, Hendrickson RC, Hergenrother PJ, Huber CG, Ivanov AR, Jensen ON, Jewett MC, Kelleher NL, Kiessling LL, Krogan NJ, Larsen MR, Loo JA, Ogorzalek Loo RR, Lundberg E, MacCoss MJ, Mallick P, Mootha VK, Mrksich M, Muir TW, Patrie SM, Pesavento JJ, Pitteri SJ, Rodriguez H, Saghatelian A, Sandoval W, Schlüter H, Sechi S, Slavoff SA, Smith LM, Snyder MP, Thomas PM, Uhlén M, Van Eyk JE, Vidal M, Walt DR, White FM, Williams ER, Wohlschlager T, Wysocki VH, Yates NA, Young NL, Zhang B. How many human proteoforms are there? Nat Chem Biol. 2018 Feb 14;14(3):206-214. doi: 10.1038/nchembio.2576. PMID: 29443976; PMCID: PMC5837046.
- Xiao H, Jedrychowski MP, Schweppe DK, Huttlin EL, Yu Q, Heppner DE, Li J, Long J, Mills EL, Szpyt J, He Z, Du G, Garrity R, Reddy A, Vaites LP, Paulo JA, Zhang T, Gray NS, Gygi SP, Chouchani ET. A Quantitative Tissue-Specific Landscape of Protein Redox Regulation during Aging. Cell. 2020 Mar 5;180(5):968-983.e24. doi: 10.1016/j.cell.2020.02.012. Epub 2020 Feb 27. PMID: 32109415; PMCID: PMC8164166.
- 5.Pimkova K, Jassinskaja M, Munita R, Ciesla M, Guzzi N, Cao Thi Ngoc P, Vajrychova M, Johansson E, Bellodi C, Hansson J. Quantitative analysis of redox proteome reveals oxidation-sensitive protein thiols acting in fundamental processes of developmental hematopoiesis. Redox Biol. 2022 Jul;53:102343. doi: 10.1016/j.redox.2022.102343. Epub 2022 May 23. PMID: 35640380; PMCID: PMC9157258.

Lecture 4 – April 13th, 2023

RNDr. Radoslav Janoštiak, Ph.D.

https://biocev.lf1.cuni.cz/janostiaklab

Title: **Biology of solid tumors and translational medicine**

Basic principles of cancer development, cancer driver mutations and targeted therapy, cancer evolution and progression, cancer cell dormancy and invasiveness, circulating tumor cells.

Study material:

- Vendramin R, Litchfield K, Swanton C. Cancer evolution: Darwin and beyond. EMBO J. 2021 Sep 15;40(18):e108389. doi: 10.15252/embj.2021108389.
- Falzone L, Salomone S, Libra M. Evolution of Cancer Pharmacological Treatments at the Turn of the Third Millennium. Front Pharmacol. 2018 Nov 13;9:1300. doi: 10.3389/fphar.2018.01300.
- Hanahan D. Hallmarks of Cancer: New Dimensions. Cancer Discov. 2022 Jan;12(1):31-46. doi: 10.1158/2159-8290.CD-21-1059.
- Fares J, Fares MY, Khachfe HH, Salhab HA, Fares Y. Molecular principles of metastasis: a hallmark of cancer revisited. Signal Transduct Target Ther. 2020 Mar 12;5(1):28. doi: 10.1038/s41392-020-0134-x.

Lecture 5 – April 27th, 2023

Assoc. Prof. RNDr. Jiří Petrák, PhD

https://www.petraklab.cz/

Title: **CLINICAL PROTEOMICS**

Using efficient separation methods and high-resolution mass spectrometry PROTEOMICS enables monitoring of quantitative and qualitative changes of thousands of proteins in biological samples. Detailed knowledge of proteome changes in cells and tissues can elucidate molecular mechanisms of physiologic and pathologic processes, and identify disease markers or novel therapeutic targets.

Study material:

- O'Neill J.R. (2019) An Overview of Mass Spectrometry-Based Methods for Functional Proteomics. In: Wang X., Kuruc M. (eds) Functional Proteomics. Methods in Molecular Biology, vol 1871. Humana Press, New York, NY
- Domon, B. (2006). Mass Spectrometry and Protein Analysis. Science, 312(5771), 212–217. doi:10.1126/science.1124619

Lecture 6– May 11th, 2023

Assoc. Prof. Ondřej Havránek, MD, PhD

https://biocev.lf1.cuni.cz/havranek-lab

Title: **GENETICS : Cancer genomes and genome editing technology**

Cancer associated acquired DNA mutations and their role in tumor development, progression, and therapy resistance. Consequences for interaction of tumor cells with immune system. Use of genome modifying technologies to create models for cancer research and options for therapy.

Study material:

- Stratton M.R., Campbell P. J., Futreal P.A., The cancer genome. Nature. Vol.458/9 April 2009. Doi:10.1038/nature07943.
- Ding L, Bailey MH, Porta-Pardo E, Thorsson V, Colaprico A, Bertrand D, Gibbs DL, Weerasinghe A, Huang KL, Tokheim C, Cortés-Ciriano I, Jayasinghe R, Chen F,Yu L, Sun S, Olsen C, Kim J, Taylor AM, Cherniack AD, Akbani R, Suphavilai C,Nagarajan N, Stuart JM, Mills GB, Wyczalkowski MA, Vincent BG, Hutter CM,Zenklusen JC, Hoadley KA, Wendl MC, Shmulevich L, Lazar AJ, Wheeler DA, Getz G;Cancer Genome Atlas Research Network. Perspective on Oncogenic Processes at the End of the Beginning of Cancer Genomics. Cell. 2018 Apr 5;173(2):305-320.e10.doi: 10.1016/j.cell.2018.03.033.
- Sanchez-Vega F, Mina M, Armenia J, Chatila WK, Luna A, La KC, Dimitriadoy S, Liu DL, Kantheti HS, Saghafinia S, Chakravarty D, Daian F, Gao Q, Bailey MH,Liang WW, Foltz SM, Shmulevich I, Ding L, Heins Z, Ochoa A, Gross B, Gao J, Zhang H, Kundra R, Kandoth C, Bahceci I, Dervishi L, Dogrusoz U, Zhou W, Shen H, Laird PW, Way GP, Greene CS, Liang H, Xiao Y, Wang C, Iavarone A, Berger AH, Bivona TG,Lazar AJ, Hammer GD, Giordano T, Kwong LN, McArthur G, Huang C, Tward AD,Frederick MJ, McCormick F, Meyerson M; Cancer Genome Atlas Research Network, Van Allen EM, Cherniack AD, Ciriello G, Sander C, Schultz N. Oncogenic Signaling Pathways in The Cancer Genome Atlas. Cell. 2018 Apr 5;173(2):321-337.e10. doi:10.1016/j.cell.2018.03.035.
- Kebriaei P, Izsvák Z, Narayanavari SA, Singh H, Ivics Z. Gene Therapy with the Sleeping Beauty Transposon System. Trends Genet. 2017 Nov;33(11):852-870. doi:10.1016/j.tig.2017.08.008.

- Hsu PD,Lander ES,Zhang F. Development and Applications of CRISPR-Cas9 for Genome Engineering. Cell 157, June 5, 2014. doi:10.1016/j.cell.2014.05.010.
- Komor AC, Badran AH, Liu DR. CRISPR-Based Technologies for the Manipulation of Eukaryotic Genomes. Cell. 2017 Apr 20;169(3):559. doi:10.1016/j.cell.2017.04.005.
- Barrangou R, Doudna JA. Applications of CRISPR technologies in research and beyond. Nat Biotechnol. 2016;34(9):933-941. doi: 10.1038/nbt.3659.
- Hoadley KA, Yau C, Hinoue T, Wolf DM, Lazar AJ, Drill E, Shen R, Taylor AM,Cherniack AD, Thorsson V, Akbani R, Bowlby R, Wong CK, Wiznerowicz M, Sanchez-Vega F, Robertson AG, Schneider BG, Lawrence MS, Noushmehr H, Malta TM;Cancer Genome Atlas Network, Stuart JM, Benz CC, Laird PW. Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000 Tumors from 33 Types of Cancer. Cell. 2018 Apr 5;173(2):291-304.e6. doi: 10.1016/j.cell.2018.03.022.
- June CH, O'Connor RS, Kawalekar OU, Ghassemi S, Milone MC. CAR T cell immunotherapy for human cancer. Science. 2018 Mar 23;359(6382):1361-1365. doi:10.1126/science.aar6711.
- Bailey MH, Tokheim C, Porta-Pardo E, Sengupta S, Bertrand D, Weerasinghe A, Colaprico A, Wendl MC, Kim J, Reardon B, Kwok-Shing Ng P, Jeong KJ, Cao S, Wang Z, Gao J, Gao Q, Wang F, Liu EM, Mularoni L, Rubio-Perez C, Nagarajan N, Cortés-Ciriano I, Zhou DC, Liang WW, Hess JM, Yellapantula VD, Tamborero D, Gonzalez-Perez A, Suphavilai C, Ko JY, Khurana E, Park PJ, Van Allen EM, Liang H; MC3 Working Group; Cancer Genome Atlas Research Network, Lawrence MS, Godzik A, Lopez-Bigas N, Stuart J, Wheeler D, Getz G, Chen K, Lazar AJ, Mills GB, Karchin R, Ding L. Comprehensive Characterization of Cancer Driver Genes and Mutations. Cell. 2018 Aug 9;174(4):1034-1035. doi: 10.1016/j.cell.2018.07.034.

Lecture 7 – May 18th, 2023

RNDr. Jiří Zahradník, PhD

https://biocev.lf1.cuni.cz/zahradnik-lab

Title: **Protein engineering in biomedicine**

State-of-the-art protein engineering is progressively asserting itself in biomedicine in a plethora of tasks such as adjustment, amplification, or attenuation of immune responses, development of new diagnostic and therapeutic modalities, and strategies to treat multiple infectious, autoimmune, and neoplastic diseases.

- Bojar D. and Fussenegger M. (2019) The Role of Protein Engineering in Biomedical Applications of Mammalian Synthetic Biology, Small 16 (27), 1613-6810, doi: 10.1002/smll.201903093

Lecture 8 – May 25th, 2023

Mgr. Miroslav Hons, PhD

https://biocev.lf1.cuni.cz/hons-lab

Title: **Leukocyte migration and immunology**

Migration of leukocytes in healthy and pathological states. Imaging of leukocyte behaviour and interactions. Cell biology of leukocyte motility.

Study material:

- Pittet MJ, Garris CS, Arlauckas SP, Weissleder R. Recording the wild lives of immune cells. Sci Immunol. 2018 Sep 7;3(27). pii: eaaq0491. doi:10.1126/sciimmunol.aaq0491.
- Miller, M. J. (2002). Two-Photon Imaging of Lymphocyte Motility and Antigen Response in Intact Lymph Node. Science, 296(5574), 1869–1873. doi:10.1126/science.1070051
- Mempel, T. R., Henrickson, S. E., & von Andrian, U. H. (2004). T-cell priming by dendriticcells in lymph nodes occurs in three distinct phases. Nature, 427(6970), 154–159. doi:10.1038/nature02238